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TOTAL DIETARY REGULATION IN THE TREATMENT
OF DIABETES

By

FREDERICK M. ALLEN, M.D., EDGAR STILLMAN, M.D., AND
REGINALD FITZ, M.D.



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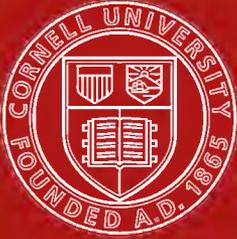
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PREFACE.

This monograph comprises the records of seventy-six out of one hundred diabetic patients treated in the Hospital of The Rockefeller Institute, and chapters on certain aspects of the clinical research. The opening chapter was written as an introduction to the publication as originally planned, and was to have been followed by chapters dealing respectively with carbohydrate, protein, fat, total metabolism, acidosis, pathology, etc., with combined animal and clinical experiments, and a fairly complete survey of the literature. Certain events, however, have interfered with this program and publication is proceeding in reverse order, the clinical part now appearing in advance of the reports of the animal experiments. The latter will shortly appear in a series of journal articles. Most of the collected bibliography, except that pertaining to the history of the subject (Introduction), has likewise been omitted from the present monograph. Reports by members of the staff of this hospital, concerning chemical aspects of the diabetic problem or methods employed, are included in the bibliography of Chapter I under the names of Cullen, Fitz, Palmer, Stillman, and Van Slyke. The cooperation and courtesy received so liberally from outside the Institute are acknowledged in the text as far as possible.

When publication is complete, it will be seen that the conclusions rest upon a unified research composed of three principal interdependent parts. One of these has compared clinical diabetes in its principal characteristics with that produced experimentally in various species of animals, and has shown that the latter, in the absence of spontaneous tendencies, is influenced by changes in the total metabolism and body weight, and not by carbohydrate ingestion alone. The second is the present clinical investigation, in which this principle has been applied to patients. The third is a pathological study, not yet finished, but included here in the form of a preliminary outline because of its important relation to the problems of treatment.

A therapeutic advance should mean a raising of the general level of clinical results, in the sense of saving life in some proportion of cases formerly fatal, and prolonging it to greater or less extent in the more hopeless cases. Expectations of an actual cure, in the sense of a restoration of the normal power of food assimilation, will necessarily be disappointed in most cases under any dietetic treatment, and the need of some more potent therapy than diet is a keen stimulus to research. The method of treatment here presented has never been proposed as such a cure, and amelioration of the existing condition and preservation of life and usefulness at the price of continued precautions have been recognized as the limit of present attainment in diabetes. As set forth in the text, the mistakes incident to the development of a new method have reduced the general results below the theoretical ideal. The severity of the test is evident, however, from the grave character of the cases chosen and their known fate under former practice. The experience as a whole is believed to sustain both the theoretical principle and its practical value for the dietetic treatment of diabetes.

TOTAL DIETARY REGULATION IN THE TREATMENT OF DIABETES.

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FITZ, M.D.

(From the Hospital of The Rockefeller Institute for Medical Research.)

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CHAPTER I.
INTRODUCTION.

HISTORY.

Understanding of the existing state of a subject is generally aided by knowledge of its history. Aside from what is given in text-books, notably those of Cantani and Lépine, the early history of diabetes has been written briefly by Hirsch, but most exhaustively by Salomon, to whom reference may be made for exact citations of most of the ancient and medieval works here quoted. A previous publication¹ has reviewed some of the theoretical and experimental features of the subject. The following account aims to trace the development of clinical knowledge and treatment of diabetes, taking note of theories and experiments only as they have influenced practice. The attempt has been made to present the true and significant, assigning credit to the successive workers as accurately as the recorded evidence permits.

It is convenient, following approximately Cantani, to divide the history of diabetes into four periods. The first extends from the most ancient times to the discovery of the sweetness of the urine by Willis in 1675, which ushered in the second or diagnostic period. The third period, that of empiric treatment, began with Rollo in 1796. The fourth, or modern period, was inaugurated in the decade 1840 to 1850, the most prominent founders being Bernard and Bouchardat. With all its imperfections, this yet merits the name of the experimental and scientific period.

¹ Allen (1).

I. The Ancient Period (to 1675 A. D.).

"In the papyrus Ebers, which is a copy of an Egyptian medical compilation already old in the time of Moses, there is mention of polyuria, and it is hard to conceive that such a marked departure from health could at any time have escaped observation" (Saundby). For explanation of the relatively late period of human history at which diabetes was first clearly recognized and described, we need not assume the absence or rarity of the disease among the ancients, but must rather consider the impossibility of their diagnosing mild cases, the natural confusion of severe cases with chronic nephritis and various forms of polyuria and with tuberculosis and other wasting conditions, and the further difficulties presented by the various complications. The differences between cases have puzzled even modern physicians to such an extent that the existence of diabetes as a unified entity rather than a disjointed symptom-complex has been disputed up to very recent years.

Hippocrates (460-377 B.C.) made no mention of any condition clearly recognizable as diabetes. A notion concerning the quantity of urine, in a passage translated by Richardson from the third book of the Epidemics,² is like that of Celsus, but the first known recognition of diabetes occurred at about the height of the Roman power:

Aulus Cornelius Celsus (30 B.C.-50 A.D.) wrote as follows:³ "When urine, even in excess of the drink, and flowing forth without

² "In some cases the urine was not in proportion to the drink administered, but greatly in excess; and the badness of the urine was great, for it had not the proper thickness nor concoction nor purged properly; for in many cases purgings by the bladder indicated favorably, but in the greatest number they indicated a melting of the body, disorder of the bowels, pain and a want of crisis."

³ Lib. iv, cap. xx, 2; ref. by Salomon: "At cum urina super potionum modum etiam sine dolore profluens maciem et periculum facit, si tenuis est, opus est exercitatione et fritione, maximeque in sole, vel ad ignem; balneum rarum esse debet, neque longa in eo mora; cibis comprimens; vinum austerum meracum, per aestatem frigidum, per hiemem egelidum; sed tantum, quantum minimum sit. Infima alvus quoque vel ducenda, vel lacte purgenda est. Si crassa urina est

pain, causes emaciation and danger, if it is thin, exercise and massage are indicated, especially in the sun or before a fire; the bath should be infrequent, nor should one linger long in it; the food should be constipating, the wine sour and unmixed, in summer cold, in winter lukewarm; but everything in smallest possible quantity. The bowels also should be moved by enema, or purged with milk. If the urine is thick, both exercise and massage should be more vigorous; one should stay longer in the bath; the food should be light, the wine likewise. In each disease, all things should be avoided that are accustomed to increase urine."

In this compressed passage, Celsus gives the first description of diabetes, introduces an error (fluid output greater than intake) destined to endure eighteen centuries, and touches some modern treatment. It is not known to what extent this knowledge was original with Celsus or handed down by predecessors. At any rate, the recognition of the disease was so new that it had not yet received a name.

Aretæus of Cappadocia (30-90 A.D.), living under the emperor Nero, and writing in Ionian Greek, was the second to describe diabetes, and the first known to have called it by the name (*διαβαλευν*, to run through; *διαβήτης*, a siphon). In a passage translated by Schnée⁴,

vehementior esse debet et exercitatio et frictio; longior in balneo mora; cibus opus est tenuis; vinum idem. In utroque morbo vitanda omnia sunt, quae urinam movere consuerunt."

⁴"Diabetes is a strange disease, which fortunately is not very frequent. It consists in the flesh and bones running together into urine. It is like dropsy in that the cause of both is moisture and coldness, but in diabetes the moisture escapes through the kidneys and bladder. The patients urinate unceasingly; the urine keeps running like a rivulet. The illness develops very slowly. Its final outcome is death. The emaciation increases very rapidly, so that the existence of the patients is a sad and painful one. The patients are tortured by an unquenchable thirst; they never cease drinking and urinating, and the quantity of the urine exceeds that of the liquid imbibed. Neither is there any use in trying to prevent the patient from urinating and from drinking; for if he abstains only a short time from drinking his mouth becomes parched, and he feels as if a consuming fire were raging in his bowels. The patient is tortured in a terrible manner by thirst. If he retains the urine, the hips, loins, and testicles begin to swell; the swelling subsides as soon as he passes the urine. When the illness begins, the mouth begins to be parched, and the saliva is white and frothy. A sensation of heat and cold extends down into the bladder as the illness progresses; and as it progresses still more there

Aretæus outlines some of the principal symptoms, the progressive course, and the fatal prognosis. He anticipates modern conceptions of a failure of assimilation, conversion of tissue into urinary products, and possible origin of some cases in acute infections. He was retrograde in treatment, for he advised a non-irritating diet of milk and carbohydrates, and hiera, nardum, mastix, and theriak (opium? sugar?) as drugs. He is commonly credited with being the first to regard diabetes as a disease of the stomach; but his vague notion of a disorder akin to ascites hardly entitles him to a claim upon this false idea which was productive of so much truth in the period from Rollo to Cantani.

Claudius Galenus (born 131 A.D.) saw two patients and introduced two ideas: first, that diabetes is a weakness of the kidneys, which cannot hold back water and also are thirsty for fluid; second, that the urine consists of the unchanged drink. Galen's great authority maintained these errors for about 1500 years, and retarded progress in the knowledge of diabetes.

Chronological order here shifts the narrative to the Far East. According to Iwai, the first oriental description of diabetes was given in the year 200 by Tchang Tchong-king, perhaps the greatest of Chinese physicians. "There is a disease called 'the disease of thirst,' in which polyuria is the characteristic symptom. One may drink as much as ten liters per day, which is recovered in the urine." A Chinese medical work of about the year 600 classifies four supposed groups of cases, and notes the symptoms of polyphagia, polydipsia, and polyuria. Still a later work mentions furunculosis. About the fifteenth century, diabetes was attributed to wine and high living.

is a consuming heat in the bowels. The integuments of the abdomen become wrinkled, and the whole body wastes away. The secretion of the urine becomes more copious, and the thirst increases more and more. The disease was called diabetes, as though it were a siphon, because it converts the human body into a pipe for the transfux of liquid humors. Now, since the patient goes on drinking and urinating, while only the smallest portion of what he drinks is assimilated by the body, life naturally cannot be preserved very long, for a portion of the flesh also is excreted through the urine. The cause of the disease may be that some malignity has been left in the system by some acute malady, which afterward is developed into this disease. It is possible also that it is caused by a poison contained in the kidneys or bladder, or by the bite of the thirst-adder or dipsas."

Among the Japanese, Kagawa Shu-An described the symptoms of diabetes as frequency of urination, with urine exceeding the drink in quantity, pale color and sugar taste of the urine, and insatiable hunger and thirst. Homma Gencho in 1864 noted the typical symptoms, the death from emaciation, and the urine so sweet as to attract dogs. These accounts show obvious European influence, and the Japanese seem to have made no original contributions. According to Iwai, this may be explained by the rarity and mildness of diabetes among them.

In Europe, Ætius of Amida (550 A.D.) accepted the Galenic doctrines, but introduced into therapy three measures long used thereafter; *viz.*, bleeding, emetics, and narcotics. According to a passage quoted from Ætius by Donkin (1), p. 128), Archigenes in the second century was the first to use opium for diabetes.

The earliest mention of the sweetness of diabetic urine is contained in the Ayur Veda of Susruta, dating from the sixth century. The disease bore the distinctive name of Madhumeha or honey-urine.⁵ Thus the most prominent clinical feature, and one of the most widely supported modern hypotheses concerning etiology, received their first mention in India. But Hindu medicine failed to advance beyond this beginning, and exerted no influence on progress elsewhere.

The Arabs are credited with nothing but passing on classical learning to modern Europe, and their two greatest physicians, Rhazes (850–992 A.D.) and Avicenna (980–1037 A.D.) are rated by Salomon as barren followers of Galen, whose observations serve only for evidence that diabetes existed among the Arabs. But Dinguizli has translated some passages which seem to establish an advanced position for Avicenna. In these passages, he remarks that diabetes is generally primary, but sometimes secondary to some other disease. He describes the irregular appetite, the great thirst, the urine *equal* to the drink, the nervous exhaustion, and the loss of sexual function and of ability to work. In suggesting that the renal weakness is due to a relaxed state of the nerve-plexus of the kidney, he propounds the first

⁵ A translation by Chunder Bose is as follows: "Madhumeha is a disease which the rich principally suffer from, and is brought on by their overindulgence in rice, flour, and sugar. The patient feels weak and emaciated, and complains of frequent micturition, thirst, and prostration. Ants flock round his urine. Carbuncles and phthisis are its frequent complications." For other quotations, see Christie.

nervous hypothesis of diabetes. "In this disease, the liver is affected, and its rôle of provider of heat is disturbed in consequence of the exaggeration of organic combustions. . . . The relations between the kidney and liver become irregular, in that the kidney attracts the humors from the liver in greater quantity than it is able to retain them." Having thus enriched the theory of the subject with the rôle of the liver, increased metabolism, and balance between organs, he proceeds to give the first description of diabetic gangrene, which spreads and causes death. Such inflammations are due to retarded circulation in the limb, or to decomposition of the blood, which results from diminution of water in the blood. Furthermore, the urine on evaporation leaves "a residue particularly scanty, of a sweet taste like honey, and resembling particles of bran." If this account proves authentic, it raises Avicenna to the rank of a clinical genius; but the second period of diabetes still begins with Willis, because only the latter's observation influenced the further development of the subject. Avicenna's treatment consisted in powders of fenugreek, lupin, and wormseed, in dosage increasing up to 45 gm. daily. This seems rather suggestive of veterinary medicine, but both Dinguizli and Robin reported patients benefited. As with so many other methods, the digestive disturbances mentioned sufficiently explain any benefit produced by the treatment of Avicenna.

Trincavella (1476-1568), a Venetian, observed three cases of diabetes. In one, the etiology was attributed to persecution and grief. In another, the relatives are said to have demonstrated the truth of the Galenic doctrine that diabetic urine is the unchanged drink, by frequently tasting the urine and finding the taste identical with what the patient had been drinking. Cantani suggests that the drink in this case was sweet tea.

Amatus Lusitanus and Zacutus Lusitanus, Portuguese physicians of the forefront of the sixteenth century, named dietary, alcoholic, and venereal indiscretions among the causes of diabetes. The latter considered the seat of the diabetic disturbance to be not only in the kidneys but even more in the stomach; he thus holds a transitional position in regard to theory between Galen and Rollo.

Aureolus Philippus Theophrastus Paracelsus Bombast ab Hohenheim (1493–1541) broke radically away from all old dogmas, in this as in other subjects. He performed the first chemical experiment, and, with surprisingly accurate insight, drew from this crude observation the first chemical concept of diabetes. The experiment consisted in evaporating the urine; it was found that a “measure” of urine yielded four ounces of “salt.” Paracelsus therefore affirmed that diabetes is a systemic disease, characterized by the formation of an abnormal salt in the blood. The polyuria is not due to a renal lesion, but the salt “makes the kidneys thirsty; for thirst always comes from salt.” He was accustomed to taste the urine of patients, but for some reason failed to discover the sweetness of diabetic urine.

Geronimo Cardano (1505–1576), an Italian, claimed that a girl of eighteen years took seven pounds of food and drink daily and excreted thirty-six pounds of urine, thus proving Celsus’ notion that the fluid output is greater than the intake in diabetes, the excess being supposedly drawn from the air. In addition to this mistake, there is evidence that the girl did not even have diabetes; but a step forward is represented by this first record of a case history and a clinical experiment.

Rembert Dodonaeus (1517–1586), a Dutch physician, first mentioned chyluria in a diabetic.⁶

Johann Baptista van Helmont (1578–1644), of Brabant, followed the chemical theory of Paracelsus and regarded diabetes as a disease of the blood. He was the first to record an observation of diabetic lipemia.⁷

Franciscus Deleboe Sylvius (1614–1672), professor at Leyden, took a step backward, in holding that the offending substance in the blood in diabetes is a volatile salt.

⁶ “Albida autem urina erat, non transparens, et paulo quam serum lactis tenuior.”

⁷ “Atque in diabete, totus cruor mutatur in lotium lacteum.”

II. The Second or Diagnostic Period (1675-1796).

Thomas Willis (died 1675), Sidley Professor in Oxford University, was the first Englishman to make an important contribution to the knowledge of diabetes. This was the simple observation that the urine is "wonderfully sweet, as if imbued with honey or sugar."⁸ He did not guess that the sweetness is actually due to sugar. He held to the theory that diabetes is a disease of the blood. The water is not properly combined with the solid matter, so that the water escapes through the kidneys, carrying large quantities of salts with it. Perhaps there is some disorder of the kidneys also. The resulting thickening of the blood causes the excessive thirst. Urine containing so much salt should taste salty; "but why it is wonderfully sweet like sugar or honey, this difficulty is worthy of explanation." He thinks it may be explained by the manner in which acids and salts alter one another's taste. Acid salts are formed in the blood in various diseases. Also a possible source of such acids is fermentation, as of wine and cider. Therefore immoderate use of these liquors is a leading cause of diabetes. It may also be brought on by bad hygiene, worry, and nervous ailments. Treatment should aim to thicken the blood and supply salts. Accordingly, milk, rice, and starchy and gummy foods are indicated; and by limiting a patient to a diet of milk and barley-water boiled with bread, Willis became the author of the first carbohydrate or undernutrition cure. He employed lime-water as a beneficial form of salt; it held a high place in diabetic therapy for well over a century, and was the first alkali to come into general use in diabetes. Certain other drugs owed their general adoption largely to his example, even though he was not the first to use them. Thus, his antimony treatment was in favor more than a century after his death and led to some interesting developments, and his Dover's powder and tinctura thebaica fastened upon the medical profession an opium habit in diabetic

⁸ "Quasi melle aut saccharo imbutam, mire dulcescere."

treatment which is very difficult to break even at the present time. Superficially, the sweet taste of the urine appears such a primitive and fortuitous observation as might have fallen to the credit of anybody in the 2000 years of European medicine from Hippocrates to Willis. But, with due allowance for the inevitable element of chance, the above record makes it clear that this, like most discoveries, fell to the lot of the man whose point of view and whose methods were capable of yielding discoveries. It marked a triumph of modern independent thought and objective clinical study over subservience to authority and dogma. It was of epoch-making importance in the history of diabetes; first, because it established a radically new and decidedly more accurate basis for diagnosis, which had previously depended upon polyuria and other uncertain symptoms; and second, because it led first to the dietary treatment of Rollo and his successors and later to the experimental work of Claude Bernard and all subsequent investigators of the normal and abnormal metabolism of carbohydrates. It may in some measure be due to the stimulus given by Willis that for nearly two centuries (*viz.*, until Bernard and Boucharadat transferred the leadership to France) the important progress in the subject of diabetes was practically confined to Great Britain.

Thomas Sydenham (1624–1689), hailed as a second Hippocrates in general medicine, contributed nothing of value in diabetes except a clearer definition as a disease of metabolism. Because the nutritive elements of the blood are not properly prepared for assimilation, they pour out through the kidneys, and the flesh and strength melt away.⁹ Later hypotheses of free versus combined sugar are here anticipated. In treatment, Sydenham prescribed narcotics and theriak; also, “Let the patient eat food easy of digestion, such as veal, mutton, and the like, and abstain from all sorts of fruits and garden stuff;” but no effective dietetic treatment grew out of this advice.

Richard Morton (died 1698) likewise regarded diabetes as “a continual flow of nutritive juice pouring out through the kidneys, which

⁹ “Succi sanguini illati per vias urinarias crudi, et inconcocti, exitum sibi quaerunt; unde sensim labefactantur vires, colliquescit corpus, et quasi substantia ejus per hanc cloacam exinanitur, cum siti, ardore viscerum, lumborum coxarumque intumescencia, et salivae spumosa exspuitione crebra.”

frequently befalls intellectual persons, and drinkers of brandy and diuretic liquors."¹⁰ He was the first to note its hereditary character. Milk diet was a feature of his treatment. He opposed the bleeding and purging in use among some physicians.

Richard Mead (died 1754) was the first to consider diabetes a disease of the liver, and brought supposed necropsy evidence in support of this view. On the Continent also began a careful postmortem search for lesions causing diabetes, but nothing of significance was found.

Matthew Dobson (1775) completed the discovery of Willis, and with his paper in English, the history of diabetes emerges from Latin into the modern languages. He first grasped the fact that the sweet substance in diabetic urine is sugar, proving this experimentally by showing that such urine was subject to alcoholic and acetic fermentation, did not coagulate on heating or addition of a mineral acid, but on evaporation four pounds of a patient's urine yielded a whitish cake weighing four ounces, two drams, and two scruples. This cake "smelt sweet, like brown sugar, and could not be distinguished from sugar, except that the sweetness left a slight sense of coolness on the palate." The urine of the same patient in convalescence yielded a less abundant dark residue which was not sweet. Dobson also was the first to discover a sweet taste in diabetic blood serum. He therefore concluded that the sugar contained in normal chyle is assimilated by the body, so that the trace in normal blood is so slight that its taste is overcome by that of the salts. In diabetes this transformation is slowed, so that sugar accumulates in the blood. Also, the quantity of sugar in some cases is too great to be derived entirely from the chyle, therefore sugar must be formed by some abnormal fermentation in the body. The diabetic loses flesh and strength because of the loss of nutritive material in the urine, therefore he should eat as much as possible to make up for this loss.¹¹

¹⁰ "Continuus succi nutritii fluxus per renes decurrens, qui cogitandibus, et vini Gallici liquorumque diureticorum potatoribus plerumque accidit."

¹¹ A prototype of the modern fallacy of replacing through the diet the calories lost in the urine.

Thomas Cawley¹² (1788) by a careful account of a single case, earned credit for the first example of diabetes decipiens, the first diagnosis of diabetes by demonstration of sugar alone, and the first description of a pancreatic lesion in a diabetic necropsy. He, however, regarded diabetes as a disease of the kidneys.

William Cullen (1709–1790) was the first to regard diabetes as a disease of the nervous system, comparing the polyuria with that seen in spastic states. He also wrote: "I think I have met with one instance of diabetes, in which the urine was perfectly insipid; and it would seem that a like observation had occurred to Dr. Martin Lister. I am persuaded, however, that such instances are very rare, and that the other is by much the more common and perhaps the almost universal occurrence. I judge, therefore, that the presence of such a saccharine matter may be considered as the principal circumstance in idiopathic diabetes." Thus, Cullen and Lister called the attention

¹² This name often appears in the literature incorrectly as Cowley. The essentials of his concise report are interesting to quote *verbatim*.

"Allen Holford, Esq., aged thirty-four years, strong, healthy, and corpulent, accustomed to free living and strong corporeal exertions in the pursuit of country amusements, in December, 1787, was seized with diabetes; but the cause of the great degree of emaciation and debility which gradually came on was not discovered until March 20, 1788; at which time his urine was found to be sweet, fermentable with yeast, and two pounds, on evaporation, yielded about five or six ounces of sweet black extract, exactly resembling that preparation of melasses made by confectioners for children, and vulgarly called *coverlid*."

"Within the above mentioned period the quantity of urine evacuated was never observed to exceed what is usual in health, or to be disproportioned to the ingesta, though the state of it had been frequently inquired into, and even the quantity of liquids drank and voided measured. For these reasons the quality of it was not suspected until it became inconceivable, considering the quantity of aliment taken in, how such a degree of exhaustion could ensue, unless the body was drained by the quality of what was rejected as apparently excrementitious."

"Variety of medicine, the usual consequence of inefficacy and despair, were successively administered. Decoction of bark with vitriolic acid and alum, with astringents and aromatics, with chalybeates, with sacc. saturni and opium, and with cantharides, together with cold bathing in salt water, were the principal means used, and at first had a very good effect; but soon afterwards every medicine disagreed with the stomach, and the patient gradually sunk and died on the 18th of June."

"The pancreas was full of calculi, which were firmly impacted in its substance. They were of various sizes, not exceeding that of a pea, white, and made up of a

of the medical profession to the possible existence of diabetes insipidus.¹³ Cullen first added the adjective "mellitus" to the name of the disease. Cullen's theory of diabetes was that of Dobson, with whom he had discussed it. "I formerly communicated this idea to Dr. Dobson, who adopted it, and published it; but I must confess that the theory is beset with difficulties, which cannot at present be solved." He gave a wholly pessimistic view of the treatment and prognosis; he had tried the known methods on twenty diabetic patients and failed to save any of them.

John Brown (1735-1788) conceived life as motion. Diabetes, as a disease of weakness, should be treated by exercise, which should be neither too slight nor too severe. But Brown's treatment was inferior to that of his predecessor Celsus, in that abundance of food and drink was also prescribed for strengthening.

Johann Peter Frank (1745-1821), the most renowned German physician of his time, gave the name of diabetes decipiens, or deceptive diabetes, to the condition of glycosuria without polyuria described by

number of lesser ones, which made their surface rough, like mulberry stones; and in all respects they appeared analogous to the calculi which we sometimes meet with in the salivary ducts. The right extremity of the pancreas was very hard, and appeared to be scirrhus."

"*Experiment I.*—A small quantity of urine, set by in a phial, spontaneously entered into the vinous, and then into the acetous fermentation, discharging a great quantity of mephitic gas. A white cloud formed in the center, which gradually fell to the bottom in the form of a white precipitate. In short, the whole of this experiment corresponded with Dr. Dobson's."

"*Experiment IV.*—A small quantity of the extract put into spirit of wine neither dissolved nor communicated any colour to it, but immediately became very hard and brittle.

"It appears, by the last experiments, that the extract consists of sugar united with gummy or coagulable matter, all of which ought to remain in the body for its support, and that little of what is excrementitious passed through the kidneys but superabundant water, the vehicle of this nutritious matter."

¹³ They did not clearly demonstrate the existence of such an entity, for Bardley (mentioned by Watt, p. 14, who gives the above quotation) criticized their findings by showing that a urine with no perceptible sweet taste might form more or less oxalic acid when examined chemically. This formation of oxalic acid on treatment with a mineral acid was the first chemical method for the demonstration of sugar in urine, and was used by Rollo and his immediate successors.

Cawley. He also established the definite division and nomenclature of diabetes insipidus or spurius and diabetes mellitus or verus.

Francis Home differentiated "watery" and "milky" diabetes.¹⁴ He proved experimentally that the urine of a diabetic patient was not in excess of the fluid in food and drink. He isolated sugar from the urine of two patients, respectively an ounce and an ounce and a half of sugar to the pound of urine. Addition of yeast to the urine was followed by fermentation; the urine lost its sweetness and acquired the taste of small beer. He failed to confirm Dobson's observation of the sweetness of diabetic serum. He upheld Dobson and Cullen's theory of diabetes as a defective assimilation of food. The sweet urine, milky in some cases, was evidence to him that vegetable foods are not properly assimilated in diabetes; the sweet chyle, which is the first product of digestion, is not converted into ammonium salts as it normally should be. Therefore diabetes should be curable by strict meat diet; but he was unable to make this theory succeed in practice, and he went on to try a multitude of drugs without result. Given sufficient courage or skill to build on this theory a successful practical method, he might have been the founder of the new era of therapy.

¹⁴ The relatively frequent mention of milky urine among early writers is remarkable. Perhaps the appearance was due to fermentation. Whether in the absence of dietary regulation there may have been occasionally a true visible lipuria is a possible question of interest.

III. The Third Period, or Period of Empiric Treatment (1796-1840-50).

John Rollo, a surgeon-general of artillery in the English army, ventured to try an entirely original method on the first case of diabetes that he had ever treated. "For the case I had seen at Edinburgh, and Dobson's account, with Dr. Cullen's opinion, had prepossessed me with the idea of the disease being a primary and peculiar affection of the stomach" (2), p. 5).¹⁵ This first patient, a certain Captain Meredith, treated in 1796, shares some of his physician's fame, not unjustly, in view of what he went through. The treatment began with bleeding, which is said to have made the patient feel better. Confinement to the house was ordered, preferably to one room, with the utmost possible quiet and avoidance of exercise. The bill of fare was as follows: "Breakfast, 1½ pints of milk and ½ pint of lime-water, mixed together; and bread and butter. For noon, plain blood puddings, made of blood and suet only. Dinner, game, or old meats, which have been long kept; and as far as the stomach may bear, fat and rancid old meats, as pork. To eat in moderation. Supper, the same as breakfast." The skin was to be greased daily with hog's lard, flannel worn next the skin, and an ulceration about the size of half a crown to be maintained opposite each kidney. At first, kali sulphuratum was ordered several times daily, but later this was exchanged for "hepatised ammonia" (ammonium sulphide), "a medicine proposed by Mr. Cruikshank, who was of the opinion that it might prove a more certain and active medicine than the other on the stomach, in diminishing its action, as well as that of the system in general." Wine of antimony and tincture of opium were to be taken at bedtime, and "in reserve, as substances diminishing action, tobacco and fox-glove." Captain Meredith's age was thirty-four, and his diabetes of seven months' standing, apparently moderate in degree. He steadily

¹⁵ This rules out the statement by various authors that Rollo received his stimulus from Home.

improved, in spite of occasional indulgence in apple pie or beer. Along with the gain in strength and disappearance of symptoms, Rollo noted diminution in the quantity and sweetness of the urine, in the amount of sugar obtained on evaporation, and in the oxalic acid test. After cessation of glycosuria, the strict diet was gradually relaxed, and it is complimentary to Rollo's judgment that the first vegetables permitted were cabbage, boiled onions, salad, mustard, common radish, and horse-radish. The patient resumed his military duties. Rollo undertook his second case, that of "a General Officer." Here the diabetes was of three years' duration, and the patient, aged fifty-seven, repeatedly broke even the rather mild regimen imposed, so that he ultimately died.

Various other matters of interest are contained in Rollo's book. The diuretic action of sugar is clearly recognized. ((2), p. 24): "The serum of the blood apparently containing less saccharine matter than the urine, may depend on the power of the kidneys in separating it in common with the other saline matters of the blood; but proving a new and peculiar stimulus, their action is increased, and the saccharine matter consequently separated speedily and in proportion to its formation in the stomach." (P. 37): "A diet of animal food, as rancid as possible, was proposed in our case, with the view of preventing the formation of sugar in the stomach, and by that means to remove the peculiar stimulus which supported the increased action of the kidneys." A number of other physicians wrote enthusiastically concerning the benefits of the new method. Currie (pp. 147 and 184 of Rollo's book, 1798) reported experiments of weighing ingesta and egesta, weighing the patient before and after bathing, etc., to refute the ancient error of excess of fluid output over intake. Marshall described a necropsy showing lipemia, "chyle in the subclavian vein;" and "there appeared to be no proper blood in the body, but instead of it, a liquid nearly resembling well made thin chocolate. All the veins were filled with this singular brown blood, which had a sickly, sweetish, slightly sour smell (not tasted)." On page 331 is the first recorded observation of an important phenomenon,—a diabetic aged twenty-five, "with the odor of decaying apples in his breath." The letters from physicians show that diabetes was a rarity and a curiosity to them. Dr. Monro is quoted (p. 364) in a statement of the nature of

diabetes, which may well bear comparison with present-day views: "Were I to give a theory of this wonderful disease, I would say that it arises from a defect of the animal or assimilatory process, by which the aliment is converted into the nature of our body." Rollo's theory was inferior to that of Dobson and Monro. He held that diabetes is a disease of the stomach, with increase of its activity, secretion of an abnormal gastric juice, and probably increased activity of the lacteals; that "the saccharine matter is formed in the stomach, and chiefly from vegetable matter." The source of sugar was to be cut off by restricting the diet to animal food; but milk was provisionally included under animal food, and, to indulge the patient, a little bread was permitted. Also, the abnormal activity of the stomach should be depressed, so as to check bulimia and restore the secretion of a normal gastric juice. Therefore, drugs were chosen to produce anorexia and nausea—ammonium sulphide, antimony, opium, digitalis, tobacco. The use of rancid fats in the diet was for a similar purpose. Fat indeed was responsible for the first fasting treatment of diabetes (Rollo (2), p. 36). "Thus Villanovanus relates that a certain man, affected with this disease, eat pot-bread dipt in lees of oil; and that a woman in the like case drank twice the melted fat of beef, with a like quantity of hot oil; and that both these patients contracted so great a loathing of food, that neither of them eat anything for five days, and so got rid of their distempers." It so happened, therefore, that the very incorrectness of Rollo's theory aided in his therapeutic success. From the results achieved with his method by himself and others, he drew the conclusion (p. 141) that "diabetes mellitus is so far understood as to be successfully cured."

Dupuytren and Thénard reported good results from the Rollo diet in France, considering it as specific for diabetes as quinine for malaria; yet they recognized that the cure is never complete, as patients relapse whenever they discontinue the diet. They investigated the properties of diabetic urine, demonstrating that on fermentation it yielded carbon dioxide and alcohol; this was considered to prove the presence of sugar, but this sugar was thought to be of a peculiar kind with little taste.

Nicolas and Gueudeville held a theory similar to that of Rollo. They regarded diabetes as a disorder of intestinal digestion; the chyle

is normally composed of nitrogenous substances, but in diabetes it contains imperfectly elaborated materials saccharine in character and unsuited for the nutrition of the body.

Robert Watt (1808), a Scotchman, reported benefit from treating diabetes with the Rollo diet, bleeding, blistering, antimony powders, and sometimes mercury. Both food and drink were severely restricted in quantity. Watt's clinical ability, and the position properly belonging to him in the history of this subject, may be indicated by quotations from his remarkable little book.¹⁶ His admonitions may be profitable to many even at the present time.

Thomas Christie (1811) first brought to European notice the fact that diabetes was known to the ancient Hindus. He described the frequency of diabetes in Ceylon, and his success with the Rollo treatment there.

¹⁶Watt, preface: "The rapid restoration of health after venesection, blistering and an abstemious diet in cases, where from the great prostration of strength and excessive emaciation, a stimulating mode of treatment seemed indicated, discloses views of the animal economy by no means favourable to some modern opinions. It is to be feared that a dread of debility and an emaciated state of body, from an inflammatory, not a hectic cause, has sometimes deterred practitioners from employing depletion, and the patient has been quietly resigned to his fate. As diabetes is so obviously aggravated by too much aliment or stimuli, and as there is such an attendant bulimia, the first aim of the practitioner should be to remove a portion of that food, which, since it does not nourish, must oppress and injure the system. Animal diet accomplishes this object to a certain extent, for during its use, the quantity of ingesta is necessarily diminished, and a partial abstinence is enforced. More might have been done if, instead of an exclusive confinement to animal food, the quantity of ingesta were gradually diminished, till no more were received than the digestive organs could easily prepare, and the functions of assimilation successfully convert to the support and nourishment of the system. Artificial depletion may, in some measure, supersede the necessity of too strict adherence to an abstemious diet; but the end will undoubtedly be more easily and effectually accomplished if the patient can exert the requisite fortitude to resist the cravings of appetite, and to repress urgent thirst. These indulgences increase the flame, which sooner or later consumes the patient. We aid the cure by a diminution of the supply, and the same means protract the fatal period, or smooth the passage to the grave, when a cure is beyond the reach of art."

Watt (p. 29 ff.) described the treatment of a laborer suffering from moderate diabetes. The man was bled daily, the quantity of blood taken being generally

Chevreul in 1815 demonstrated that the sugar of diabetic urine is identical with glucose.

Latham (1811) distinguished two forms of diabetes, the saccharine and the serous. Likewise Gregory (1825) described the differences between diabetes mellitus and diabetes insipidus. Such observations were of importance in settling the existing doubts among the medical profession as to the decisive import of glycosuria for the diagnosis of diabetes.

Pelham Warren (1813) may be mentioned as the leading English opponent of the Rollo treatment. He regarded dietary restriction as of merely secondary importance, and voiced the frequent objection that patients would not adhere to such a diet. He placed chief dependence on large doses of opium, by which, without dietary regulation, he obtained diminution of glycosuria and polyuria. Some authors have referred to him as the originator of opium therapy. He

fourteen or eighteen ounces, but on one day twenty-four ounces. The bleedings were well borne, and after twelve days there was marked improvement. Antimony powders were also used, and the patient in consequence "was very sick and uneasy all day; had no appetite for food." Again (p. 35): "The antimonial powders appeared to have a more decided effect. They produced very severe sickness, vomiting, and commotion in the stomach and bowels. The night after taking these, the urine was greatly reduced, and next day he found himself uncommonly well. On repeating them, they had not such violent effects, nor was the relief obtained so decisive. . . . Anything which produces sickness has a temporary effect in relieving diabetes, by diminishing the quantity of ingesta. The antimonial powders seemed to possess no other specific action. During the two days he was under their influence, he vomited everything, and was not disposed to take either meat or drink, hence when the supply is cut off, the excretion must diminish of course." (P. 204): "The loss of balance between the digestive and assimilative organs may be produced in two ways" (underfunction of lungs or overfunction of lacteals). (P. 205): "In some diseases the receptive power is not only continued but even increased, while the assimilative powers remain at or below their normal level." Finally, (p. 212): "Diet. From the very nature of the disease, abstinence becomes an indispensable part of the practice. This doctrine, however, is often very contrary to the feelings of the patients, who are apt to urge in their defence that nature is the best judge of what is necessary for their support. They feel weak, they have a strong craving for food, and they can see no reason why they should be deprived of what makes other people strong. These arguments are frequently repeated, though every meal might convince them that it has added to their burden and not to their strength."

failed to take account of the effect of opium upon appetite, and he may be considered the founder of the erroneous belief, still widely prevalent, that opium has an actual specific effect upon diabetes.

Rollo's treatment seems to have met with chiefly an adverse judgment in Germany.¹⁷ It never gained general adoption by the medical profession of any country, unless perhaps England; and though it always had eminent supporters, and more or less restriction of carbohydrate continued to prevail, yet the weight of opinion and practice even in England gradually turned against strict animal diet. The decline in popularity may be attributed to the crudeness and imperfections in the method itself, the careless and faulty application of it by most physicians, the rebellion of patients—who generally, sooner or later, secretly or openly broke the intolerable dietary restrictions and relapsed—the failure of the method to check the severest cases, and the frequent bad results, well understood nowadays, of changing diabetic patients suddenly from mixed diet to strict protein-fat regimen.

Prout, though transitional in time and influenced in his later years by Bouchardat, may be mentioned as closing this period. Naunyn (5), p. 388) credits him with being, in the 1820 edition of his book, the first to restrict protein in diabetes; but such instructions (1848 edition, p. 40) were intended only to forbid overloading the stomach at any one time, so that Prout's advice was not superior to Rollo's and far inferior to Watt's. His treatment was based on the theory (p. 38) "that diabetes is nothing more nor less than a form of dyspepsia; that this dyspepsia principally consists in a difficulty of assimilating the saccharine alimentary principle." He did not approve of strict animal diet, but gave especially green vegetables with it. He (p. 44) introduced the use of bran bread, to be made with eggs and milk, the bran being finely ground to avoid irritation of a sensitive intestine,¹⁸ and washed in a cloth till the water came through clear to remove

¹⁷ Cf. unfavorable experiences reported by von Stosch, Wolff, and Horn, ref. by Ebstein (2), p. 11).

¹⁸ Camplin (1858) stated that the use of bran for diabetic bread had been known for a long time, but it was not highly considered. He was a diabetic treated by Prout, and suffered diarrhea from bran bread; therefore he originated the plan of having the bran ground very fine in a special mill.

starch. He limited drink as well as food. He employed bleeding, Dover's powder, antimonials, and other drugs, but cathartics only as needed to regulate the bowels. In thirty years of practice he saw 700 diabetics. He considered that cold, dampness, or malaria brings on the disease in predisposed persons. He described the frequency of phthisis as a fatal complication, the liability to sudden death from indigestion, travel, or exhaustion; and in particular, he was the first to mention coma as the typical termination of diabetes, as follows: (pp. 28-29) "The person and breath of the patient often exhale a sweetish hay-like odour. Accompanying these bodily symptoms there is great depression of spirits and despondency. . . . The breath becomes short, and there is more or less of cough and expectoration. . . . The emaciation and debility now rapidly approach the maximum; the tongue and fauces assume a dark red colour, and often become aphthous; the urine generally diminishes in quantity, and loses much of its saccharine property; the feet and legs become edematous; and, finally, after almost a total suppression of the renal secretion, the patient becomes comatose, in which state he expires." Also (p. 61): "In young children, the sudden withdrawal of fluids, as well as the use of opium, require caution, from the tendency of these expedients to cause a suppression of urine, which is almost certain to terminate in coma and death."

IV. Modern or Experimental Period.

Though this period began in the decade 1840 to 1850, the way was prepared, as usual, by a few brilliant forerunners, who may properly be included here.

Lavoisier¹⁹ (1743-1794), who discovered the most important properties of oxygen, substituted chemical union for the phlogiston hypothesis, and determined that plants consist essentially of carbon, hydrogen, and oxygen, while animals contain also nitrogen, pointed out the relation of oxygen to the processes of life. He proved that it, and not nitrogen, is essential for respiration. He recognized that animal life and heat are dependent on oxidation. He performed the first experiments concerning human respiratory metabolism, and actually obtained correct values for the normal oxygen consumption of man, and demonstrated the increase due to cold, work, and digestion. Such an achievement is a most remarkable display of genius in a man whose work preceded Rollo's publication, and whose career was untimely ended by the guillotine of the French Revolution. Further research was lacking in this line until Regnault and Reiset in 1849 conducted experiments with a respiration chamber for animals.

Tiedemann and Gmelin (1827) in animal experiments proved that sugar is normally formed from starch in digestion. By the fermentation test they also demonstrated sugar in the portal and systemic blood of animals after carbohydrate feeding, but supposed it to be absorbed through the chyle.

Ambrosiani, also Maitland,²⁰ by the same method discovered the presence of fermentable sugar in the blood of diabetic patients, though Claude Bernard criticized their results because white of egg was used to clarify the solution. M'Gregor claimed to find sugar in the vomitus of a diabetic who for three days had received only roast beef and water, thus supposedly demonstrating the origin of diabetes in an abnormal

¹⁹ See Lusk, Chapter I.

²⁰ Mentioned by M'Gregor.

gastric function. He also reported the presence of sugar in diabetic saliva and feces. Also, by fermentation, he demonstrated sugar in the blood of a considerable number of his diabetic patients, and found traces in the blood of normal persons during digestion of starch. Magendie and von Frerichs confirmed these blood sugar findings.²¹ Meanwhile Thomson had attempted the first quantitative determination, finding by fermentation only 0.03 to 0.06 per cent of sugar in chicken blood.

Other movements in science about this time must be borne in mind in connection with the remarkable new developments in the field of diabetes: Wöhler's synthesis of urea in 1828, breaking down the supposedly absolute barrier between the domains of the organic and inorganic; the cell theory enunciated by Schleiden in 1838 for plants, and by Schwann in 1839 for animals; the beginning of Virchow's work on cellular pathology with his appointment as Privatdozent at Berlin in 1847; and meanwhile the laying of the foundations of physiological chemistry by Liebig. In addition to the deeper problems thus thrown open, certain chemical tests deserve notice; these were the polarimetric determination of sugar discovered by Biot in 1833, the first copper reduction qualitative test devised by Trommer and announced after his death by Mitscherlich in 1841, and the quantitative method of Fehling in 1850. It is hard to overestimate the important influence of these easy and striking sugar tests upon the development of the theory of diabetes. Also, by furnishing the first means for the accurate qualitative and quantitative detection of sugar even in small quantities, they had a great and immediate effect on both diagnosis and treatment.

Claude Bernard contributed nothing directly to the treatment of diabetes, but stands as an epoch-making figure of the new period because of the extensive physiological researches by which he not only founded modern knowledge of carbohydrate metabolism, but also clearly established animal experimentation as a method for solution of the problems involved. His scientific career began in 1847, his first work being the demonstration of sugar in the right-heart blood of dogs fed exclusively on meat. This inconclusive experiment seemed then

²¹ For other early literature see von Mering (1), p. 386).

to overthrow the prevailing doctrine that only plants and not animals can form sugar from non-carbohydrate materials. By this and other experiments Bernard founded the theory of sugar formation from protein, which was not to receive actual proof until some years later. He performed the first reasonably accurate quantitative determinations of blood sugar, some of his values being too high, presumably because of injury and excitement of the animals, but other figures, such as 0.107 per cent, being of a character now recognized as normal. He discovered glycogen and the glycogenic function of the liver; he considered that glycogen is formed from either the carbohydrate or the protein of the food, and that the liver from its glycogen supplies sugar to the circulation in the intervals between digestion. He observed sugar formation from glycogen in the liver post mortem, and proved that the process was due to a diastatic enzyme, which was held to be the agent of this action also during life. He discovered curare glycosuria, and, more important, the glycosuria produced by puncture of the floor of the fourth ventricle, giving the first experimental foundation for the conception of nervous glycosuria. To Bernard, diabetes and *piqûre* glycosuria were temporary and permanent forms of the same thing. The nervous irritation was supposed to cause splanchnic vasodilatation and hyperemia of the liver; this produces increased contact between liver glycogen and blood diastase, and the resulting acceleration of glycogenolysis floods the body with sugar, the excess of which flows away in the urine. It was thus a pure over-production hypothesis, and the liver was in Bernard's opinion the organ principally concerned.

Mialhe in 1845 announced the discovery of the diastase of saliva. Apparently as an outgrowth of his diastase studies, he set up the hypothesis that diabetes is a primary acidosis, that the blood of patients has an acid reaction due to ingestion of too much acid, or to deficient sweating and the resulting retention of acids; and he introduced a treatment with large doses of alkali, especially sodium bicarbonate and magnesium hydrate. Though claiming some benefits at first, he and those repeating his attempt soon met failure. Under the tests of Bouchardat, Griesinger, Külz, and others, both theory and therapy fell. Later Mialhe (3) concluded that the primary cause of diabetes does not consist entirely in an abnormal composition of the blood, but

in an essential nervous disorder. The fallacious comparison between the diabetic process and the rôle of acids in the hydrolysis of starch or glycogen *in vitro* has caused such a theory to reappear in various forms from that time to the present.

Though Bouchardat (1806–1886) read his first memoir to the Academy of Sciences in 1838, and the final edition of his book appeared in 1875, he came into prominence through important contributions in the decade 1840 to 1850. Like Rollo and all other founders of the dietetic treatment, he considered diabetes a disease of digestion. According to his theory, normal gastric juice has no action upon starch, which is digested in the intestine; but in diabetes, an abnormal ferment digests starch in the stomach, and glycosuria, polyuria, and other symptoms result. He claimed to demonstrate the presence of diastase in the vomitus of diabetics and its absence in that of normal persons.²² Hypertrophy of the stomach and atrophy of the pancreas in diabetic necropsies were also held to support his theory; and he was thus the first to suggest an influence of the pancreas in the causation of diabetes, and the originator of the attempt to produce it by pancreatectomy in dogs.²³ For sugar determination in urine, he used fermentation, the polariscope, and the Frommherz copper reagent. By the fermentation method he showed the presence of sugar in diabetic blood, but found none in normal blood. At how low an ebb was the Rollo treatment at this time is shown by the pleading and

²² Various other authors reported similar results: cf. Griesinger, pp. 41–42.

²³ Some authors attribute the first pancreatectomy to Brunner in 1686, but his extirpation aimed only to produce hypertrophy of the duodenal glands named after him, and involved less than half of the pancreas. Bouchardat (2), p. 108) ascribed to Haller (1708–1777) the observation that depancreatized dogs show polydipsia, polyphagia, emaciation, and death. This statement has been widely copied in the literature. But pancreatectomy to the point of diabetes was scarcely possible at such an early date, and as Haller apparently never published any such work (cf. Sauerbeck), the entire myth seems to have originated in a mistake of Bouchardat. The first attempt at total extirpation and the first idea of producing diabetes by this means were represented in Bouchardat's publication in 1846 of experiments undertaken with Sandras to support the pancreatic origin of diabetes. The dogs did not survive pancreatectomy, and ligation of the pancreatic duct did not produce diabetes. The undeveloped state of surgery therefore barred Bouchardat from reaping the fruits of his brilliant intellectual perception in this field.

arguments of Bouchardat ((1), p. 10). He begs all friends of truth to hear him; whatever be the original cause of glycosuria, diabetics, who otherwise all die, are actually saved when his dietetic treatment is used. Bouchardat in the clinical field ranks with Claude Bernard in the experimental field. He is easily the most brilliant clinician in the history of diabetes. He resurrected and transformed the Rollo treatment, and almost all the modern details in diabetic therapy date back to Bouchardat. He was first to insist on the need of individualizing the treatment for each patient ((2), p. 150). He disapproved the rancid character of the fats in the Rollo diet, but followed an intelligent principle of substituting fat and alcohol for carbohydrate in the diet. He forbade milk because of its carbohydrate content. He urged that patients eat as little as possible, and masticate carefully; also (1841) he inaugurated the use of occasional fast-days to control glycosuria. Subsequently he noted the disappearance of glycosuria in some of his patients during the privations of the siege of Paris. Though the introduction of green vegetables is credited by Prout (p. 45) to Dr. B. H. Babington, the honor of thus successfully breaking the monotony of the Rollo diet properly belongs to Bouchardat. He recommended them as furnishing little sugar, a little protein and fat, but especially potassium, organic acids, and various salts. He also devised the practice of boiling vegetables and throwing away the water, to reduce the quantity of starch when necessary. As a similar trick ((2), p. 217) he "torrefied" (*i.e.*, charred and caramelized) bread to improve its assimilation; possibly this is the origin of the widespread medical superstition that diabetics may have toast when other bread must be forbidden. He invented gluten bread; this started the idea of bread substitutes, from which sprang the bran bread of Prout and Camplin, Pavy's almond bread, Seegen's aleuronat bread, and the numerous later products. Bouchardat also first introduced the intelligent use of exercise in the treatment of diabetes, and reported the first clinical experiments proving its value. He showed that carbohydrate tolerance is raised by outdoor exercise; and to a patient requesting bread, he replied ((2), p. 228): "You shall earn your bread by the sweat of your brow." There is a modern sound to his complaints ((1), p. 47) of the difficulties of having treatment efficiently carried out in hospitals, of

the lack of adequate variety of suitable foods, of deception by patients, and of how, even when improved in hospital, they break diet and relapse after returning home. He advocated ((2), p. 330) daily testing of the urine, to keep track of the tolerance and to guard against a return of sugar without the patient's knowledge. He followed Mialhe in giving alkalies, *viz.* sodium bicarbonate up to 12 to 15 gm. per day, also chalk, magnesia, citrates, tartrates, soaps, etc., also ammonium and potassium salts; he found them often beneficial to the patients but not curative of the glycosuria. He told a patient ((2), p. 120): "You have no organic disease; there is merely a functional weakness of certain parts of your apparatus of nutrition. Restore physiological harmony and you will attain perfect health." He used glycerol for sweetening purposes, and introduced both levulose and inulin as forms of carbohydrate assimilable by diabetics, for reasons which well illustrate his intellectual keenness. On giving cane sugar to diabetics, he had found only glucose excreted. Was the levulose utilized or changed into glucose? Levulose proved under certain conditions to be more easily destroyed *in vitro* than glucose. Accordingly he gave levulose and inulin to diabetics, and found no sugar in the urine. Therefore he recommended levulose for sweetening purposes, and inulin-rich vegetables for the diabetic diet.

Sir Henry Marsh (Dublin, 1854) criticized the Rollo diet as impossible to follow because of the indigestion and repugnance to food resulting, but he followed the Bouchardat plan with vegetables, and also used exercise, warm clothing, and baths, restriction of fluid intake, Dover's and James' powders, and alkalies (lime-water and hartshorn, recommended by Colles). He condemned bleeding, and found opium temporary in effect. He noted that an attack of vomiting frequently leads to death; also, "I have seen three cases of diabetes terminate in fatal coma."

Petters (1857), in the clinic of von Jaksch, investigating the peculiar smell noted by various authors, obtained from the urine of a coma patient a small quantity of a liquid giving the reactions of acetone. An extract of the lungs also yielded acetone. He therefore attributed the cause of coma to poisoning by acetone produced by digestive disorder. Kaulich distilled 700 pounds of diabetic urine, and purified enough acetone to identify it by elementary analysis.

Trousseau condemned the Rollo diet. "I cannot too emphatically raise my voice against the abuse of giving an exclusively animal diet in diabetes." Intolerable loathing and impairment of health were alleged against it. Trousseau followed Bouchardat's method, and especially advocated exercise; but he also allowed fruits and even a small quantity of bread, and confessed that patients in the emaciated stage were beyond hope. He was the first to mention bronzed diabetes.²⁴

Piorry of Paris, "a man who loved to turn everything upside down,"²⁵ brought into some prominence in 1857 a notion which was more excusable when first suggested by Chevallier in 1829. Since sugar is lost in diabetes and is indispensable to life, it was proposed to replace the loss by feeding sugar. Piorry gave only a very incomplete description of one case, apparently mild, which he treated by almost complete withdrawal of fluids, and by giving daily 125 gm. of sugar candy "and two portions of meat." The polyuria necessarily ceased, and the sugar excretion remained high in percentage but diminished in total quantity. If the author's statement represents the entire diet, his treatment was a crude carbohydrate and undernutrition cure. It had disastrous consequences. Owen Rees and others are said to have taken it up. Schiff—a physiologist of some repute, an opponent of Bernard on certain details of the glycogenic hypothesis, and a careful investigator of nervous glycosuria, and one of those who removed the pancreas (in birds) without discovering diabetes—also followed it, and upon becoming diabetic, he applied this treatment to himself. Although the diabetes had appeared late in life, it ran a quickly fatal course, apparently because of the treatment.²⁵ Naunyn (5), p. 383) gives another example of injury from this treatment, as applied by a quack. Though such a method now seems foolish, it should be noted

²⁴ (P. 501): "I was struck by the almost bronzed appearance of his countenance, and the blackish color of his penis." Autopsy showed a cirrhotic liver twice the normal size.

²⁵ Griesinger, p. 67. The quack practice of compelling patients to drink their own urine is mentioned as something similar.

²⁶ Naunyn (5), p. 388). It is interesting that Schiff (p. 128) had described a slight alimentary glycosuria in himself and his brother, without suspecting its warning significance.

that the orthodox treatment of severe cases has represented a similar attempt to fill a sieve—the calories lost in the urine being replaced by fat in the diet, which merely brings the fatal end more slowly and in a different form than does sugar.

Griesinger in 1859 published an analysis of 225 cases of diabetes; and though only eight were his own and the others all from the literature, his contribution was valuable for clinical experiments and sound judgment. He compiled the first evidence indicating excess in sugars and starches as a cause of diabetes, but concluded that it could not be the most important cause, or many more persons and some entire races would have diabetes. He overthrew various current errors, but somehow convinced himself in painstaking experiments that diabetics may excrete large quantities of sugar in the sweat, as reported by several other authors. From the negative findings in necropsies, he regarded diabetes as generally a functional disorder. His most notable achievement was the demonstration, in three separate experiments on a single patient, of sugar excretion equalling exactly 60 per cent of the protein of the diet. "These facts, remaining constant under varied conditions, cannot be accidental; they seem much more to contain the law of the relation in which, in this individual on exclusive meat diet, the production and excretion of sugar stands to the quantities of ingested meat."

Frederick William Pavy²⁷ (1829–1911), in the year that he received his doctorate (1853), visited Claude Bernard. He soon became one of the latter's opponents on the glycogenic theory, and, in particular, overthrew Bernard's claim that the hepatic or right-heart blood of a fasting or meat-fed animal contains notably more sugar than the systemic or portal blood. He accepted Bernard's view that diabetes is essentially a disorder of the liver, but denied that the liver normally supplies sugar to the circulation, and maintained that sugar is transformed in passing the intestinal wall, that sugar reaching the circulation as such is non-assimilable, and that the formation of any large quantity of sugar by the liver during life would make everybody diabetic. His theories were largely incorrect, but his experimental work was scrupulously careful and exact and still furnishes useful

²⁷ See article by Hopkins.

information. The study of diabetes was the dominant interest of his life; and though a clinician with a large diabetic practice, he has the credit of perceiving that progress could come only from fundamental physiological investigations. The flippant remark of Sir William Gull,²⁸ "What sin has Pavy committed, or his fathers before him, that he should be condemned to spend his life seeking for the cure of an incurable disease?" is a compliment to Pavy rather than to its author. Clinically, Pavy proved the transitory nature of the apparent benefit from opium. He took a step backward by ignoring the quantity of the diet aside from carbohydrate. He was among the first²⁹ to make the following observation ((1), p. 167): "Another feature of peculiarity belonging to the complaint, is the inability that is experienced to render the urine alkaline by the administration of the fixed alkalies and their vegetable salts. Although I have given the carbonate of soda to the extent of four drachms a day; the acetate of potash, half an ounce; the tartrate of potash and soda or Rochelles salt, six drachms, and even an ounce; and the citrate of potash, six drachms; yet, I have never succeeded in rendering the urine alkaline, or in any way approaching this character."

Seegen was also prominent in the battle over the glycogenic hypothesis. He laid down the principle that every prolonged glycosuria should be considered an incipient diabetes. His therapy was retrograde in two points: he ignored the total quantity of protein and fat ingested, and he denied the value of exercise, in the belief that it was based on a false theory.

Von Pettenkofer and Voit published the first study of the respiratory metabolism of a diabetic patient. They made the interesting remark that they dared not inflict much fasting on a diabetic, because of the great hunger and the difficulty of rebuilding lost tissue. Their work was originally supposed to show a subnormal oxygen consumption by the diabetic. Reynoso had previously attributed diabetes to diminished respiration. Ebstein (1836-1912) devoted extensive labor to the attempt to prove that as CO_2 inhibits the diastase of saliva, pancreatic juice, and organ extracts, so also it inhibits diastase in the living body,

²⁸ Cf. Editorial, *J. Am. Med. Assn.*, 1913, ix, 1159.

²⁹ For earlier, less definite observations, cf. Griesinger, p. 59.

and that diabetes is due to abnormal diastatic activity resulting from subnormal production of CO_2 in the tissues. In treatment he advised the usual diet, also carbonated waters. He (1) claimed priority as being the first to point out the danger of coma when antidiabetic diet is suddenly begun. He opposed inanition, but considered exercise beneficial through increased CO_2 production. Schnée and a few others followed this doctrine.

Kussmaul, a pupil of von Frerichs, in 1874 gave the first detailed description of diabetic coma, distinguished it from pulmonary disease, uremia, and other terminal processes, called attention to the characteristic dyspnea, and from the physiological action of acetone observed in man and animals cast doubt on acetone intoxication as the cause of the condition.

After Bouchardat, the most powerful impetus to the rigid dietetic treatment of diabetes came from Cantani (1837-1893). A pupil of von Jaksch, he was at once a clinician and an enthusiastic chemist and theorist. His preface preaches that, however great the achievements of morphologic pathology, it can show only the form, and never the process at work; only chemistry can give the solution, and he presents his findings as a beginning in the pathology of metabolism. His first chapter lays down the principle that metabolism is disturbed by excess of any constituent in the diet, and if the excess is prolonged, the disorder becomes permanent; diabetes and gout are examples. In an analysis of 218 careful case histories, he showed that carbohydrate had practically always predominated in the diet; but critics must observe that Cantani practised in Rome. He believed the greater frequency of the disease in Italy as compared with Germany and Austria to be due to centuries of over-rich carbohydrate diet. When nervous shock or other causes seem to bring on diabetes, he thought that the incipient disease was generally present before. He admitted that a primary predisposition must precede, because so many persons can live on excessive carbohydrate diet and never develop diabetes. He considered the seat of diabetes to be in "the abdominal organs of digestion, the chylopoietic glandular organs" (1), p. 363). Atrophy of the pancreas present in some of his own cases and those in the literature was interpreted by him as the result and not the cause of diabetes. He believed (p. 331) that sugar is mostly absorbed through the thoracic

duct and only a small portion enters the liver through the portal vein; and (p. 257) quoting Kühne's 1868 text-book of physiological chemistry against the glycogenic theory, he expressed surprise that a chemist like Pavy should believe that the liver could change sugar into glycogen. He thought it probable that the blood sugar in health fails to pass into the urine because burned in the epithelial cells of the kidney.³⁰ Diabetic symptoms were attributed to the non-combustion of sugar and its circulation in excess. He claimed to show (pp. 274-275) that the sugar of diabetic blood is a so called para-glucose, which is reducing but non-polarizing and non-assimilable; the kidneys transform it and excrete it in the urine as true glucose. He regarded acetone formation and coma as due to the digestive disorder, and as accidental in character. His treatment set an entirely new standard of strictness; this was the essential contribution made by Cantani. He isolated patients under lock and key, and allowed them absolutely no food but lean meat and various fats. In the less severe cases, eggs, liver, and shell-fish were permitted. For drink the patients received water, plain or carbonated, and dilute alcohol for those accustomed to liquors, the total fluid intake being limited to one and one-half to two and one-half liters per day. For flavoring were permitted acetic and citric acids, and distillate of orange blossoms. Lactic acid was given regularly as the best substitute for carbohydrate and to aid digestion; Cantani deemed that by means of it he was enabled to keep patients on a more rigid diet than any of his predecessors. The quantity of protein was carefully limited; 500 gm. of cooked meat per day were considered enough for any diabetic, and 300 to 400 gm. sufficient to maintain strength. The value of vigorous muscular exercise was recognized, and it was proved by clinical tests that glycosuria was thus diminished or abolished without change in the diet. If the glycosuria was not otherwise controlled, fast-days were imposed, as often as once a week if necessary. On these days nothing was allowed but water, or sometimes bouillon three times a day. The protocols show a sharp drop in the glycosuria on fast-days.³¹ The duration of this treatment

³⁰ This idea has lately been supported by Reicher, by Pierce, and by Woodyatt.

³¹ Stokvis (1886) considered fast-days as having only experimental interest, stating that in Cantani's records, the glycosuria returned promptly in every case and not one showed any clinical benefit.

is also a noteworthy step; the regular period was three months, and it was extended to six or even nine months if necessary to achieve sugar-freedom. After two months of absence of glycosuria, green vegetables were begun; and later wine, cheese, nuts, sugar-poor fruits, and finally small quantities of farinaceous foods were added. Notice was taken of the different tolerance for different forms of carbohydrate (p. 230). Glycerol³² was found to produce a return of glycosuria in sugar-free patients (p. 258). The urine was analyzed daily during treatment, afterward once every week, then every two weeks. The least trace of glycosuria (p. 229) called for one or two months of absolute protein-fat diet. The patient who could return to moderate carbohydrate diet was considered genuinely cured. If a more generous diet brought a return of glycosuria, it was regarded not as a relapse but as a fresh attack, caused by the same excess in carbohydrate which produced the diabetes in the first place. This determined insistence upon sugar-freedom was Cantani's best contribution; but it was marred by faults which have persisted since, namely, the high calory fat diet, the belief (p. 231) that gain in weight is one of the most important benefits, and (p. 386) that a slight glycosuria is preferable to undernutrition. Regarding his failures, Cantani believed (p. 356) that as long as the pancreas alone, or perhaps the stomach alone, is diseased, the diabetes is curable in all cases, but after the liver is involved a cure is impossible. He acted (pp. 369-370) on the theory of sparing a weakened organ. He held the modern view that diabetes is a unit, and that the varying cases represent different degrees or stages, not different diseases. He distinguished two groups: cases in which sugar disappears on meat diet, and those in which it does not disappear. He judged that the lowered temperature and the slowed respiration were evidence of a diminished metabolism in diabetes. He thought (p. 203) that diabetes is better borne by fat than by thin people because of their lower metabolism, and that the greater severity of diabetes in young persons and children is explained by the higher metabolism. The diminution of glycosuria on fasting was held (p. 190)

³² Glycerol in the treatment of diabetes was first used by Basham (*Lancet*, January, 1854). It was especially advocated by Schultzen (*Berl. klin. Woch.*, 1872, No. 35) on the basis of an erroneous chemical theory. Cf. Naunyn ((5), p. 441).

to prove that the diabetic's own tissues are not convertible into sugar, though the glycosuria on meat diet shows that sugar can be formed from ingested protein. The description (p. 302) of a case of cerebral tumor, causing paralysis of the optic and oculomotor nerves, with polyuria and 3 per cent glycosuria, which cleared up after several months, while the tumor progressed and caused death, may now receive probable interpretation at the first mention of hypophyseal diabetes. The infectious nature of tuberculosis being unknown, the development of pulmonary tuberculosis in a diabetic was to Cantani (pp. 113, 233) a sign that the glycosuria could never be abolished, that the breakdown in metabolism was hopeless, and death inevitable.

The authors who described gross lesions of the pancreas in diabetic necropsies are named by Bouchard ((1), p. 171) as follows: Cawley, Elliotson, Bright, Bouchardat, Griesinger, Hartsen, Fles, von Recklinghausen, von Frerichs, Klebs, Harnack, Kuss, Cantani, Silver, Friedrich, Haas, Lecorche, Lancereaux.³³ Zimmer in 1867 supposed that carbohydrates are normally split to lactic acid in the intestine, but in the absence of pancreatic juice the process stops at the stage of glucose, with resulting glycosuria; but later he considered diabetes as a defect of muscular metabolism. Popper (1868) assumed that diabetes is due to lack of pancreatic juice, causing disturbance in fat digestion and secondarily in glycogen storage in the liver. Lancereaux, a pupil of Claude Bernard, described a form of diabetes characterized by sudden onset, marked emaciation, polyphagia and polydipsia, characteristic feces, and early death. He correctly interpreted this complex as evidence of a pancreatic lesion. Hirschfeld later described similar cases. But Lancereaux and his pupil Lapierre proceeded to assume that all diabetes with emaciation is due to a gross pancreatic lesion; to this *diabète maigre* or pancreatic diabetes they opposed the type of *diabète gras* or fat diabetes, supposedly not pancreatic in origin. They also added later a "constitutional" or "arthritic" diabetes and a "nervous" diabetes. This classification has been generally discredited but still persists to some extent in France.

Baumel was the first to set up the hypothesis that all diabetes is

³³ Other literature is given by Sauerbeck, Rosenberger (p. 206), and Allen, (1), Chapter 21).

pancreatic in origin. When no gross or microscopic alterations could be found, he assumed the presence of a nervous or circulatory disturbance. Lack of pancreatic diastase was imagined to be the essential factor, and the inhibition of secretion of pancreatic juice by stimulation of the central end of the vagus was considered illustrative of what might occur in diabetes of functional origin.

Bouchard followed Lancereaux in regarding diabetes with emaciation as pancreatic in source. He upheld the doctrine of diminished utilization as opposed to Bernard's view of simple overproduction of sugar, and he classified diabetes among the diseases due to retardation of metabolism.

Friedrich Theodor von Frerichs (1813–1885) published a work of careful objective description, free from theories and preconceptions, based on an experience of 400 cases and 55 necropsies. His preface states that he began with the exact science chemistry, passed thence to physiology, and thence to the clinic, and writes now in the autumn of life to present the fruits of nearly forty years' experience. The thorough study and analysis of his cases, clinically, chemically, and pathologically, constitute the author's chief merit in extending the knowledge of diabetes. He distinguished three forms of sudden diabetic death; *viz.*, cardiac failure, collapse, and the Kussmaul coma. Today it seems probable that all three are manifestations of acidosis. By clinical experiments he made the acetone intoxication theory improbable. Ehrlich, with von Frerichs, investigated the glycogen in diabetes, not only post mortem but by liver puncture during life. Ehrlich likewise discovered the so called glycogenic degeneration of the renal tubules in diabetes.

Richard Schmitz of Neuenahr was the first to give conclusive demonstration of complete recovery in a few cases of diabetes. Also, among his 2320 cases he observed 26 in which the diabetes, in absence of any other discoverable cause, seemed so definitely to come on after close association with another diabetic (through marriage or otherwise) as to suggest an infectious transmission. Senator, Oppler and C. Külz, and others have made it reasonably certain that such cases represent mere coincidence.

Rudolph Eduard Külz (1845–1895) was a similar and even more notable example of a painstaking, unbiased investigator. To him,

diabetes was a mystery, toward the solution of which theorizing was futile and only the gathering of the most complete and exact data possible could be valuable.³⁴ In journal articles Kütz published many laboratory investigations, especially concerning glycogen. Also, he discovered the oxybutyric acid in diabetic urine simultaneously with Minkowski, and was first to observe it to be levorotatory. His clinical experience of twenty-five years covered 1100 carefully studied cases of diabetes, of which 711 were chosen for publication. Probably no other man ever did so much to clarify the subject by proving all things and holding fast that which was good. His experiments were the last which finally ended the error of excess of fluid output over intake in diabetes. He found sugar absent from the sweat. He showed the uselessness of lactic acid and the harmfulness of glycerol. He proved the absolutely negative effects of various drugs, notably sodium bicarbonate and arsenic, for diminishing glycosuria, aside from the illness and digestive upsets produced; this lesson of Kütz concerning Fowler's solution still needs to be learned by many today. He demonstrated with exactness that Carlsbad water has no effect upon diabetes. Although no valid evidence has ever shown that any kind of water anywhere has specific influence upon diabetes, this superstition is still so prevalent among both physicians and patients that diabetics continue to flock by thousands to mineral springs like pilgrims to medieval shrines. Kütz disapproved of the methods of Bouchardat, who jumped at truths without pausing to prove them; and much of his constructive work actually consisted in establishing on a substantial basis the suggestions of the brilliant Frenchman. He tested the tolerance of many patients for many forms of carbohydrate, finding (2), p. 528) that the assimilation is better for green vegetables than for the equivalent of starch in other forms; and that lactose, levulose, and even cane sugar are often better borne than glucose, but results are variable and levulose is often harmful and utilized no better than starch. He was unable to formulate any fixed rule whether glycosuria is increased by alcohol or not. By careful com-

³⁴ Preface to "Beiträge:" "Mein Bestreben ging vor Allem dahin, möglichst exacte Beobachtungen zu liefern. In wie weit mir dies gelungen ist, in wie weit diese Untersuchungen geeignet sind, unsere Kenntnisse von diesem in vieler Beziehung noch so räthselhaften Leiden zu erweitern, mag die Kritik entscheiden."

parison between periods of days of rest and corresponding periods with exercise, he reached the conclusion that exercise is beneficial in strong patients with mild diabetes; in severe diabetes, where sugar is excreted on carbohydrate-free diet, exercise may diminish glycosuria, sometimes only transitorily, or it may have no effect; and in weak individuals with severe diabetes, there was no benefit from exercise.³⁵ The great experience of K \ddot{u} lz was probably the most powerful factor in establishing the modern view of the unity of diabetes. His cases were classified in three groups; first, a mild group, becoming sugar-free on strict diet; second, a "mixed" or intermediate group; and third, the group of severe cases, with glycosuria continuing on restricted diet. The numerous careful case records showed such an abundance of gradations and transitions between these groups, from the mildest to the most severe, that fixed distinctions between types of diabetes were shown to be impossible. K \ddot{u} lz made no use of undernutrition or fasting. He treated severe cases by gradual withdrawal of carbohydrate to avoid coma, reduced protein not below 110 gm. daily, and was one of the first to calculate diets according to the caloric requirement. He was the first to introduce the practice of systematically testing the carbohydrate tolerance of each patient. Rumpf³⁶ claims as the greatest merit of the K \ddot{u} lz system the inauguration of individually planned diets instead of indiscriminating general rules. Notwithstanding the universal adoption of this plan by specialists and the better informed physicians, it is a regrettable fact that the majority of the profession have not yet come up to the standard of K \ddot{u} lz, and the majority of diabetics still receive treatment by means of printed lists of "allowed" and "forbidden" foods. K \ddot{u} lz founded a numerous and influential school. Of the three editors of his posthumous work, Aldehoff is known for various clinical and experimental studies, Sandmeyer chiefly for the diabetes produced in dogs by pancreatic atrophy, and Rumpf as a prominent clinician, who made early studies of dextrose-nitrogen ratios in human patients (1, 2, 3), and

³⁵ This was not only the most thorough investigation of exercise in human diabetes, but also an important independent discovery, for K \ddot{u} lz did not know of any previous use of exercise till after completion of his experiments.

³⁶ Preface to K \ddot{u} lz (2).

first (3) warned against loss of body fluid as an important factor in bringing on coma.

Joseph Friedrich von Mering (1849–1908) was trained under von Frerichs and Hoppe-Seyler. Though a clinician of high standing, his fame rests upon his numerous experimental works, among which may be mentioned his metabolism studies with Zuntz, the discovery (1886) of phloridzin glycosuria, and the discovery with Minkowski (1889) of pancreatic diabetes in dogs.

Bernhard Naunyn (born 1839) was the pupil of Lieberkühn, Reichert, and von Frerichs. Though the author of a number of researches, they include no important discovery. His position as the foremost diabetic authority of the time rests upon his influence for the advancement of both clinical and experimental knowledge; upon his judgment, his teaching, and his pupils; upon the fact that from his great Strassburg school have come the soundest theories, the most fruitful investigations, and the most effective treatment. In birth, it is to be noted that Naunyn preceded Külz, and was only two years younger than Cantani. He came into this field in the pioneer period when the principle of dietetic management was generally recognized, but the average practice, especially in regard to severe cases, was still a mass of ignorance and inefficiency. As late as 1886, Naunyn (1) stood as the champion of strict carbohydrate-free diet in a German medical congress where most of the speakers opposed it. As one of the few early German followers of the Cantani system, he maintained its feasibility and ultimate benefit, and locked patients in their rooms for five months when necessary for sugar-freedom. With experience, he gradually introduced modifications, until the rigid and inhuman method, which a majority of physicians and patients would never adopt, became a rational individualized treatment, with a diet reckoned according to the tolerance and caloric requirements of each patient. The work of various pupils requires mention in this connection. Important investigations of metabolism established the basis for this treatment, the most notable being that of Weintraud, who proved that, instead of having an increased food requirement, diabetics could maintain equilibrium of weight and nitrogen on a diet as low as or a little lower than the normal. Minkowski discovered with von Mering the

diabetes following total pancreatectomy in dogs,³⁷ and established the doctrine of the internal secretion of the pancreas, as well as the first clear conception of a dextrose-nitrogen ratio. After the early acetone investigations and Gerhardt's discovery of the ferric chloride reaction had failed to reveal the cause of coma, the Naunyn school accomplished almost the entire development of the subject of clinical acidosis in the following sequence. Hallervorden (1880) discovered the high ammonia excretion, confirming an earlier discredited observation of Boussingault. Stadelmann (1883) established the presence in the urine of considerable quantities of a non-volatile acid supposed to be α -crotonic, correlated the condition with Walter's previous acid intoxication experiments, and theoretically suggested the treatment with intravenous alkali infusions. Minkowski proved the excreted acid to be β -oxybutyric, and demonstrated the presence of this acid in the blood and a diminished carbon dioxide content of the blood. He, also Naunyn and Magnus-Levy, applied the alkali therapy in practice, and the latter carried out chemical and metabolism studies which made him the recognized authority in this field. Naunyn introduced the word acidosis, saying in definition (4), p. 15): "With this name I designate the formation of β -oxybutyric acid in metabolism." The Naunyn school have consistently maintained that this acidosis is an acid intoxication in the sense of Walter's experiments. They demonstrated striking temporary benefits from the alkali therapy, particularly in diminishing the danger of the change from mixed to carbohydrate-free diet; but the practical results were never equal to the theoretical expectations. With Naunyn, also, acidosis became the principal criterion of severity for the clinical classification of cases. As regards other theories, the Naunyn school have upheld the deficient utilization as opposed to the simple overproduction of sugar in diabetes. They have clearly recognized the necessary distinction be-

³⁷ This is commonly supposed to have been an intentional following up of the observations of Cawley, Bouchardat, and others. But according to Dr. A. E. Taylor (personal communication) the epoch-making discovery was accidental. Dogs depancreatized for another purpose were in a courtyard with other dogs. Naunyn, perhaps mindful of the part played by insects in the history of diabetes, asked, "Have you tested the urine for sugar?" "No." "Do it. For where these dogs pass urine, the flies settle."

tween diabetes and non-diabetic glycosurias.³⁸ Naunyn was next after Klemperer to recognize clinical renal glycosuria. Though observing that "the course of the disease is as variable as can be conceived," he nevertheless upholds the essential unity of diabetes, finding in heredity a link which often connects cases of the most varied types. In regard to the etiology, he considers that "it is certain that disease of the nervous system and of the pancreas can produce diabetes;" other causes seem more doubtful. The nervous disorder supposedly acts indirectly by setting up a functional disturbance in the pancreas or other organs directly concerned. Underlying everything in most cases is, in his opinion, the diabetic "Anlage" or inherited constitutional predisposition. Naunyn has particularly supported the conception of diabetes as a functional deficiency, to be treated by sparing the weakened function. He wisely emphasized the importance ((5), p. 391) of doing this at as early a stage as possible, before the tolerance has been damaged and the glycosuria has become "habitual." His plan of treatment is to withdraw carbohydrate gradually, giving large doses of sodium bicarbonate in cases with acidosis as a further precaution against coma. A brief increase of the ferric chloride reaction is not allowed to interfere with the program. When the glycosuria is successfully cleared up, the aim ((5), p. 396) is if possible to place the patient on a Rubner diet, representing 35 to 40 calories per kilogram of body weight and about 125 gm. protein (pp. 407-408), carbohydrate being gradually (p. 415) added and then kept (p. 416) at a figure safely below the tested tolerance. The views concerning exercise (p. 432) agree with those of previous authors; brisk walking, etc., is found beneficial; but overexertion is harmful, especially in severe cases; and some patients seem to do best on a rest cure. When sugar-freedom is not attained on simple withdrawal of carbohydrate, protein may be reduced as low as 40 to 50 gm. daily ((4), p. 22) and the calories also diminished, since ((4), p. 22; (5), p. 397)

³⁸ Magnus-Levy ((2), p. 8), concerning pancreas-diabetes: "Dieser Diabetes ist der einzige experimentelle, der tatsächlich als Diabetes zu bezeichnen ist." Naunyn ((2), p. 3130): "Einen Diabetes melitus haben die Experimentatoren vor Minkowski und von Mering nie erzeugt. Der sogenannte Kurare, der Kohlenoxyd, etc., der Stichdiabetes und selbst der Meringsche Phloridzindiabetes, sie alle tragen diesen Namen mit Unrecht."

diabetics may remain in equilibrium on as little as 25 to 30 calories per kilogram. When necessary as a final resort, temporary under-nutrition may be employed ((5), pp. 392, 409); but prolonged under-nutrition or the loss of more than 2 kilos weight should be avoided ((4), p. 15). Loss of weight continuing over the third week of treatment requires adding carbohydrate and abandoning the attempt to stop glycosuria ((5), p. 414). Occasional fast-days are advised if necessary ((5), p. 409), but only when previous treatment has reduced the glycosuria below 1 per cent; otherwise their effect is indecisive ((5), p. 426). It is stated ((5), p. 425) that such fast-days are practicable for even the severest cases, and heavy acidosis is not a contra-indication (p. 426); the ferric chloride reaction may diminish on a fast-day (p. 414). Naunyn has not stated what limitations apply to the use of such occasional fast-days, but Magnus-Levy ((2), p. 67) stipulates that they must never be more frequent than one in eight or ten days, and in very thin patients must be avoided altogether. Fasting is nowhere recommended as a treatment for coma by Naunyn. On the contrary, when restriction of diet produces really threatening symptoms, his plan is to add carbohydrate and give up the attempt to abolish glycosuria ((2), p. 3144; (5), p. 414). Even the persistence of a very heavy ferric chloride reaction longer than two or three days is a signal for adding carbohydrate (p. 425). The treatment for impending coma consists in maximal doses of bicarbonate and the free use of carbohydrates, especially milk ((4), p. 28; (5), pp. 350, 351; also Magnus-Levy, (2), p. 77). Naunyn had some conception of limiting the total metabolism ((4), p. 14), but meant by it only a bare maintenance diet, or the slight and temporary undernutrition mentioned above. Naunyn ((4), p. 13) states that fat does not appreciably increase glycosuria; elsewhere ((6), p. 741) that in very severe cases it may slightly increase glycosuria; Magnus-Levy ((2), p. 21) that it never gives rise to glycosuria. Like others, Naunyn considers that fat is the chief food for the diabetic ((5), p. 449); that the introduction of fat is the most important art in diabetic cookery ((6), p. 741). He uses it to complete the full number of calories when other foods are restricted ((5), pp. 408, 447); this applies even to the severest cases on carbohydrate-free diet with strict limitation of protein, where accordingly much fat is given (p. 424); his principal care is that the

patient shall take enough of it (p. 395); the only reason for limiting the quantity is the danger of indigestion (pp. 395, 424), except when coma impends, in which case fats are replaced by carbohydrates, and butter is especially shunned because of its content of lower fatty acids (p. 350). Even when sugar-freedom is attainable, certain cases are believed to show an inherent progressive downward tendency ((2), pp. 3135-3136; (5), p. 390). Concerning patients emaciated down to 50 kilograms, with heavy ferric chloride reaction and the usual accompaniments, it is said (p. 425): "In the face of these great difficulties and dangers, which accompany the energetic management of these very severe cases, the prospects of being successful in permanently removing glycosuria are in general not very great, and usually one will be content with a limitation of it which suffices to bring the patient into nutritive equilibrium, that is, down to 60 to 80 gm. sugar in 24 hours."

Lenné of Neuenahr is known chiefly for his advocacy of low protein diet. His plan is to reduce the nitrogen intake until the output falls to his so called "normal" figure; *viz.*, 0.37 gm. urea or 1.1 gm. *absorbed* protein per kilogram of body weight (about 1.3 gm. per kilo in the diet). Carbohydrate is also limited, but the protein restriction is considered more important. He classifies cases into four groups: those in which (1) the glycosuria ceases on diminution of protein without diminution of carbohydrate and the protein requirement falls to 1.1 gm. per kilo; (2) this result is achieved only by reducing carbohydrate as well as protein; (3) limitation of protein and carbohydrate stops glycosuria but the protein requirement never falls to 1.1 gm. per kilo; (4) glycosuria continues and nitrogen remains high in spite of complete withdrawal of carbohydrate and strict limitation of protein. He believes in simple overproduction of sugar without impairment of utilization as the explanation of diabetes, and in the correlated doctrine of sugar formation from fat. He states ((1), p. 82) that it is not necessary to assign any upper limit for fat, since appetite and digestion set the limit; later (2) he speaks in favor of fat restriction, but only in the sense that the diet should be adequate but not excessive. He does not limit fat even for the sake of acidosis, since he disbelieves in the acid intoxication theory of coma, and cites ((3), pp. 252-253) the example of a patient whose urine became free

from diacetic acid on carbohydrate abstinence, insufficient protein, and excess of fat. He insists on abolishing glycosuria and hyperglycemia if possible, and opposes ((1), p. 74) von Noorden's opinion that some diabetics, especially the elderly, can be indulged in eating as long as sugar is not excreted above 20 gm. daily. Nevertheless he refuses (p. 83) to prolong absolute carbohydrate-free diet for a week or over. For stubborn glycosuria he has used fast-days, but prefers to avoid any complete abstinence. His protocols show the benefits of protein reduction, but also indicate the failure of the method in numerous cases of only moderate severity.

It is desirable at this point to introduce a digression, for the purpose of considering the so called "carbohydrate cures" as a group.

It will be observed that carbohydrate has been the touchstone of diabetic therapy since the time of Rollo. All the orthodox theories have agreed in holding it as the one offending substance, and a large proportion of physicians today still conceive of dietotherapy as limited to prescribing a list of carbohydrate-poor foods. On the other hand, the vast majority of diabetic patients have (following or defying advice) never undergone rigid deprivation of carbohydrate for any long time, the specialists of highest repute have granted it in the later stages of the more severe cases, and there has grown up a line of treatment characterized by diets heavy in carbohydrate.

The milk diet is historically first. According to Stokvis, milk was recommended for diabetes by almost all authors in the eighteenth century. The Karel cure, published in 1866 and still well known in the treatment of obesity and other conditions, was a diet limited strictly to 60 to 200 cc. of skim milk four times daily. Richardson credits "Dr. Smart of Edinburgh" with priority in the use of a formal "milk cure" in diabetes. A skim milk treatment was advocated by Donkin (1869) on the claim that it was pleasanter than the Bouchardat plan and also more effective, as casein is better assimilated than other proteins, and lactose than other forms of carbohydrate. Balfour, Oettinger, Winternitz and Strasser, Maurel, Landouzy and Cottet, and numerous others championed the milk treatment, but K ulz, von Frerichs, and most authorities condemned it. Strasser advised three days of milk, then three days of strict diet, and so on alternately—a schedule which might rank high among carbohydrate "cures."

Prasad asserts that in India a diet chiefly of milk permits mildly diabetic patients to live fifteen or twenty years. Naunyn considers that it is hard to get along without milk in treating diabetes, and that milk "cures" are often beneficial. He and his followers have used it as the principal means to ward off acidosis. Guelpa's use of milk is mentioned later. Recently (1915) Farges has taken up the original belief concerning milk, holding that not only is lactose perfectly assimilated in mild diabetes, but that it actually improves the tolerance for other carbohydrates.

Sour milk and its commercial preparations have been used to some extent, but according to von Noorden (1), p. 315) only 10 to 15 per cent of the sugar is destroyed in the natural curdling, and souring beyond this point makes the taste too unpleasant for use; he therefore rates sour milk as neither better nor worse than sweet milk. The status of the typical milk cure as a form of undernutrition treatment is universally recognized.

Second chronologically was the treatment of von Düring of Amsterdam, often incorrectly styled the "rice cure." The first edition of this author's book appeared in 1868, the fifth edition in 1905. He limited his patients to three or four meals daily, representing a total of 80 to 120 gm. of any cereal (frequently rice, least often oatmeal because of its tendency to ferment), up to 250 gm. meat, moderate quantities of stewed fruits, and small allowances of stale bread, milk, and wine. His general position was a protest against overeating and luxurious living, and a "back to nature" attempt in food, exercise, and general hygiene. He was a pioneer in sanitarium discipline and restriction of the total diet. One interesting trick was his use of ice and ice-water to combat polyphagia. He was a zealot in his beliefs, but frankly acknowledged numerous failures. His method may be interpreted as a mixed ration rather low in protein and calories, not infrequently proving preferable to the protein-fat excess of which his earlier contemporaries were signally guilty.

Dujardin-Beaumetz (1889) first recommended potatoes for diabetics in quantities below 100 gm., because they contained less carbohydrate than the usual gluten bread. Mossé (first publication 1898) believed potatoes to be far superior to other forms of carbohydrate for assimilation in diabetes, and attributed the supposed virtue to their content of potassium, and perhaps also of organic acids, traces of manganese, or oxidases. He gave as much as 1500 gm., or in polyphagia 3000 gm., not as occasional "cures" but as regular additions to the daily diet. His records and graphic charts of comparisons between potatoes and bread reveal in many instances a much smaller quantity of carbohydrate in the potato diets; in other cases the quantity of carbohydrate was kept equal, but it is doubtful if patients taking such large quantities of potatoes would eat as much of other kinds of food as when taking bread. The alleged advantage of potatoes is thus readily explained. Also the treatment was very bad throughout, for though the cases were mild, there was no pretense of stopping glycosuria, which was high even in the cases showing the imagined benefit. The treatment thus poorly founded gained widespread adoption only in France. Rathery refers to the numerous patients there who complain of glycosuria uncontrollable by strict diet, when inquiry shows that they are consuming potatoes liberally in the belief that they are harmless and beneficial. He finds it necessary to point out the smaller percentage of starch in them as compared with bread or cereals. Labbé, by testing a series of mildly diabetic patients with allowances slightly above their tolerance, composed a list of carbohydrates in descending order of assimilation, as follows: potato, oatmeal, macaroni, chestnuts, rice, beans, lentils, peas, milk, bread, sugars. Linossier,

discussing certain of these papers, properly called attention to the lower protein and calories of the potato diets. The facts concerning potatoes are fully explained by their relatively low food value, in that they carry little protein or fat and only a fraction of the carbohydrate percentage of bread or cereals, while their bulkiness tends to diminish the consumption of other foods. They are a higher homologue of the green vegetables, and may be used correspondingly in the milder grades of diabetes.

Von Noorden made the chance observation that certain patients showed marked improvement in their diabetes, even to cessation of glycosuria, when placed because of digestive disturbances on a diet of oatmeal gruel. It is probable that such rations were rather low in protein and calories. In 1902 he announced his formal "oat-cure." Though there were already facts in the literature to indicate the true explanation, the diminution or disappearance of glycosuria on change from strict to carbohydrate-rich diet impressed von Noorden and the contemporary medical world as an astounding and mysterious phenomenon. Naunyn held a skeptical attitude throughout. He favored the untenable hypothesis of intestinal fermentation supported by his pupil Lipetz, but he also (4A) early classed all carbohydrate "cures" together and declared that the essential benefit lay in undernutrition. Kolisch's correct suggestion of the importance of a low protein intake was supposedly disproved by the incorporation of eggs and vegetable protein in the oat diet. Falta and others employed smaller quantities than the established 250 gm. of oatmeal; but none perceived that the value of the "cure" diminished as the quantities of foods were increased. The therapeutic endeavor was to make up a full Voit diet to avoid undernutrition, depending on the supposed virtues of oatmeal and special proteins to achieve assimilation. Differences in the manner of cooking, and even distinctions between brands of oatmeal, were asserted and accepted. The experimental goal was to discover the reason for the superiority of oatmeal over other carbohydrates, and thus much fruitless labor was spent upon oat extracts, digestion, renal permeability, and intestinal bacteriology. Thus the entire clinical and experimental development of von Noorden's primary observation followed mistaken lines. Blum in 1911 attacked the foundation of the error, by comparative tests showing the equal assimilation of oatmeal and other carbohydrates when administered to diabetic patients under identical conditions. He likewise overthrew the perplexing claim that the severe cases are the ones that assimilate oatmeal best; and it is now generally recognized (cf. Magnus-Levy (2), p. 70) that cases doing well on carbohydrate "cures" are essentially mild even though they may have appeared severe. Also in 1911, Klemperer showed that even sugar behaves similarly when given in divided doses. The von Noorden school has maintained, with diminishing force, that oatmeal possesses some degree of superiority, and has arranged a scale of assimilability, in which bananas and barley stand next to oatmeal, and wheat and rice are at the lower end. The literature up to 1913 permitted no positive conclusion. Minkowski (4), in a sweeping criticism of the Vienna doctrines, acknowledged the benefits of the oat cure. Magnus-

Levy added his experience in support of the relatively better assimilation of oat starch. It has since become clear that the mixed or indecisive clinical observations of von Noorden, Lampé, Werbitzki, Piskator, Richartz, Weiland, and other authors previously referred to furnish no sound evidence of any peculiar assimilability of oatmeal. On the contrary, accurate comparative tests by Petersen, Wolff, and Falta have fully confirmed Blum's position. Jastrowitz found complete similarity between oats and wheat in experiments on totally and partially depancreatized dogs. Csonka lately proved the equal and complete elimination of the carbohydrate of wheat and oats as glucose by phloridzinized dogs. The absence of any specific ease of assimilation of oatmeal by human patients has been demonstrated in the blood sugar investigations of Schirokauer, Severin, Lampé and Strassner, Wolf and Gutmann, and Menke, and in the studies of respiratory metabolism by Schilling, Rolly, Róth, Joslin (2), and Allen and DuBois.

The buckwheat (Alvord), raisin, and other sporadic "cures" require no special discussion. All the early carbohydrate treatments laid stress on the restriction to only one form of starch, but the benefit of such limitation was always incomprehensible and is now recognized as imaginary. The later recommendations offer greater variety. Labbé has introduced a "dry legume cure," with a diet of 300 gm. beans (including lima, soy, or other varieties), peas, or lentils, 150 gm. butter, 3 to 6 eggs, 3 to 6 aleuronat or gluten cakes, green vegetables, and wine. The main thing avoided is meat. Falta, having renounced his old allegiance, now uses "mixed cures" planned after the oat cure except that monotony is avoided by means of alternation of all sorts of carbohydrate foods, with addition of green vegetables.

The rationale of the carbohydrate "cures" appeared mysterious when diabetes was regarded as a deficiency of carbohydrate assimilation, but becomes clear with the understanding of diabetes as a general disorder of nutrition. Most of the diets represented some degree of undernutrition. In the oat cure, this was attained by the preceding and following vegetable or fast-days, adopted from Bouchardat, Cantani, and Naunyn. Temporary relief from the overload of protein and fat diet was afforded by the substitution of an excess of carbohydrate. The experience showed that the latter is, at least for short periods, often less injurious and dangerous than the former. The successful results demonstrated the surprisingly high tolerance still retained in a large proportion of diabetic cases heretofore classed as severe. The invariable failure encountered in truly severe cases follows as a simple corollary to the definition, since the nature of severe diabetes involves inability to metabolize such quantities of carbohydrate, protein, and fat.

Aside from the carbohydrate "cures," there have long been practitioners of higher and lower degree who have upheld the opposite of Rollo's animal diet, namely, a pure vegetarian diet. Harley employed it for cases of a certain type. Kolisch may be mentioned as the principal champion of this system. He argues that diabetes does

not consist in a lowered tolerance for carbohydrate, because a small quantity of carbohydrate often causes less glycosuria than a large quantity of protein. He regards the disorder as an overproduction of sugar, derived from unknown compounds in the tissues. The improvement of tolerance on carbohydrate-free diet, also the cessation of glycosuria in cachexia observed by Cantani and Naunyn, are explained as due to impoverishment in sugar-forming material. Food, especially protein, is supposed to irritate the tissues so as to stimulate sugar formation. Therefore the author reiterates Bouchardat's advice, "*manger le moins possible*," and particularly restricts protein. He regards fat as the food which sets up the least stimulus to sugar formation and which never gives rise to glycosuria ((1), p. 248). He enforces vegetarianism, because patients are thus kept in equilibrium on 20 to 25 calories per kilogram of weight with a diet bulky enough to satisfy, and because he believes that this maintenance requirement is lower than on animal food, that vegetable protein has a superiority over animal protein in contradiction to the caloric theory, and that the vegetable diet is intrinsically less irritating to the diabetic process. Milk is regarded as somewhat similar. Fast-days are supposed to benefit through absence of food irritation, but they are held ((1), p. 252, and elsewhere) to have little practical value, because their effect is transitory and glycosuria always returns. Kolisch (2) makes a trenchant criticism of the Külz method of testing tolerance, objecting that this shows merely the result of adding relatively small quantities of carbohydrate to large quantities of protein and fat. Instead, he advocates trying various combinations of foods, and choosing the one which permits maintenance on the lowest number of calories, also the taking of as much carbohydrate as possible without harm. Here a critic will necessarily ask for a definition of the phrase "without harm." Von Noorden ((1), pp. 369, 372) calls attention to the phenomenon studied by Leo, Rosenfeld, and Kolisch, that up to a certain point many diabetics assimilate more carbohydrate as the quantity ingested is increased (paradoxical law); the practice of giving such a ration as will cause the greatest possible combustion of carbohydrate is called the method of Rosenfeld and Kolisch; von Noorden opposes this method for mild or moderate cases, but endorses it for severe cases. Roubitschek and Gaupp are among the recent advocates of this "best

oxidation level" program, naming Klotz also in support of it. This is one phase of the method of the so called "carbohydrate balance," under which physicians everywhere have been greatly concerned over the relation between the quantity of carbohydrate ingested and the quantity of sugar excreted, and, especially in threatening acidosis, have juggled the diet in every possible way to make the former greater than the latter. The method has also been used very widely and by the highest authorities for the sake of mere comfort and temporary well-being of the patients; for example, von Noorden's advice, criticized above by Lenné; the advice of Naunyn ((4), p. 20) that not more than 0.5 per cent glycosuria is allowable in mild cases; and the statement of Magnus-Levy ((2), p. 67) that the advantage of 100 gm. bread in the diet is worth the excretion of 20 or 25 gm. sugar as long as no complications are present. This entire method is fundamentally vicious and in the end defeats every purpose for which it is employed. On the other hand, there is interest in the view of Kolisch, similar to that of Lenné, that the patients with milder diabetes are injured by heavy protein-fat diet, even though glycosuria and other symptoms are absent; and that the ultimate consequence is that they progress downward and later show the severe form. For such cases Kolisch favors a low calory mixed diet, containing little meat and plenty of vegetables, with carbohydrate in quantity just short of producing glycosuria.

Albu is the author of the most recent vegetarian system for diabetics.

Carl Hanko von Noorden has occupied a position of eminence among diabetic specialists in the generation after Naunyn. He was trained under Hensen, Riegel, and Gerhardt, has directed important clinics at Frankfort and Vienna, and by his writings has done much to diffuse knowledge of the rational treatment of diabetes. The investigations of his large and influential school are voluminous, but belong mostly to the theoretical side of the subject. He long maintained the deficient utilization of carbohydrate in diabetes, but in the later editions of his text-book went over to the pure overproduction hypothesis. He also supported the polyglandular doctrine, which assails the unity of diabetes; but, though still nominally defending it, and assigning great importance to the liver and the thyroid, his later writings con-

cede the essential contentions of his opponents ((2), p. 69): "But really these differentiations do not shake the essential unity of the metabolic disturbance in diabetes in the very least. I think I shall be voicing the opinion of all pathologists when I say that every individual who has a diminished tolerance for carbohydrate, either permanently, or extending at least over a considerable period, and thus exhibits the most important clinical symptom of diabetes, must be considered as a subject of pancreatic insufficiency. We need not always expect to find perceptible anatomical evidence, for there may be functional impairment where no macroscopic or microscopic pathological appearances can be discovered." Von Noorden has been unfortunate in his support of false theories, but he deserves credit as the principal upholder against the Naunyn school of two doctrines which now appear to be justified by facts: first, that diabetic acidosis represents something more than lack of carbohydrate; second, that the symptoms of acidosis, including the fatal termination, are due to something more than simple acid intoxication. Von Noorden's clinical work has consisted chiefly in systematizing and improving the Külz method in some details. He justifies the Külz treatment by the statement that he has under his care some of Külz's patients who have remained in good condition for seventeen years. The one distinctive feature introduced by von Noorden, the oat cure, was previously discussed. Though he stands as the most prominent believer in the formation of sugar from fat, this belief has not influenced his treatment; for he "perhaps gives diabetics greater quantities of fat than anybody else;" he regards fat as the anchor of their salvation; he has almost never seen increase of glycosuria from it, except when digestive upsets occur, in which many diabetics immediately excrete more sugar ((1), p. 96). Nevertheless he recognizes occasional "fat-sensitive" cases. High fat intake, greatly in excess of the requirement, is said to increase metabolism, like every overabundant diet, and therewith increases the sugar excretion. But in order to produce this increase of glycosuria, the quantities of fat required are so high as to be superfluous and of no practical importance in treatment. In the presence of severe acidosis, it is held that butter should be avoided, but that ordinary animal and vegetable fats cause no increase of ketonuria in a patient accustomed to strict diet ((1), p. 141), and even

during the transition to strict diet the administration of alkali is an adequate precaution (p. 293), so that fats are given freely even under these circumstances. In addition to alkali, von Noorden formerly treated impending coma with carbohydrates, especially oatmeal, milk, and levulose; but recently he has found that one or two fast-days are far more effective. On these days the only food is alcohol in large doses, up to 200 to 250 cc. cognac. As soon as the glycosuria and acidosis are thus partially controlled, he hastens to inflict an oat cure ((1), p. 388). Here also the fat intake is limited, thus contradicting his previous contention. A large proportion of severe cases are conceded to be hopeless; here a liberal varied diet is allowed, the glycosuria being merely limited and the strength maintained ((1), p. 371; (2), p. 151) and 15 to 20 gm. sodium bicarbonate and about 6 gm. calcium carbonate given daily for the acidosis ((1), p. 389). Not only strict diet or vegetable days, but also actual fast-days, are interposed in this program. ((2), p. 93): "There are but few diabetics who do not become sugar-free on these days,³⁹ and you will at the same time notice an enormous fall in the acetonuria. Fast-days, combined with bed-rest, are excellently borne. I never find that the patient's strength is unduly diminished by them. An important result is regularly attained in the immediate and well-marked rise of tolerance which follows." Again ((2), p. 152): "We need have no fears that the hunger day will damage seriously the general nutrition. Of course the body weight falls on the fast-day, but the loss is rapidly made up, and by this combined method we often obtain considerable increases in weight." Von Noorden refers to these fast-days as "metabolic Sundays." The metaphor is striking and accurate, but the insufficiency of the metabolic rest and the attempt to build up weight in the presence of glycosuria and acidosis are fatal to the patients and to the method.

Weichselbaum and Stangl in 1901 first observed the specific "hydropic" degeneration of the islands of Langerhans. It is remarkable that one of the most important contributions to the morphologic

³⁹ Remarks of this sort show the actual mildness of many cases classified by writers as severe.

pathology of diabetes should have met with such a complete lack of confirmation or credence.

Among English writers, Williamson in 1898 published a text-book possessing permanent value by reason of the author's great experience and wide knowledge. Recently (2) he has made some use of a diet consisting only of casein and cream given in small quantities every two hours. He attributes the benefit to this latter device and to the reduction in the total quantity of food, but says: "In the most severe forms of diabetes with marked diacetic reaction in the urine, I do not at present feel justified in recommending the casein treatment."

Cambridge (1), p. 297) held that with impaired fat metabolism indicated by wasting, lipemia, and acetonuria, a limitation of fat in the diet and its partial replacement by carbohydrate is advisable, even though glycosuria be increased. More recently (2) he has advocated a treatment resembling that of Lenné. He aptly remarks that fat and protein metabolism should be considered as well as that of sugar, and that the absence of any striking color reaction for protein disturbance, comparable to those for detecting sugar or diacetic acid, goes far to account for the neglect concerning the protein metabolism. The treatment consists in reduction of protein, rest in bed, and opium when nitrogenous equilibrium cannot be established by any other means. In adopting recently the fasting treatment, he has emphasized the study of the protein metabolism for judging the condition and progress.

Modern France has not lived up to Bernard and Bouchardat in this field. Not only has it remained relatively barren of important original contributions, but also, outside the practice of a few specialists, the knowledge and management of diabetes seem to fall below the high general standard of French medicine. A French physician on a recent visit to America remarked that patients in France were less willing than those in other countries to adhere to restricted diet, and demanded a cure which would enable them to eat freely.

Lépine has published a very large number of studies especially concerning blood sugar and glycolysis, but his comprehensive text-book alters nothing in the accepted treatment of diabetes. The same is true of his recent review of the therapy (2, 3).

Fasting has been employed in diabetes not only by specialists in

this subject, but also by enthusiasts who advocate it as a panacea.⁴⁰ Of these the most prominent is Guelpa of Paris. Starting from an incorrect observation of Dujardin-Beaumetz in typhoid fever, "that the more regular and rapid the patient's loss of weight, up to the disappearance of the pyrexia, the quicker and more favorable was his course to recovery," Guelpa applied the principle first to infections. "I have found it an invariable rule that, in febrile affections, the more promptly emaciation sets in, and the more definitely it establishes itself, the more sure and rapid is the patient's progress toward recovery. Conversely, when the patient fails to exhibit an emaciation proportional to the intensity of his pyrexia, the illness is always graver and of longer duration, and the convalescence more prolonged and more interrupted. All this, it seemed to me, proved, so to speak, mathematically, that disease is a state determined and kept up by the presence within the body of a quantity of products of fermentation—toxins and the debris of poisoned tissues—which the organism must eliminate before it can return to a condition of health." Having set up the theory of autointoxication as the dominant feature in all disease, Guelpa proposed fasting—generally in three-day periods—as the sovereign remedy. Symptoms of weakness, headache, and malaise during fasting, and the sensation of hunger itself, were attributed to autointoxication; food relieves the symptoms by combining with the toxin, while purgation also relieves by sweeping out the toxin; copious purgation—a bottle of hot Hunyadi-János water daily—was accordingly added to the treatment. Among the conditions for which the fasting-purgation treatment is recommended, with confirmatory histories of grateful patients, are gout and rheumatic troubles, anemia, bronchitis and asthma, herpes zoster, eczema and other dermatoses, various ophthalmic conditions, some gynecological conditions (including postpartum hemorrhage), digestive complaints, nervous disorders, insanity, epilepsy, drug addictions, various infec-

⁴⁰ Some of these are outside the ranks of the medical profession. Hereward Carrington, in his book, "Vitality, Fasting and Nutrition," New York, 1908, p. 187, mentions a patient with incipient diabetes who fasted twenty days continuously, becoming free from glycosuria and remaining so for two months thereafter, when he was lost from observation. In the same place is a reference to a previous example recorded by C. C. Haskell.

tions, postoperative complications, etc. Important in the list is diabetes, where alone the results have attracted widespread notice. A diabetic is given the usual fasting and purgation for three to five days. Other features of the treatment are best shown in Guelpa's own words ((5), p. 131):

"It is necessary to insist on the absolute necessity of repeating the cure from time to time, and of imposing, during the intervals, which should be carefully lengthened, a carefully restricted diet. As regards the latter, it is my custom to complete the first period of the cure (three or four days) by a week of milk diet, the amount of milk taken daily not to exceed $2\frac{1}{2}$ pints. At the end of this week, however satisfactory the condition of the patient, I prescribe a second period of cure (three or four days) to be followed by a week or a fortnight of a régime mainly of vegetables, which satisfies the patient by filling his stomach, but, in reality, *under-feeds* him, the object being to continue the process of forcing the organism to live partially on its reserves and to burn off its debris. The following is a menu of the diet I generally adopt: Breakfast, coffee or tea without milk; Lunch, clear soup, salad, one or two apples or pears; Dinner, as lunch. As drink, tea or other non-nutritive drinks *ad lib*. In certain special conditions I allow an ounce or so of bread, or a diet of cooked vegetables. I increase the amount of food after each repetition of the cure, taking as my guide an analysis of the urine. Since I adopted this régime, I have obtained more rapid and stable cures, without discouraging relapses. I wish also to draw attention to what I believe to be a deplorable error; namely, the doctrine that milk is very harmful in the treatment of diabetes. This is a mistaken view, based on a false interpretation of a single fact. It is quite true that diabetics kept on milk diet almost always pass an increased quantity of sugar. This increased excretion, is, however, only temporary. From the fact of the increased glycosuria, the conclusion has been drawn that milk is harmful in diabetes. The deduction is the result of a too superficial process of reasoning. It would be as logical to conclude that rest and warmth were harmful in the treatment of rheumatic conditions, from the fact that they lead to an increased discharge of urates. In the case we are considering, the milk merely hastens the expulsion of sugar, which is injuring and impeding the tissues, relieves the hematopoietic function, and contributes to a cure, if the mistake is not made of overwhelming the blood-forming organs by administering a quantity of milk beyond the metabolic powers of the liver to deal with."

Afterward, potatoes, bread, and other elements of a mixed ration are gradually added, with general admonitions against overeating. Acidosis is not mentioned in the records of Guelpa's early "cures." About 1911, something seems to have called his attention to acidosis, for he suddenly (7) added a new chapter to his theory of diabetes.

Here he announces that diabetes is the type disease of hyperacidity. Glycosuria is merely one of the multiple forms of defense of the organism against acidosis caused by food pernicious in its quantity and especially in its quality. There are several stages of the process, first increase of urea, later glycosuria, later acetonuria, etc., and the sixth and final stage is coma. The body defends itself by breaking down its less useful elements, notably fat; an indication is the acetonuria, which like the glycosuria is helpful and not harmful in the process of acidosis. He denounces the overfeeding in the usual treatment of diabetes, and denies that his method is unsuited for *diabète maigre*. As evidence, he cites the example of a patient aged sixty-five years. This man underwent a "cure" of five days' fasting with 40 gm. sodium sulfate daily. The subsequent diet of vegetables, fruits, and 60 gm. bread daily caused return of glycosuria, whereupon the five-day "cure" was repeated, followed by a similar diet. The duration of this "dix-toxication cure" was a month, and the result was that the patient became free from his former glycosuria, albuminuria, and joint infection. For threatened coma, Guelpa (7 and 11) advises copious drinks and enemas of sugar and weak alkaline solutions, oxygen inhalations, bleeding, and intravenous injections of physiological saline or weak alkali.

The Guelpa treatment has gained followers chiefly in France and England. Cammidge ((1), p. 343) mentions authors reporting favorable results, but states that he has never been able to persuade any patient to undergo it. A recent favorable report is by Hume.

Clear recognition should be accorded to Guelpa for the following points of merit. First: without being guided by knowledge of earlier undernutrition cures, and entirely from his own original and independent thought, he devised the first plan of treating diabetes by a radical initial fast, longer than any previously recommended for this purpose. Second: these fasts were repeated a number of times, with intervening periods of diet very low in calories and protein and relatively rich in carbohydrate, and the increase toward a living ration was made gradually. Third: he emphasized loss of weight as a potent factor in the improvement, and carried the reduction of weight to a more extreme point than ventured by anyone before him, and did this even in patients complaining of weakness. Fourth: he was first to demonstrate the beneficial effect of fasting upon certain complications,

notably diabetic gangrene. The dietotherapy of gangrene is familiar in text-books, but the important observation of Guelpa was that fasting benefited the gangrene, instead of making it worse by weakening the patient. Fifth: fasting periods were employed not only whenever glycosuria or other symptoms appeared but also as a prophylactic against their return. Certain contrary facts must also be given proper weight. The Guelpa treatment, in spite of its ease and simplicity, failed of acceptance at the hands of diabetic specialists and the immense majority of medical practitioners in all countries. The explanation of this fact necessarily casts discredit either upon the medical profession or upon this mode of treatment, and the latter alternative is the true one. It is frequently repeated that the cases treated successfully by Guelpa's method were severe, and that "the usual anti-diabetic régime had failed;" but the details of the unsuccessful diets are not given and the assertion cannot be accepted as correct in a single instance. In age, the patients were almost without exception above forty and frequently above sixty; many were obese; their complaints were largely the natural consequence of their mode of life at their time of life; on cessation of overeating and a lively purge they were astonished how much better they felt, and their diabetes was so slight that it was controlled by these simple measures with little or no subsequent restriction of carbohydrate. The two most severe cases of the series, namely that of the man described by Arnold⁴¹ and that of the woman described by Bardet,⁴² cannot be considered

⁴¹ Introduction to translation of Guelpa's book.

⁴² Bardet narrates that in the therapeutic clinic of Beaujon was a woman with diabetes of several years' duration, excreting 800 gm. sugar daily. Emaciation was not extreme and acutely threatening symptoms were absent. Nothing resembling the Naunyn treatment was undertaken. "She was placed for several weeks under the ordinary treatment of M. Albert Robin, namely alternate medication with antipyrine and arsenic, without its being possible to reduce the quantity of sugar below 160 gm. After a series of this medication, the patient was left free from all treatment, and followed the routine diet of the diabetics of the service: meat 500 gm., potatoes 500 gm., green vegetables 500 gm. At the time of beginning the experiment (*i.e.* absolute fasting), she was passing 12 liters of urine in 24 hours, and on the final day showed an elimination of 760 gm. sugar." Here is seen a combination still too frequent in all countries; absence of rational treatment, dependence on drugs, the use of routine instead of individualized diets, and the physician's ignorance that the alleged sugar excretion on the diet stated is impossible.

examples of severe diabetes; at the utmost, they would fall in the class of "medium severity" according to von Noorden or Naunyn; they are of the type easily cleared up under the Naunyn plan of regulated diet, restricted protein, and intercalated fast-days, and neither of them remained clear under the Guelpa method. So far from this method being an improvement over the known treatment, a physician confronted with the choice of referring a patient to Guelpa or to Naunyn could have no possible ground for hesitation in choosing the latter. The Guelpa plan is applicable only to mild diabetes, and here (notwithstanding the quick temporary clearing of glycosuria) a permanent success is attained only in a longer, harder, and less certain manner than under the usual treatment. For diabetes of even moderate severity, the attempt to fast, purge, and undernourish a patient until he is able to tolerate carbohydrate-rich diet is inevitably disastrous. In undertaking to apply the mode of treatment described in the present monograph, the most common difficulty and mistake of inexperienced physicians has been to fast the patient till free from glycosuria, then to give a diet permitting its return, then to fast, then to proceed with improper diet, so that weight and strength are lost while tolerance is injured instead of improved, and the end in any severe case will be fatal. In the one young patient of his series, a youth of sixteen years, with actually severe diabetes, Guelpa ((5), p. 112) achieved sugar-freedom after fifteen days, but relapse followed because the patient finally found the program unendurable. There may be justifiable surprise that Guelpa describes only successes; in his half dozen or less of partially successful cases the blame for mishaps is placed entirely upon the patients. Inasmuch as common knowledge and Guelpa's own experience ((1), p. 506) make it clear that purgation does not prevent acidosis during fasting, it would be remarkable if so many diabetics should be treated without encountering some of those severe cases of long standing who go into fatal acidosis on fasting. There is still more noteworthy absence of a record of any young patient with impending coma who was cleared up and kept clear of both glycosuria and acidosis. It is improbable that Guelpa avoided such cases altogether; it is certain that his treatment must fail in the vast majority of them; and his record of success limited to mild cases constitutes sufficient evidence of his failure in more severe cases, even of the grade that can

be managed successfully under the Naunyn plan. On the one hand, Guelpa should receive due credit for boldness, enthusiasm, originality, and some new observations growing out of a new clinical procedure. On the other hand, it cannot be maintained that Guelpa devised a good treatment for diabetes. The lesson of his work cannot be overlooked; but the information and encouragement derivable from his long fasts in mild cases are less than from the shorter fasts of Naunyn and von Noorden in severe cases, so that the proposed treatment of severe cases by fasting is a development of the Naunyn method rather than of the Guelpa method.

America has not been prolific of diabetic text-books. A notable early example is that of Tyson, the frontispiece of which shows the intraocular picture by which diabetic lipemia can be diagnosed.

The first great contribution of this country to this subject was Opie's hypothesis that diabetes is due to alterations in the islands of Langerhans, on the basis of findings of hyaline, fibrous, and other destructive changes in the islands in a series of cases where the acinar tissue was relatively little affected.

Mandel and Lusk demonstrated the dextrose-nitrogen ratio of the phloridzined dog in a human diabetic, and drew attention to the prognostic value of this ratio. Lusk's "Science of Nutrition" treats a subject of such dominant importance for intelligent dietotherapy that it may be placed in the highest rank among text-books of diabetes. The most extensive investigation of the respiratory metabolism in diabetes is that of Benedict and Joslin.

Hodgson treated over 1100 patients in the twenty years preceding 1911. He worked out a plan of treatment without drugs, using a mildly alkaline mineral water freely. He held that patients "should be kept mentally indolent and physically active. . . . One other essential must be made plain to the diabetic, and that is the quantity of food eaten is just as important as the kind of food. . . . It is a fact that many mild cases of diabetes will show a diminution of sugar almost to the vanishing point when the patient is merely compelled to eat a very moderate ordinary diet. That is to say an antidiabetic diet is not always necessary to reduce the glycosuria; a reduction in the amount of ordinary food will sometimes accomplish the same end. . . . Again it should be stated that the quantity of all food, even

if it is carbohydrate-free, must be greatly restricted. The number of calories that the body ordinarily requires is no safe criterion for the amount of food that should be given a diabetic. It is not the quantity of food that should be metabolized, but the quantity that can be metabolized that should determine the amount given to the patient. All in excess of the quantity that the patient can actually use burdens the already overtaxed excretory organs and retards improvement." In cases severe enough that sugar did not disappear after two weeks of strict diet, the patient was put to bed and allowed one raw egg and two ounces of olive oil three or four times a day. If diacetic acid appeared, the oil was diminished and some carbohydrate added. Hodgson's statistics show a high percentage of favorable results in cases not too severe in type.

Foster's manual (1915) is not only an excellent brief presentation of the Naunyn system, but distinctly goes beyond this in the more radical employment of undernutrition, with correspondingly better results. He lays down the wise rule (p. 165) in contradiction to some European authorities, that it is not safe to disregard diabetes even in advanced life. By the use of repeated fast-days, vegetable days, and restricted diet he achieves freedom from glycosuria in cases of the type given up as hopeless by many writers. The procedure in such cases is slow, and the control transitory (p. 216). "By the enforcement of rest in bed and a stringent diet the urine can be freed of sugar in the vast majority of cases. With early cases the result is often effected within a few days; when the disease is advanced and there is a complicating severe acidosis, months may be necessary. . . . These are the most discouraging cases, as they never approach a semblance of health. . . . At once on being released from incessant control, there is an inevitable transgression beyond the path of safety in diet and exercise. . . . With severe cases of diabetes coma develops finally in spite of the best endeavors."

Mosenthal applied the hospital class system to the care of diabetics.⁴³ The method is particularly adapted to a disease in which instruction of patients is so essential as in diabetes, and it is the most effective practical measure in the organization of a clinic, both for the care of

⁴³ Cf. Joslin ((4), pp. 327 and 409).

ambulant cases and for guarding against relapse in patients after discharge from hospital. More widespread and effective social service along these lines offers one of the most important means of diminishing the death rate from diabetes.

Woodyatt (1) was one of the very few who in 1909 held clearly to the conception of diabetes as a deficiency of the internal function of the pancreas.⁴⁴ Woodyatt (3) has recently suggested that the weakness of the pancreatic function here concerned may not always be an inherited or constitutional defect in the Naunyn sense, but may sometimes be acquired, especially through infections which selectively injure either the pancreas or the nervous mechanism controlling it.

⁴⁴ "Diabetes mellitus is a disease in which the body has in part lost its ability to utilize sugars. Sugar arrives at the point where it should burn, but fails to do so, and accumulating in the blood creates an hyperglycemia. Disregarding accessory factors, which may play a part, we can say that ultimately the failure of sugar combustion in diabetes mellitus depends upon lack of 'a something derived from the pancreas.' The pancreas, like other glands, is capable of being stimulated into a state of fatigue. It may be conceived that excess of sugar in the blood of healthy individuals acts directly or indirectly (*e.g.* through nerves) as a stimulus to the pancreas, as a result of which more internal secretion is set free and the excess of sugar thereby automatically taken care of. This removed, the stimulating influence ceases and the pancreas rests. In diabetes it may be assumed that the pancreas is functionally weak. A small excess of sugar in the blood, let us say, calls for a response from the pancreas, and as in health the excess may be removed. Sooner or later, perhaps as a result of some dietary excess, or of some shock to the nervous system which results in an outgush of sugar from the glycogen depots of the liver, an unusual hyperglycemia occurs. This calls for a strong pancreatic response, more than the functionally weak gland can give, and some excess of sugar remains unutilized in the blood. If hyperglycemia persists for any appreciable time the continuous pancreatic stimulation thereby engendered results in glandular fatigue. Less and less secretion is elaborated, less and less sugar utilized, the hyperglycemia grows progressively worse and a vicious circle becomes established. The condition of the pancreas then corresponds to that of a heart with broken compensation, and as the treatment for such a cardiac condition is rest, so in diabetes rest is needed for the pancreas. To secure this we must control the stimulating hyperglycemia, which means primarily the withdrawal of carbohydrates from the diet, secondarily reduction in the amount of protein, until absence of glycosuria tells us that the blood sugar percentage is approximately normal. After prolonged rest of this sort a return of the pancreatic function to its previous state is frequently spoken of as an increased body 'tolerance for sugar.'

"Such restoration of sugar-burning capacity, such increase in 'tolerance' is the

Raulston and Woodyatt in 1914 described a case of diabetes, for which fasting had been used.⁴⁵ Woodyatt (2) said at a symposium on diabetes before the Association of American Physicians in 1915: "For eight years at the Presbyterian Hospital we have regularly used starvation in the treatment of diabetes, following principles with which I became acquainted in the clinic of Müller in Munich. We have fasted patients for the purpose of desugarization for periods of one, two, three, and in one case five days, and have kept patients for prolonged periods in semistarvation. There can be no doubt of its value in certain phases of treatment. As to its safety, I have seen two deaths apparently from spread of infection immediately following a period of fasting."

first aim of diabetic therapy. There are cases in which the ability of the body to utilize carbohydrate has sunk so low that as a result certain secondary changes in the fat metabolism have supervened. These changes are mainly responsible for the condition spoken of as acidosis. In health and in diabetes withdrawal of carbohydrate from the diet frequently causes the appearance of a previously absent acidosis or an increase in the severity of an already existing one. These aggravations are temporary. Still in such cases as already have a dangerously large amount of the acetone bodies in the blood no increase at all is permissible. In these cases, and only in these cases, should one refrain from an attempt to improve tolerance. Just where to draw the line is a matter for individual judgment. Where means are at hand for accurate quantitative measurements of the daily excretion of acetone bodies one may be justified in closely approaching the danger point. When these means are not available a more respectful margin of safety must be maintained."

⁴⁵ "We made a transfusion of blood into the veins of a patient suffering from diabetes mellitus, one for whom all known expedients had been exhausted and who was approaching the end. . . . The patient, a man, aged thirty-four, had first shown symptoms of diabetes six years previously. . . . For two years the symptoms had been severe, and for eighteen months prior to the transfusion he had been constantly under observation in the Presbyterian Hospital, Chicago, where on numerous occasions his metabolism had been studied for prolonged periods. Prior to entering he had twice become unconscious with what had been diagnosed as diabetic coma, and on several occasions afterward coma was averted only by the enforcement of complete bodily rest and the use of maximum doses of alkali and wine. He became fully educated with regard to the requirements of a metabolism study and voluntarily cooperated in a highly intelligent way. He knew that the expectancy of life was very limited and solicited the trying of any new line that might even temporarily mitigate his condition or

In the same discussion, Billings (1) spoke to similar effect.⁴⁶ Recently Billings (2) has written, "In the service of the Editor in the Presbyterian Hospital, Chicago, in collaboration with Dr. R. T. Woodyatt, the treatment of diabetes by a preliminary absolute fasting period, until the urine is sugar-free, has been followed for nine years. We have fasted patients for as long as eight days. The patient is encouraged to drink water freely. Acidosis usually diminishes rapidly. One may give whisky or sour wine during the fasting period. Soda bicarbonate may also be used in persistent acidosis. All that is said by Allen and Joslin concerning the treatment we can affirm."

To clear up possible misunderstandings, the following may be remarked:

(1) Friedrich Müller has published nothing in regard to the principles attributed to him. On the contrary, Stäubli published (1908) the records of one clinic patient and two private patients of Friedrich Müller, showing that they were treated by the Naunyn method, and though the treatment continued for a number of months and the cases were not extremely severe, they continually showed marked glycosuria and ketonuria and were dismissed with these still present. Further-

delay the end. On several occasions his glucose to nitrogen ratio closely approximated 3.65 : 1 on a diet aggregating 2,500 calories (due allowance having been made for ingested carbohydrate). Nevertheless his urine could always be rendered sugar-free by fasting, and on semistarvation (the Falta-Lusk quotient) could be reduced from 100 or thereabouts to the neighborhood of 50, as it was on the diet used at the time of transfusion. During the time of observation the patient remained quietly in bed. *Diet.*—For two weeks prior to the transfusion and for five days afterward the diet consisted of 800 cc. of 16 per cent cream, three eggs (150 gm.), and water, clear tea or coffee to make the total volume of fluid two liters daily." The patient died shortly after this time.

⁴⁶ "I am surprised to hear it said that the method of starvation of diabetic patients is new. We have used that method in Chicago for a number of years and patients have been fasted for as long as eight days. The adoption of the method there was due to the work of Woodyatt. A point to be remembered is that the study of patients at rest in a hospital is only part of the problem; it is necessary to study them after exercise, after return to ordinary mode of life. For years, I have taught patients how to examine their own urine. While it may be harmful to give fats in general in diabetes, butter fat is not harmful. Diabetics may take butter fat or bacon fat and may do so for years. Whatever may be said, it is impossible ever really to control diabetic patients; they will do as they please as soon as they get beyond the observation of the doctor."

more, personal letters recently received show that Friedrich Müller has no knowledge of the proposed treatment, and considers it theoretically inadvisable because of the supposed danger of acidosis.⁴⁷ Such an attitude on the part of one so widely informed concerning diabetes and so familiar with the Naunyn method, affords some evidence of the newness of the proposed treatment and the principles underlying it.

(2) Though Woodyatt states (1915) that an initial fast has been used for eight years, and Billings (1916) that it has been used for nine years, the above quoted therapeutic program of Woodyatt (1) makes no mention of the use of such a method in 1909; on the contrary, it is there advised, in harmony with Naunyn, that in cases with very dangerous acidosis one should "refrain from an attempt to improve tolerance." No description of the new method has since been published by either of these authors.

(3) The paper of Raulston and Woodyatt makes incidental reference to fasting and semistarvation. It seems evident that the plan of fasting used and referred to by these authors resembled that of von Noorden, the only difference being that the periods were sometimes longer; the effect is a temporary cessation of glycosuria

⁴⁷ One letter was addressed to Professor Graham Lusk, and another to one of the present authors. Liberty is taken to quote from the latter, under date of August 1, 1915.

"Die Frage einer kalorisch armen Ernährung bei Diabetes ist vor einigen Jahren in der deutschen Literatur durch Schlesinger erörtert worden, und er hat gezeigt, dass Diabetiker häufig bei einer an Kalorien auffallend armen Nahrung sich erhalten. Ein Nutzen für die Kranken wird aus dieser Arbeit nicht erkenntlich. Dann hat Weintraud vor Jahren in seinen aus der Naunynschen Klinik kommenden in der Bibliotheca medica erschienenen Arbeit auf die Bedeutung einer zeitweiligen Unterernährung hingewiesen, und Sie finden diese Gesichtspunkte in dem Buch von Naunyn über Diabetes ausführlich dargelegt. Wir verwenden in Deutschland zeitweilige Unterernährung, sogenannte Hungertage, ganz gewöhnlich zur Reduktion des Zuckers, und scheuen uns nicht das Körpergewicht dadurch zu reduzieren. Freilich gelingt es nur selten durch solche Hungertage die Acidosis zu vermindern, da ja der Hunger an sich auch bei gesunden Menschen ausgesprochene Acidosis zu erzeugen pflegt. Jeder Hungerzustand führt zu Verbrennung von Körperfett und erzeugt daher bei Mangel an Glykogen eine Acidosis. Bei Diabetes, wo der Glykogenvorrat ohnedies reduziert ist, und wo die Zuckerverbrennung häufig schwer geschädigt ist, tritt die Hungeracidosis gewöhnlich noch stärker hervor, und erschwert die Behandlung durch Unterernährung. Eine generelle Verordnung der Unterernährung bei Diabetes dürfte schon aus dem Grunde nicht ganz ohne Bedenken sein, weil die Diabetiker unter einander so ungeheure Verschiedenheiten zeigen, dass man sich hüten muss alle Fälle nach derselben Regel zu behandeln. Das letzte Wort in dieser Frage hat jedenfalls nur die Erfahrung, nicht aber die Theorie."

and diminution of ketonuria at the price of a certain amount of weight and nutrition, but the diet after the fast permits a quick return of the symptoms. It is expressly stated that in the semistarvation periods the Falta-Lusk quotient⁴⁸ was still about 50, which means serious glycosuria; and it is obvious that marked ketonuria was constantly present. Billings' opinion concerning fat, and the high fat diet used by Raulston and Woodyatt, suffice to explain such a result, for without fat restriction these patients cannot be kept free from such symptoms.

Misunderstanding of the incomplete description of the method in the brief preliminary communications was evidently responsible for the early criticisms of this character. Aside from the fundamentally new principle of total caloric regulation, it has been necessary to develop many practical details. The discussion of the resulting system has in general remained free from questions of priority.

Joslin has had the largest experience in the treatment of severe diabetes in this country, and has published the latest as well as the most advanced and authoritative text-book. No other American clinician has followed the scientific study of diabetes so long and intensely. His careful records cover approximately 1000 diabetic patients treated during the past eighteen years, and are particularly valuable because the great majority of the cases have been accurately followed up to death or to the present time. His definition is one which when generally adopted will tend to lower the death rate from diabetes and its complications. "My rule in the treatment of diabetes is to consider any patient to have diabetes mellitus and treat him as such, until the contrary is proven, who has sugar in the urine demonstrable by any of the common tests. This method of procedure is safer for the patient than to make use of the term glycosuria, which begets indifference." He has laid emphasis upon the necessity of keeping patients supplied with sufficient quantities of fluid and salts. He has been closely in touch with the development of the fasting treatment from the outset. He was informed in advance concerning the first clinical results, and has treated a greater number of severe cases of diabetes by this method than any other individual. The rapid general adoption of the method has been largely due to his example and influence, and in his various publications he has formulated a detailed program which many practitioners have followed. The reversal of conditions is shown by the fact that whereas fat was formerly the only food not restricted,

⁴⁸ Cf. Lusk (2).

Joslin now begins treatment by withdrawing only fat. His statistics support the belief that the life of diabetic patients is lengthened by the new method, and in his judgment they enjoy also better strength and comfort. References to and comparison with Joslin's results afford valuable information on the questions discussed in the ensuing chapters, and certain topics can be here omitted altogether because of the manner in which he has handled them on the basis of a wider experience.

One of the present writers⁴⁹ previously published work which seemed to promise the possibility of investigating diabetic therapy by animal experiments. The conception underlying the subsequent research at this Institute had a threefold origin. One lay in considerations from the literature as above mentioned, and also the reports of cessation of diabetes in various forms of cachexia (*loc. cit.*, p. 800 ff.). The second was found in certain of the preceding observations; *viz.*, that in dogs with severe diabetes not too far advanced, glycosuria ceased and the diabetes seemed more or less improved on fasting alone (*loc. cit.*, p. 480, Dog 64), or together with ligation of the pancreatic duct (Chapter XXII). The latter experiments were repeated and the rôle of impaired food absorption and undernutrition demonstrated by Homans. The third suggestion was furnished by Joslin,⁵⁰ who in a conversation called attention to his observations that though infections are generally so serious in diabetes, tuberculosis with rapid emaciation had seemed sometimes, notably in one very carefully studied case, to be accompanied by diminution of both glycosuria and acidosis.

On these various grounds, animal experiments were begun with a view to the possibility that diabetes is a disorder of the total metabolism and not of carbohydrate utilization alone, that the entire diet and maintenance of the entire body mass constitute a load upon the internal function of the pancreas, and that accordingly in the treatment of diabetes increase of diet and of body weight increases the strain upon this function, and reduction of the total diet and weight relieves this strain more effectively and permanently than restriction of carbohydrate alone. A series of animal experiments seemed to support this

⁴⁹ Allen (1).

⁵⁰ Cf. Benedict and Joslin, p. 55, Case R; also Joslin, Treatment of Diabetes Mellitus, 2nd edition, 1917, p. 409.

conception, which was then applied to the treatment of diabetic patients. Some of the results have been outlined in preliminary communications, which, however, have not been sufficient to convey an accurate knowledge of the details, and results have varied somewhat with the different applications of the method in different hands.

Among authors who have reported favorable experiences are: in America, Barker, Bookman, Christian, Friedenwald and Limbaugh, Greeley, Halsey, Hamburger, Heffron, Heyn and Hawley, Hill and Eckman, Hill and Sherrick, Jeans, Jones, Lemann, Levy, Lovewell, Marshall, Martin and Mason, McNabb, Moses, Paley, Potter, Robbins, Stengel and collaborators, Strouse, and Williams; in England, Cammidge, Fenwick, Leyton, Spriggs, and speakers discussing their papers; in Ireland, Nesbitt; in India, Waters. Its adoption by specialists and institutions, and by a still greater number of general practitioners, has furnished gratifying evidence not only of its theoretical soundness but also of its feasibility for successful practical application under the many varied conditions of medical work and environment. Geyelin and DuBois, and Jonas and Pepper, have demonstrated the possibility of beneficial results in the most intense uncomplicated cases ever described in the literature of diabetes.

Aside from any benefits inherent in the treatment itself, it has apparently served to stimulate interest in diabetes among members of the medical profession, and to promote the understanding and employment of rational dietetic management of this disorder, than which none has been more poorly understood or treated. Such knowledge and confidence concerning the rational therapy will diminish the use of the worthless or harmful remedies which appeal to ignorance or despair. The history of the development of the scientific treatment, and of some among the many contributors to it, may fittingly be closed with a quotation from Naunyn (5), p. 452). "The interest in novelty may be granted also to physicians, and the lack of prejudice with which we accept for trial all things, even the strangest and from the worst source, may—so far as one may believe in it—be praised; but every physician must beware of undertaking such special treatments or of recommending them, without ascertaining their relation to what science has established and teaches concerning the therapy of our disease. If this is not possible for him, then the employment of them

is not permissible. The therapy of diabetes has been well founded by painstaking labor highly fruitful in all directions; we may be proud of that which has been achieved and attained here. The physician who here frivolously abandons the scientific basis must, if he wishes to be deemed honorable, submit to the accusation of ignorance."

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CHAPTER II.

GENERAL PLAN OF TREATMENT.

This chapter, like the later ones, aims only to present the methods and experience of the present investigation. A multitude of questions and details concerning the treatment of diabetes must necessarily be left to general text-books on the subject. Discussion of the observations and suggestions of others who have used this treatment must also for the most part be omitted in the interests of brevity. For details of the laboratory methods employed, reference may be made to the original papers or to the excellent description in Joslin's text-book.

As emphasized from the outset, every case of diabetes must be managed according to its own requirements, and the best results are obtainable only when the treatment is intelligently individualized. At the same time, a basic plan is essential, inasmuch as one general principle underlies the treatment of all cases, and organization and routine conduce to both ease and efficiency. The system developed in this hospital may be described under the following headings:

- I. General measures.
- II. Treatment up to cessation of glycosuria in simple cases.
- III. Complications and emergencies (acidosis, infections).
- IV. Treatment following cessation of glycosuria.
- V. Ideals of diet and laboratory control.
- VI Practical management of diets.

I. General Measures.

A. THE ROUTINE CARE OF PATIENTS.

1. *Hospital Observation.*—All the cases treated have been under direct hospital observation. Between February 24, 1914, and July 1, 1917, altogether 96 patients were received, for a total of 165 admissions, an average of 1.72 admissions to each patient. The greatest number of admissions for a single patient was five. The total number of days of diabetic treatment was 11,308, giving an average of nearly 69 days to each admission. The longest single admission was 304 days, the shortest a few hours (acute death). Hospital observation has seemed advisable for the following reasons: (a) to obviate possible danger from acidosis during the active treatment of the disease by the fasting method; (b) to govern with the greatest possible accuracy the individual diet, while the preliminary tests of tolerance are being made, a ration built up, and its suitability demonstrated; (c) for the instruction of the patient, in order that he may carry out his diet and tests properly after leaving the hospital.

2. *Confinement to Bed.*—Unless made advisable by some complication or by a dangerous degree of acidosis, the patients have not been confined to bed. Even during the most trying period of treatment, namely the initial fast, it has not been uncommon for patients to lessen the tedium of treatment by going to theatres, concerts, etc.

3. *Clothing.*—As many patients show a decided susceptibility to cold weather, they have been advised to dress warmly, but without specific instructions. The use of exercise, as discussed in Chapter V, has obviated this condition to some extent, especially for that great majority of diabetic cases which rank as relatively mild. But the extremely low diets required for the very severe cases provide so little combustible material that body heat must be conserved as carefully as possible.

4. *Baths.*—It has not been attempted to gain effect through hydrotherapy. Bath temperature has been left to individual inclination. Patients with severe diabetes have naturally chosen warm water.

5. *Catharsis*.—Chronic and obstinate constipation has been a rule with few exceptions in the past history of these as of other severely diabetic patients. It was regulated by cathartics before bran was incorporated into the dietary of the hospital. This and the bulky vegetables have almost banished constipation. When something more active has been needed, the usual cathartics (castor oil, salts, cascara sagrada) have been employed.

6. *Medication*.—The principle has been followed of giving drugs to diabetic patients only as they would be used for other persons. No medicines have been employed with a view to influencing the diabetes, and no effect upon the diabetes has been observed from any of those employed for incidental purposes. The recommendations of various drugs in the past have probably been based upon inadequate control and study of the cases. Special mention may be made of the dangerous possibilities of anesthetics, especially chloroform. It is well known that drugs of the chloroform class most easily injure the liver when it is poor in glycogen. The visceral disturbances set up by general anesthesia readily explain the production of either glycosuria or acidosis, as so frequently described. The dangers are greatest where the treatment is poorest, and the majority of diabetics under thorough treatment are able to undergo suitable anesthesia without glycosuria and without dangerous acidosis.

7. *Complications*.—The experience with these has not been large. It is discussed in Chapter VII and in the individual case histories. The treatment of the acute forms is described under Section III of the present chapter. Metabolic complications in general do not interfere with the treatment of the diabetes; the present diabetic diet does not conflict, for example, with the usual treatment of nephritis. In regard to infectious complications, it may be said that the ideal of treatment is to make the patient as nearly like a normal person as possible by means of diet, and then to use as nearly as possible the measures considered best for normal persons. The recently debated question of the relation of infections, sometimes focal and minor in degree, to the etiology of diabetes is discussed in Chapter VIII. Certainly bad tonsils, teeth, and other foci are sources of injury for diabetic patients, which in acute attacks often give rise to glycosuria and acidosis, and which may interfere seriously with the success of

dietetic treatment. It has been the policy with this series of cases to have teeth or tonsils removed or other operations performed on the same basis as advised for normal persons by conservative specialists. Experience has indicated that such measures are beneficial from the standpoint of the general health and also of the diabetes, in obviating chronic and acute disturbances and the downward progress associated with them. No patient has died or suffered harm from such operations performed while on the dietetic treatment, and it appears that there is less danger from performing needed surgery than from omitting it. On the other hand, if toxic absorption causes diabetes, evidently the damage has mostly been done before the case has come under treatment, for in no instance has the removal of a focus of infection been followed by cure of the diabetes or by improvement beyond that seen in other patients.

B. WARD REGULATIONS AND CLINICAL REMARKS.

1. Respiration, pulse, and temperature have been recorded at 4 hour intervals when fever was present or when acidosis or other crisis threatened. Otherwise they have been taken every 12 hours. Some of the information which may be gleaned from these signs in diabetic patients follows.

Respiration.—Increased breathing is one of the classical indications of acidosis, the increase generally applying to both volume and frequency. Ordinarily it is a fairly constant and reliable index of danger, unless obscured by the use of alkali; but in the type of acidosis produced by fasting, it may, like the drowsiness and other symptoms, be far less prominent than in typical diabetic coma.

Pulse.—It may some day be possible to analyze the records of these cases with respect to the pulse rate. F. G. Benedict has noticed a relation between pulse and metabolism, and he and Joslin reported acceleration of the pulse in proportion to increased metabolism in severe cases of diabetes with active symptoms present. Patients in the present series entering the hospital with intense diabetes and threatening acidosis have regularly shown rapid pulse, which has become slower under treatment. A few examples appear in tables in certain of the case histories. Marked bradycardia has been observed

in some of the patients subjected to extreme undernutrition and the corresponding reduction of metabolism, but this has not been constant. The conditions are evidently not simple. On the one hand, the tachycardia out of proportion to any possible exaggeration of metabolism in impending coma is clearly an effect of intoxication upon the circulation. On the other hand, Dr. Alfred Cohn has observed in radiograms of some of these emaciated patients a diminution of the cardiac shadow even out of proportion to the thinning of the chest. This wasting of the heart muscle, like other states of general or circulatory weakness, might of itself alter the rate, especially in the direction of tachycardia. With the uncertainty concerning the respective influence of metabolic and other factors, a uniform interpretation may be difficult.

Temperature.—It being understood that the temperature of diabetic patients typically is normal, notice should be taken of variations in two directions. Elevation of temperature often accompanies severe acidosis, as illustrated in a few of the case records in this series. Otherwise, fever of any grade generally points to infection, and ceases with the finding and removal of the cause. Subnormal temperature is common in proportion to malnutrition, whether the latter is due to failure of assimilation of food with active diabetes, or to therapeutic restriction of diet. In the most severe cases of this series under treatment, the rectal temperature has commonly been below 98° and above 96°F. An important practical point is to watch the temperature when children must be subjected to extreme undernutrition. Even though the weakness is not visibly graver than before, a fall of temperature to the neighborhood of 96–95°F. is a signal of danger, which generally comes in time to permit warding off death by giving food. If acidosis or stubborn glycosuria makes a full diet inadvisable, even protein alone may support strength to the point where fasting can be continued. More careful attention to this point might possibly have prevented the fatal collapse which occurred in several children of this series. The low temperatures in severely diabetic patients are readily explained by the failure to receive or to assimilate (according to the treatment) enough combustible material. The same circumstance may wholly or partly explain another important clinical phenomenon, namely the absence or diminished grade

of the febrile reaction to infection in some cases. Joslin called attention to the possibility of an almost complete lack of symptoms with tuberculosis, even in an advanced stage. Something similar may be witnessed occasionally with other infections. Either the weakened individual is deficient in reactive power, or possibly the resultant of a subnormal temperature and a febrile tendency may be something like a normal temperature. This possible fallacy regarding fever should be borne in mind, and if a patient under rigid dietary control begins to do badly without apparent cause, careful search should be made for the infection which is often responsible.

2. *Blood Pressure.*—Aside from extraneous causes of hypertension, the blood pressure of diabetic patients is generally normal or below normal. Not only weakness, but also the intoxication of acidosis, is responsible for the depression. Several patients received in extreme stages have had a systolic blood pressure below 80, and in certain others the circulation was so feeble that it was not possible to determine the pressure accurately. In such cases the question always arises whether the patient can endure the week or more of absolute fasting required to control his diabetes. In actual fact, every adult has passed successfully through such fasting, not only without collapse, but generally with more or less gain in strength, as indicated for one thing by a rise in blood pressure. It thus appeared that intoxication was the most dangerous factor in the depression, and relief from it even at the price of fasting was necessary to save life. Therefore a dangerously low blood pressure is not necessarily any contraindication to fasting. On the other hand, it is possible that a fall in blood pressure during fasting or extreme undernutrition may be a signal of danger, but the clinical observations have not been sufficient to show whether this is a reliable warning or whether it comes in time to permit of averting the danger.

3. *Body Weight.*—All patients have been weighed naked each morning after voiding urine and before breakfast. The weight has been recorded in kilograms. The weight is very valuable among the criteria of treatment, though it is well known to be only a crude measure of the true body mass. Patients with intense active diabetes sometimes seem to be dried out by diuresis; they may hold or gain weight by water retention during fasting and for days or weeks on inadequate

diet thereafter. Fall in weight is sometimes sudden, to the extent of a kilogram or two on a fast-day, without evident significance. Fat diet following carbohydrate diet gives rise to such a water loss. The commonest cause of precipitous fall in weight for a series of days is acidosis. This melting away of weight and strength is seen in its most alarming degree in the occasional cases combining intense acidosis, maximal D:N ratio, exaggerated nitrogen loss, and, with these, rapid water loss. The opposite condition of sudden gain in weight represents water retention, sometimes associated with relief from glycosuria or acidosis, or with carbohydrate feeding, but frequently from obscure cause. Even without nephritis, it is commonly connected with salt retention and removed by salt-free diet. It may differ in degree at different times and especially in different patients, from invisible storage to extensive edema. Edema, sometimes huge, has been well known in connection with the large salt intake in "oat-meal cures," and especially with high dosage of sodium bicarbonate. In Joslin's experience, water loss is one of the most dangerous, and water retention or edema one of the most favorable conditions when combating a dangerous acidosis. On the other hand, the more severe cases have the greatest tendency to edema. This edema may therefore be classed among the indications of severity, though not all severe cases show the tendency equally. Apart from any mere changes in the function of the kidney for salt, it is likely that there is some unknown metabolic cause affecting the general tissues, either belonging in some measure to diabetes itself, or perhaps largely or wholly a phenomenon of undernutrition. It may possibly belong in a series of dropsical conditions due to malnutrition, a related member being the "hunger swelling"¹ of the wretchedly poor classes in Poland on an almost exclusive potato diet in the present war, another representative being the "epidemic dropsy"² of famine times in India, another being the edema of cachectic children, while at the farther extreme is beri-beri.

¹ Budzynski, B., and Chelkowski, K., abstracted in *J. Trop. Med.*, 1916, xix, 141-42.

² Megaw, J. W. D., *Indian Med. Gaz.*, 1910, xlv, 121; *J. Am. Med. Assn.*, 1911, lvii. 826.

4. *Measurement of Fluids.*—It is well known and has lately been emphasized by DuBois that an accurate water balance is one of the hardest of all things to determine. In our cases the fluid intake and output have been measured daily, and occasionally gross retention or loss of water has been thus demonstrated. The information afforded is necessarily vague and inaccurate. No allowance was made for the water content of foods, and especially the large quantities of vegetables generally given made this unknown factor a considerable one. Most of the apparent discrepancies of intake and output shown in the graphic charts are thus explained.

(a) *Intake.*—Thirst is not of abnormal degree in ordinary diabetic patients under proper treatment, one of the advantages of which is the relief from the discomfort of polydipsia and the inconvenience of polyuria and nycturia. Severely diabetic patients on very low diets generally drink rather freely, merely for the sake of something to fill the stomach. There has been no need to restrict fluids, except temporarily in a single patient (No. 1) who had formed the habit of excessive drinking, and in a few others during periods of marked edema. There is also no need to urge drinking of mineral waters or anything else under the conditions of proper diet, there being no poisons to wash out of the system. This may be an important advantage in cases with a complicating nephritis, with limited ability to excrete fluid. The one emergency which demands the forcing of fluids to capacity is dangerous acidosis, as mentioned later in this chapter.

(b) *Output.*—If an occasional patient drinks so little that the urine is unduly concentrated, a troublesome turbidity may cloud the sugar reactions; and instead of using chemical reagents for clearing, the best plan all around may be to urge the patient to drink a normal quantity of water. Usually in the severe cases the urine is very pale and clear, both because of the excessive drinking stimulated by hunger and because of the small total content of solids. It thus resembles in appearance the traditional diabetic urine, but a sharp difference is found in the very low specific gravity. Delicate sugar reactions are easily seen. The total 24 hour urine is saved in four separate portions each day, the divisions coming at mealtimes. During all the earlier and greater part of the investigation, days were counted from 7 a.m. of

one day to the same hour the next day. More recently, for general hospital convenience, a change has been made to the less commendable method of counting from midnight to midnight. Accordingly at present the order of periods is as follows:

- Period I. Midnight to 7 a.m.
- Period II. 7 a.m. to 11:30 a.m.
- Period III. 11:30 a.m. to 5:30 p.m.
- Period IV. 5:30 p.m. to midnight.

Two considerations favor this latter plan, namely that all urine is recorded under the date on which it was voided instead of being distributed over two dates, and second that the separation of days is made at a time when there is little work in the hospital instead of at the busy hour of 7 a.m. The arguments against this plan and in favor of the former plan are more weighty, first that patients are subjected to the inconvenience of being wakened at midnight to void urine, and second that the urine of a day does not correspond correctly to the diet of the day, inasmuch as the break between days is made at a time when the digestion of the last meal is not finished. The segregation in four periods has a decided value. Patients are not free from glycosuria unless the test is absolutely negative in every period. Even when the reaction seems negative in the mixed 24 hour urine, tests of the separate specimens may show not only the presence of faint traces but also after which meal they appeared. Also a transgression of diet is sometimes revealed by a marked reaction occurring suddenly in some period and clearing up thereafter, whereas a slight reaction in the mixed 24 hour urine might be of doubtful interpretation.

5. *Meals.*—Food has generally been served in three meals, with sometimes an additional lunch at bedtime. In the past, minor peculiarities in the relation between meals and glycosuria have been described, generally glycosuria after carbohydrate ingestion and clearing up during the night, more rarely glycosuria only at night, absent during the day perhaps because of exercise. Also, it seems a promising plan to give carbohydrate distributed in numerous small fractions at intervals, or in slowly digestible form, so as to avoid flooding

the system suddenly; and from such work as that of Thomas,³ it might appear that the best assimilation of protein would be obtainable by the same scheme. Undoubtedly it is possible to flood the system, especially with a quickly absorbable carbohydrate such as sugar, when the same quantity in divided doses would be assimilated without glycosuria. But under the ordinary conditions of diabetic treatment, the essential cause back of either regular or irregular glycosuria is a diet in excess of the tolerance or a persistently high blood sugar. As for distribution of foods between meals, a mild case of diabetes on a proper diet should be independent of such variations within limits of reason. With severe cases, the difficulty lies in the persistence of the hyperglycemia set up by either carbohydrate or protein, so that before the effect of one ingestion has subsided the next is superimposed upon it. In general, the total diet is the important thing, and little is to be hoped from unusual fractionation. A ration so close to the verge of tolerance as to require such aid will not be permanently tolerated. On the other hand, when the blood sugar is kept normal by a total diet truly within the assimilative power, glycosuria or other trouble does not result from any arrangement of meals that is likely to be made.

6. *Regulation of Habits.*—Precision regarding diet has been the chief essential. In other matters, it seems advisable, in brief, that patients should do whatever is necessary to maintain the best possible general health, while restraining their activities within the limits set by their diet and tolerance. With a more hopeful general prognosis, it becomes highly important to guard patients against alcohol and drug habits; and especially as opium and other drugs are worthless or harmful, and alcohol as a means of adding calories is also inadvisable, it is important that their widespread use in diabetic treatment be stopped. With other indulgences, such as tobacco, tea, and coffee, there are two opposite considerations. On the one hand, these articles in excess probably injure all persons, and even in moderation apparently injure some persons. On the other hand, the diabetic is denied so many enjoyments in diet that it is a pity to deprive him of any pleasures unnecessarily. Accordingly, the patients have been enjoined

³ Thomas, K., *Arch. Physiol.*, 1910, 249-285.

to use such moderation in these respects as is advisable for normal persons. Smoking within careful limits has seemed very enjoyable to men long addicted to it. All habitual users of coffee have derived the utmost comfort from it, especially during fasting. From one to three cups a day has been the allowance, and decaffeinated coffee has been used if there was any suspicion of harm. In all other matters, the usual life of the patient should be altered just as little and just as much as demanded by the particular case. It will be seen that frequently in this series men have continued business, children have attended school, and everything possible has been done to keep patients contented and useful. Especially those with milder diabetes are able to pursue practically a normal existence with care only in diet, and this fact is one of the most hopeful elements in the prognosis and one of the greatest encouragements to fidelity in diet. Either mental or physical overstrain is injurious to such a degree as to be out of the question for the severest cases and inadvisable even for the milder ones. Healthful rest, short of ennui, is important. Exercise is discussed in Chapter V. While reduction of weight and diet to a certain point is known to be compatible with physical and mental efficiency, with more extreme diminution these are progressively impaired, until in the severest cases emaciation and invalidism are chronic. Even in these worst cases, much depends on the individual disposition, and light employment or amusement aids in keeping the mind off the subject of food. If it comes to a choice, neurasthenia is preferable to overfeeding. Finally, one of the most important points in the hygiene of diabetics is the avoidance of infections, either great or small. This need not contraindicate outdoor exercise in cold weather, which may be one means of building up resistance for patients who can stand it. For some, however, it means avoiding crowds or any places where colds or influenza may be caught. For others, it means the removal of foci of chronic or recurrent infection, even at the risk involved in surgery. The best possible care of the teeth, skin, and body in general is advisable at all times, though the extreme susceptibility of diabetics to troubles from these sources is greatly diminished under proper diet.

II. Treatment up to Cessation of Glycosuria in Simple Cases.

Any fixedly prescribed routine is opposed by the necessity of individualizing treatment to suit the special needs of every case, and by the desirability of free play for the physician's individuality and adjustment to environment. The basic principle of undernutrition being grasped, the application can be made in various ways. This period is occupied by the observation diet (if used) and the initial fast.

A. THE OBSERVATION DIET.

All sorts of possibilities are of course open in the choice of an observation diet. One conservative plan is to leave the patient for a short time on as nearly as possible the same diet he has been taking, to guard against the danger of any sudden change, especially in the form of carbohydrate reduction. In order to establish data for comparing cases with one another and also with cases in the literature treated by older methods, the majority of patients in this series have been placed for a few days (2 to 5) on a diet somewhat as follows:

Protein per 24 hrs.	Carbohydrate per 24 hrs.	Fat per 24 hrs.
1.5 gm. per kilo.	10 to 25 gm.	Sufficient to bring total calories to 35 per kilo body weight.

This is essentially the traditional "carbohydrate-free diet," for the low carbohydrate allowance is given only in the form of green vegetables, such as have usually been included in diets of this description in the past. With close laboratory and clinical observation, no hesitation has been felt in placing patients abruptly on this diet; and even though this was done in some very severe cases, such as No. 8, the ability to control acidosis when necessary by fasting prevented any mishap. This plan was necessary for the accurate study of the earlier cases. Also, it frequently shortened the requisite period of fasting,

when the previous diet had been grossly improper. In general, it is not therapeutically advisable, and was seldom used when the patient's condition at entrance seemed dangerous. More recently, this observation period has been omitted, treatment has been begun immediately, and the severity of the diabetes has been judged by the subsequent progress and food tolerance.

B. THE INITIAL FAST.

If diabetes is deficiency of the function of food assimilation, logically the most effective method of relieving strain upon this function should consist in withholding food. The benefit of such relief should apply not only to glycosuria but also to acidosis, irrespective of whether the latter is wholly secondary to glycosuria or is partly a specific diabetic phenomenon; and the slight ketonuria developed by normal persons on fasting should not serve to confuse this expectation.

With regard to the initial tests on dogs, it may be mentioned that irregularities in the glycosuria following total pancreatectomy are well known, and in particular the urine may become free from sugar just before death from starvation or weakness; but the fatal diabetic cachexia is always present and freedom from glycosuria never avails to save the lives of such animals. Also, partially depancreatized dogs, of the type best suited for therapeutic experiments, in the severest stage continue to show glycosuria through the most prolonged fasting, up to death or the hopeless exhaustion just preceding death. It was a serious question whether the severest clinical cases are in a similarly hopeless state, or whether they still correspond to the type of dogs which can be freed from glycosuria by fasting and then kept symptom-free at a more or less reduced weight by suitable regulation of the total diet. Some encouragement was found in the results of the shorter therapeutic fasts employed by former writers, but there was nowhere in the literature any description of such a procedure as contemplated, or any information as to what might happen if a patient with the worst type of diabetes were suddenly subjected to absolute fasting until sugar-free. Accordingly, as noted in the history of patient No. 1, the first attempt was made with considerable caution. It so happened that this patient, although of the type in which glyco-

suria and acidosis had formerly been viewed as hopeless, and though chosen as one in whom at least no great harm could be done, responded with rather exceptional ease to this treatment, and both glycosuria and symptoms of impending coma quickly disappeared. If this first experience had concerned a case, such as frequently encountered later in the series, requiring from a week to 10 days for sugar-freedom, it is a question whether courage would have held out; and if by any chance this first case had been one of the rare ones which develop fatal acidosis on fasting, the proposed treatment might have ended there. The first fact demonstrated was that even the severest cases of human diabetes almost invariably become free from glycosuria and as a rule also improve markedly as respects acidosis upon fasting.

Regarding the practical carrying out of the initial fast in ordinary cases, the following details may be noted.

Water.—It is advantageous on general principles that the total daily intake of fluids be at least 1500 to 2000 cc., and patients have therefore been encouraged to drink tap water or any kind of mineral or table water rather freely. In hot weather, cracked ice has sometimes been relished. No limit is placed on the fluid intake if patients desire more than the above quantity.

Alcohol.—The use of alcohol was one of the early precautions adopted to support strength during fasting. According to some earlier literature, it not only produced no glycosuria but also might diminish acidosis. In a number of cases, 50 to 350 cc. whisky or brandy were given daily, in small divided doses every hour or two, the limit for any individual being always short of producing subjective or objective symptoms. A rather general misapprehension was created by the first papers published, as it was not clearly understood that the use of alcohol was not new but was adopted entirely from previous writers, that it was used for cases with extreme weakness or for other special purposes, and that it was never a primary or essential feature of the treatment. Experience has tended to discredit it even for the purposes for which it was first employed. It is a decided comfort during fasting to persons already habituated to its use. In other persons, especially women and children, it often excites discomfort or even nausea, and is therefore detrimental. It has an unmistakably bracing action in weak patients, but its real effect is probably more

harmful than beneficial. Soup and coffee are preferable in almost every case.

Soup.—In the great majority of cases, clear meat soup has been allowed in quantities up to 600 cc. daily during fasting. The trivial quantities of protein contained are harmless, but even such can be avoided if desired by substituting beef extract. Soup is very comforting, and the fluid and salts may be valuable.

Coffee.—One to three cups of coffee or Kaffee Hag daily are pleasing and supporting to most fasting patients. It is not advisable to cultivate the coffee habit in children or other persons not addicted to it.

Solids.—Three to six of the bran muffins described subsequently in this chapter have generally been allowed daily during fasting. They are of some use in diminishing the feeling of emptiness. Theoretically, small quantities of thrice cooked vegetables might be permissible in the milder cases, but have very seldom been used, because there is no use in trying to trick the appetite too far, and it is better for patients to learn to bear rigorous fast-days.

Purgation.—The habitual constipation of most diabetics renders a cathartic advisable at the outset. With the use of bran, there is generally more natural tendency to defecation. On a prolonged fast with only fluid intake, the patient may safely go for a week or more with no bowel movement. There is no specific virtue in purgation.

Edema.—As mentioned, water retention even to the point of visible edema is sometimes observed in fasting, especially in the more severe cases. It seems never to have been reported in normal persons on simple fasting, but only in connection with prolonged malnutrition and abnormal living. Diabetics vary in susceptibility, but the immediate cause of edema is usually the salt of the above ingesta, especially the soup. No harm has ever been observed from the fluid retention. The prevention or remedy consists in the restriction or exclusion of salt.

Comfort and Strength.—Fasting, sometimes up to a month or more in duration, has been a well known practice for purposes of metabolic studies and sometimes for public exhibitions, and the subjects have retained physical and mental powers through these long periods and have denied any real suffering. Fasting has also been one of the com-

monest religious customs of numerous peoples and sects. On the other hand, the omission of a single meal is often felt as a great privation, and a few days' abstinence from food is viewed as something serious and alarming, not only by people in general but even by numerous physicians. The most profoundly emaciated and cachectic diabetic patients undergo even a 10 day fast with ease and safety. The refusal of a patient to undergo fasting is generally as much the fault of his physician as of himself, provided he is of a type who will faithfully carry out any kind of careful dietetic treatment. The first fast generally dispels the dread, and furthermore is valuable for discipline.

As described in the histories, the fasting treatment has been applied to patients in all physical states, from those appearing in full health and strength to those seeming at the point of death from weakness and emaciation. The effect upon the immediate comfort has varied with individuals. Some patients have entered with nausea or vomiting which prevented eating; others rejoiced in quick relief from acidosis symptoms; others had been overfed till fasting was agreeable in itself. At the other extreme are the occasional patients who, whether in good or poor health and flesh, feel weak, uncomfortable, and depressed whenever they fast. In the intermediate position are the great majority of patients, who find fasting more or less inconvenient but no serious hardship, and who carry on their usual activities or amuse themselves in various ways during either long or short fasts. As stated elsewhere, some very weak patients have unmistakably gained strength on fasting. More or less decline in strength is the rule. Even in the most extreme cases, no adults have died from weakness either during or within any short time after fasting to sugar-freedom. Two small children (cases Nos. 45 and 71) entered with such a combination of extreme diabetes, acidosis, and weakness that the choice between coma and starvation could not be avoided; and it is conceivable that such a dilemma may be possible in very rare adult patients. The use of levulose as a restorative in sudden collapse of strength is illustrated in cases Nos. 4 and 45.

Laboratory Control.—Laboratory tests are qualitative and quantitative. So much information is derivable from the former that it is generally possible to carry through a fast successfully by their guid-

ance alone. The qualitative test for urinary sugar has been the keystone of the plan, since fasting is terminated on the day after it becomes negative. Acidosis can also be judged fairly safely by the increase or diminution of the ferric chloride test of the urine and of the Rothera test applied to the blood plasma (Wishart), and by the acid or alkaline reaction of the urine; by simply noting the dosage of alkali required to turn the urine alkaline, the latter test acquires a quantitative significance. Also, in default of accurate measurements of blood alkalinity, the test proposed by Yandell Henderson⁴ should not be overlooked; namely, that normal persons can hold the breath 30 or 40 seconds without specially deep preparatory inspiration, but that this period diminishes somewhat in proportion to the reduction of blood alkali.

Of quantitative tests, that for blood sugar is of minor practical importance during the fast. Generally the blood sugar falls; sometimes it rises at first even when glycosuria is diminishing and the general condition improving; and in the rare cases where fasting results badly, the persistence or increase of hyperglycemia may be one significant feature; but other tests are more important danger signals. Also, the quantity of sugar excreted in the urine is of little practical importance in the great majority of cases, though persistence or increase of glycosuria gives warning of the failure of fasting, and likewise of the danger of coma even independently of direct acidosis tests.

Quantitative nitrogen determinations are of significance for the rapidity of protein destruction and the D : N ratio, which is an important index of severity. Increase of the quantity of amino-acids in blood and urine also marks the severe cases.

Possibly some significant behavior of the blood fat may later be found, but at present such analyses have no established value as a guide for treatment at this stage. In dogs it seems probable that fasting acidosis is sometimes accompanied by increased lipemia, but in human patients fasting generally produces no increased turbidity of the plasma.

The essential danger that threatens during fasting is acidosis, therefore the tests for it are preminent. All analyses of the urine are un-

⁴ Henderson, Y., *J. Am. Med. Assn.*, 1914, lxiii, 318.

reliable. Very high excretion of acetone bodies is dangerous, but yet the progress may be favorable; while lower excretion may indicate either less acidosis or more dangerous retention. The urinary ammonia is governed not only by the degree of acidosis but also by other factors such as the total nitrogen output and the alkali dosage. The recently developed blood tests are the most convenient as well as the most trustworthy. The Van Slyke method⁵ of determining the CO₂-combining power of the blood plasma has been used in the present series of cases, because of its combination of ease and accuracy. Methods showing the carbon dioxide tension of the alveolar air⁶ are simple and almost equally reliable. Those requiring the patient's cooperation encounter difficulty in coma or similar states, and even the bag or mask methods are subject to possible errors from circulatory or other causes. The air analyses are specially useful to those desiring to avoid the taking of blood, but both physicians and patients should learn that blood ought to be taken for various analyses as a means of intelligent diabetic treatment. The hydrogen ion concentration of the blood, determined by either the gas-chain method, the oxyhemoglobin dissociation, or the more convenient procedure of Levy, Rowntree, and Marriott,⁷ has recently attracted attention clinically as well as experimentally, but is not so early or delicate an indicator of danger as the CO₂ capacity. Quantitative analyses for acetone bodies⁸ in the blood may sometimes be of practical service. For example, if high and increasing, they may give warning of impending coma, even if this is not revealed by any of the above mentioned tests. On the other hand, the danger in different diabetic cases by no means runs parallel to the ketonemia, neither has any infallible index yet been derived from the relative proportions of β -oxybutyric and acetoacetic acids.

In summary, therefore, all laboratory tests are open to more or less fallacy. The more tests performed, the more easily and accurately can the condition be judged and needful measures instituted. If it

⁵ Van Slyke, D. D., and Cullen, G. E., *J. Biol. Chem.*, 1917, xxx, 289.

⁶ Fridericia, L. S., *Berl. klin. Woch.*, 1914, li, 1268. Marriott, W. M., *J. Am. Med. Assn.*, 1916, lxvi, 1594.

⁷ Levy, Rowntree, and Marriott, *Arch. Int. Med.*, 1915, xvi, 389.

⁸ Van Slyke and Fitz, *J. Biol. Chem.*, 1917, xxxii, 495.

comes to a question of the absolute minimum of laboratory work on which fasting can justifiably be conducted, the methods of choice are the Benedict qualitative sugar test for the urine and the Van Slyke determination of the bicarbonate reserve of the blood plasma, together with the nitroprusside reaction in the plasma.

III. Emergencies and Complications.

A long list of greater or lesser troubles associated with diabetes might be enumerated here. As mentioned in Chapter VII, the present experience indicates that these traditional complications, which have been the cause of so much suffering and fatality in diabetes, are for the most part avoidable under efficient treatment; and when already present, it is believed that the best and quickest means of curing any of these or hindering their further advance lies in fasting followed by restriction of the total diet as described. A physiological condition which stands as a real complication in the management of diabetes is pregnancy. It was encountered in only one instance in this series, namely case No. 38, where it was associated with a hopeless complex of infections. Joslin's experience has proved that the formerly grave prognosis for both mother and child can now be much brighter; and unless deterred by eugenic considerations, the possibility exists for women with not too severe diabetes to go through pregnancy successfully. The essential requirement is the same thorough dietetic treatment as for other patients. By far the chief emergencies or complications, however, which are liable to be encountered in undertaking the fasting treatment, are acidosis and infection.

A. ACIDOSIS.

1. *Definition.*

If the normal resting metabolism upon which calorimetric studies are based be accepted as a standard, acidosis may be broadly defined as any departure from this normal tending to turn the reaction of the body to acid. It may thus include all possible states of increased production or deficient destruction of acid, administration of acid, retention of acid, or deficient supply or abnormal loss of bases. The most important clinical type of acidosis is a ketosis; namely, the occurrence of abnormal quantities of the so called acetone bodies—

whether due strictly to excessive formation or deficient utilization is uncertain. Therefore, in accordance with Naunyn's dictum, acidosis is present in diabetes whenever an abnormal increase of acetone substances is demonstrable in the urine or blood. Attempts to replace this metabolic or biological definition by purely chemical conceptions of alteration of reaction, derived from experiments *in vitro*, have thus far been scientifically fallacious, on grounds which need not be reviewed here, and clinically are open to the following objections: (a) these changes represent no independent phenomenon, but only some late stage of a process which should properly be regarded as a unit from beginning to end; (b) the striking abnormal production of acid in the protoplasm, perhaps up to 100 gm. of β -oxybutyric acid daily, is the essential disorder to be defined, and the mere neutralization of the products by alkali cannot properly be regarded as abolishing this biological acidosis; on the contrary, the necessity of ammonia formation or alkali dosage to maintain neutral relations should in itself be considered evidence of acidosis; (c) the therapeutic point of the whole matter is that attempts to treat by neutralization of products are often illusory and sometimes dangerous even as temporary measures, and lead always to failure in the end, while successful treatment can only consist in stopping the abnormal acid production which is the essential disturbance.

2. Fasting and Undernutrition Treatment in Various Types.

The ordinary acidosis of severe diabetes is no contraindication to beginning a fast, and, as already stated, typically diminishes progressively during the fast. The more severe the acidosis, and the more imminent the impending coma, the more urgently is fasting demanded, so that the patients of this series who have entered in the most dangerous condition have been placed immediately on strict fasting. The results have been favorable, as shown in Chapter VII.

In the milder cases of diabetes, including those previously free from acidosis, some degree of ketonuria, generally slight, sometimes rather heavy, may develop during fasting, without danger or any need for changing the fasting program. Exceptionally, however, in cases inherently either mild or severe, blind persistence in fasting may result

in dangerous or fatal acidosis, as happened in one case (No. 30) in the present series. This difficulty, though exceptional, is certain to be encountered if any considerable number of cases are treated; and the fact that it had not formerly been known is one evidence of the newness of the fasting method.

This atypical behavior may sometimes be expected in middle-aged or elderly patients, who have carried their diabetes for possibly 5 to 15 years with little or no apparent harm, whose glycosuria may be heavy or moderate, whose acidosis may be chronic but slight, and whose bodily state may be that of good nutrition or slight obesity. Such a case may appear very promising for quick and gratifying results. During the fast, glycosuria may persist or diminish; ketonuria is generally qualitatively heavy, but quantitatively may not be great, especially if alkali is not given. What is seen clinically is first a vague malaise, often with headache or pains elsewhere, dizziness, and increasing prostration. Nausea seems to be invariable, and the gravest stage is when vomiting is established. Though the condition is acidosis, the appearance is not that of typical coma. Dyspnea may not be prominent, and the consciousness may be clear up to the last hours or minutes of life. The end comes with uncontrollable vomiting and profound and rapidly progressive weakness.

Treatment in this final stage offers little hope. Glucose or levulose, orally, rectally, subcutaneously, or intravenously, should theoretically be most important, provided the diabetes is inherently mild enough to permit any effective utilization. A few patients elsewhere are said actually to have been saved by such means. If food can be taken at all, whatever protein-carbohydrate diet promises to be best retained is indicated. The use of sodium bicarbonate is customary; it is probably best given intravenously, possibly by rectum, to avoid nausea. If carbohydrate or protein as above described succeeds in arresting the underlying intoxication, it is possible that the cautious use of bicarbonate may guard against death from simple deficit of alkali and thus may be a temporary assistance in tiding over the crisis. The traditional large doses of alkali are dangerous. If the other measures fail to arrest the underlying toxic process, alkali in any dosage is useless, and the patient dies just as certainly whether the blood alkalinity is low or high.

The essential treatment lies in prevention, and with simple care these unnecessary accidents can be avoided. For this purpose, Joslin has introduced a precautionary program, which, briefly, consists first in omitting fat from the diet, then gradually diminishing protein and finally carbohydrate, down to complete fasting unless glycosuria ceases before. This is opposite to the orthodox treatment of a few years ago, which started with a gradual reduction of carbohydrate. The plan is theoretically sound, embodying the same general principle of under-nutrition which underlies all this treatment. Besides the usual loss of a little time, there is an imaginable disadvantage in very rare cases, which might be controllable by immediate fasting but within a few days might be advanced past hope; also it is a possible question whether a threatening acidosis may ever be aggravated by food of any sort, even protein and carbohydrate. The only concrete observation is in case No. 55 of this series, where it must be confessed that the diet which made trouble on November 5 did contain an appreciable quantity of fat. In favor of the gradual procedure are the following considerations: first, in Joslin's experience, which is larger than any other, dangers such as here suggested have not actually been met; second, the duration of the initial fast is shortened; and third, the occurrence of fasting acidosis has been entirely prevented. This modification has therefore been widely adopted and will doubtless continue in extensive use. Though Joslin's own cases are studied by complete laboratory methods, the modified treatment becomes more important in proportion as laboratory control is lacking.

As already stated, the method of immediate fasting has been employed in the whole of the present series. Since the early experience (case No. 30) calling attention to the occasional danger, it has been a simple matter by combined clinical and chemical observation to avoid further mishaps. The practical management of dangerous cases of acidosis may be discussed according to the three classes into which they fall.

(a) *Typical Coma*.—Patients in actual deep coma generally die. The considerable proportion of recoveries in this series shows that treatment is not entirely useless. With coma impending but not yet complete, death was the usual outcome under former methods, but under fasting treatment the usual outcome is recovery. It is be-

lieved that immediate fasting, with the adjuvants mentioned below, is the safest general rule for cases of threatened coma. Generally the improvement is quick, and may be evident within twenty-four hours or less. Sometimes the patient may appear more stuporous on the second day than on the first, and the blood alkalinity may be almost stationary or may even fall a little. In all the favorable cases seen, there has been unmistakable improvement by the third day. It is worth noting that cases of ordinary coma, coming on in the usual manner on any kind of diet, have never shown injury from fasting; *i.e.*, fasting acidosis has not developed where the threatened coma was due to feeding. The patients whom inexperienced physicians are likely to be afraid to fast are the ones who usually need fasting most and who usually show the most striking benefits.

(b) *Fasting Acidosis*.—As stated, occasional patients, in no immediate danger of coma on whatever diet they may be taking, react to fasting with an increase of acidosis, sometimes to dangerous degree. The reason for this peculiarity is unknown, and there is also no known way of foretelling which cases will exhibit it. Examination of the case records in this series will show that neither the mildness or severity or duration of the diabetes, nor the initial degree of acidosis, nor the intensity or persistence of glycosuria, nor the store of reserve fat represented by obesity or emaciation, nor the supply of circulating fat as represented by lipemia, necessarily stands as a determining factor. The same patient at different times may behave oppositely. Thus, several cases in this series displayed more or less tendency to fasting acidosis at first, while at subsequent periods they reacted to fasting with the usual decrease of acidosis. The essential treatment for fasting acidosis is food; and the only known rule of procedure up to the present is if a patient develops acidosis on feeding to fast him, and if he develops acidosis on fasting to feed him. The kind of food seems to be of subordinate importance. Thus the fasting acidosis symptoms of patient No. 35 ceased entirely on an orthodox protein-fat diet, which represents the surest means of producing acidosis in most patients. Nevertheless, it should not be considered that the choice of diet is immaterial. Fat is theoretically disadvantageous. Carbohydrate may be beneficial if the diabetes is not too severe, but should be closely limited to avoid too great hyperglycemia and gly-

cosuria. Protein is on general principles the most valuable food, and either alone or with such carbohydrate as may seem advisable, it makes up a low caloric diet which both relieves fasting acidosis and at the same time continues the benefit of undernutrition. After a few days of feeding, a second fast is generally well borne, and both glycosuria and acidosis are brought under control as usual. After thorough and successful treatment, all patients become able to undergo fasting without danger from acidosis.

(c) Indistinctly separated from the above two groups are the occasional examples of extraordinary intensity. Some cases of diabetes almost from the outset, and others after a longer or shorter course of ordinary symptoms, reach this degree characterized by maximal dextrose-nitrogen ratios, enormous protein breakdown, high amino-acid values in blood and urine, and extremely threatening acidosis. Unless further improvement in the treatment is devised, probably a majority of such patients will continue to die, as did several in the literature, and patient No. 39 in the present series. Some of them apparently represent a degree of diabetes which is uncontrollable by fasting, perhaps because fasting is not sufficiently potent to check the rush of metabolism. There are three favorable considerations in regard to this condition: first, though familiar in dogs, it is rare in human patients; second, it is sometimes controllable by skillful treatment; and third, a distinction exists between intensity and severity, for if it is possible to weather the immediate storm of symptoms, these extremely intense cases sometimes turn out later to be less severe than anticipated. Thus, the patient of Geyelin and DuBois gained a tolerance running into hundreds of grams of carbohydrate, and the patient of Jonas and Pepper seemingly recovered from his diabetes altogether. In Chapter VIII it is shown that the distinction rests upon the apparently functional nature of the chief disturbance underlying the intense symptoms, while anatomic destruction of the islands of Langerhans, which is the fundamental basis of true severity, has not necessarily advanced very far in these cases. As regards acidosis, it may be assumed as a general principle that if fasting does not control glycosuria the result will be coma. These cases differ from those of group (b), which somehow react unfavorably to fasting irrespective of the presence or absence of glycosuria. The fatal acidosis

from prolonged fasting in the present group seems to occur only because of the persistence of high glycosuria. Successful treatment has consisted in replacing fasting by an undernutrition diet of carbohydrate or protein. Carbohydrate may be helpful for diuresis, but with a maximal D:N ratio its value otherwise is questionable. Protein offers theoretically the greatest advantages, in that it furnishes carbohydrate and urea for diuresis and ammonia for neutralizing acids, and at the same time is the most important food for maintaining strength and protecting body nitrogen. Successful treatment with carbohydrate and protein is illustrated by the cases of Geyelin and DuBois and Jonas and Pepper above mentioned. Success with pure protein diet is illustrated by case No. 37 in this series. This boy had first entered the hospital with impending coma which had developed on a mixed diet and which cleared up smoothly on fasting. In a relapse 11 months later, he was readmitted with glycosuria which had resisted 8 days of fasting and acidosis which threatened early coma if fasting were continued. By a practically pure protein diet for 10 days, the acidosis and other symptoms were relieved, and then glycosuria was easily abolished by fasting. As mentioned, in some cases fasting, feeding, alkali, and all other measures are unavailing, and here death occurs from acidosis or exhaustion within a few days. Obviously, all cases of this group should be under the care of the most experienced specialist available.

3. *Adjuvant Measures and Remarks.*

(a) *Emptying Alimentary Canal.*—When it is known that food has been recently eaten, lavage of the stomach is advisable in impending coma, and if there is any doubt, it is a wise precautionary measure. Joslin makes it a routine for children with dangerous acidosis. It is also important to empty the intestine thoroughly by a combination of any vigorous purgative and high colonic irrigation. There may be some incidental benefit from absorption of saline solution if this is used for the colonic injections, or of alkali if the irrigation is performed with sodium bicarbonate solution. Case No. 25 illustrates the great difficulty of securing adequate intestinal evacuation in some instances, and also its importance.

(b) *Drugs*.—Except in accidental emergencies, it is doubtful if drugs ever rescue patients from acidosis. Such an emergency is shown in case No. 11. This patient was not actually saved; but if there is cardiac and renal failure along with acidosis, it is evidently possible that life may be preserved by medicines which restore circulation and excretion. When any patient is sinking into the stupor of ordinary coma or the weakness of fasting acidosis, there is always the inclination to stimulate heart, brain, and kidneys by such drugs as caffeine and digitalis, if only in the hope of supporting strength until other measures have time to take effect. The liberal use of coffee, as illustrated in a few cases in this series, may be of some slight service. But whether employed early or late, drugs are probably never able to change the result in uncomplicated cases. If a large dose of alkali is given intravenously, there is a possible question whether some circulatory stimulant might be of value for guarding against the sudden death which sometimes follows within a few hours.

(c) *Sugars*.—Glucose and levulose have received long and extensive trial as weapons against acidosis in the past. Their promise of usefulness is greatest in fasting acidosis, at the stage when all ordinary food is vomited. They may then be given, preferably in 5 per cent solution, rectally, subcutaneously, or intravenously. For the latter purpose, a slow continuous infusion by some such device as that of Woodyatt⁹ appears obviously best. For ordinary coma, sugar might have some value as a diuretic, and also for diminishing the formation of acetone bodies if it can be burned. But as a rule, the blood sugar is already undesirably high, and little if any sugar can be metabolized. It is well known that the attempted sugar treatment of coma has in general been such a failure that it has been abandoned by the best authorities. Von Noorden¹⁰ found absolute fasting more effective than levulose, milk, or oatmeal for coma. Anything that aggravates the diabetes and delays the clearing up of glycosuria may possibly act injuriously also upon the acidosis. For these reasons it is believed that as a rule sugar or carbohydrate should not be used for the treatment of ordinary cases of acidosis.

⁹ Woodyatt, *J. Biol. Chem.*, 1917, xxix, 355–365.

¹⁰ von Noorden, C., *Zuckerkrankheit*, 1912, 388.

(d) *Alcohol*.—So far as observable empirically, alcohol has shown no specific value in connection with acidosis. Some experiments to be published later agree with the finding of Higgins, Peabody, and Fitz¹¹ that it tends rather to increase acidosis. One objectionable feature is its frequent nauseating effect. For these reasons, the use of alcohol is considered inadvisable even for weak patients with serious acidosis.

(e) *Salts*.—The value of inorganic salts and the danger of extreme loss of salt have been emphasized especially by Joslin. Sodium chloride is valuable as a diuretic; also, its retention is associated with edema, and only one patient with edema in Joslin's experience has ever died in diabetic coma. Therefore sodium chloride may be administered by mouth in quantities up to 20 or 30 gm. daily unless prevented by nausea or other contraindication; physiological saline solution also is useful, by rectum, subcutaneously, or intravenously, for conveying salt as well as fluid. In case No. 1 and a few others, trial was made of giving also salts of potassium, calcium, and magnesium, with a view to physiological balance, but no apparent advantage has been found in this plan over the use of sodium salts alone. Soup is valuable partly for the salts it contains.

(f) *Fluids*.—As already mentioned, the conduct of fasting with ordinary moderate acidosis calls for only moderate quantities of liquids. On the other hand, the largest practicable fluid supply is one of the most essential matters in the treatment of threatened coma. Authorities from Rumpf to Joslin have recognized the danger of desiccation of the body, especially with the vomiting which occurs so frequently. The further use of fluids is to promote the freest possible diuresis. Joslin set the standard of 10 liters a day when possible. If the patient can drink and retain sufficient liquid, it need not be given in other ways. The patient should be persuaded to take water as much and as often as possible, either hot or cold, and free use should also be made of coffee, tea, soup, cracked ice, or whatever else will aid in introducing fluid and perhaps also in preventing nausea. If drinking is insufficient—for example, if an adult with impending coma cannot retain 5 liters per day—recourse may be had to

¹¹ Higgins, H. L., Peabody, F. W., and Fitz, R., *J. Med. Research*, 1916, xxxiv. 263-272.

corresponding quantities of 0.85 per cent sodium chloride solution by rectum, subcutaneously, or intravenously. From 500 to 1000 cc. salt solution at a dose intravenously is considered by Joslin often preferable to alkali, because less dangerous. Here again the Wood-yatt injection apparatus might be advantageous. The reasons for the importance of keeping up copious diuresis by fluids are the following. First, the possible concentration of acetone bodies in the urine is limited (the highest observed by Fitz was between 9 and 10 gm. per liter); for this reason the excretion can often be multiplied by almost as much as the quantity of urine is multiplied, and large quantities of dangerous material thus removed. A high excretion, e.g. 50 gm. or more of total acetone bodies daily, is never possible except with abundant diuresis. Second, β -oxybutyric and acetoacetic acids circulate in the blood only in the form of salts. They are partly eliminated as salts, but also to an important extent the kidney saves the base for the body and excretes the free acids. Through this saving of base by the acid-secreting power of the kidney, the administration of fluid is equivalent in some degree to the administration of alkali, without the special disadvantages or dangers of the latter.

(g) *Laboratory Guidance.*—Mention has already been made of the various routine tests for acidosis, and preference expressed for the Van Slyke plasma bicarbonate method. More reliance can be placed upon the blood alkalinity, determined by this or by one of the less direct methods, than upon any other single feature of the condition, and without this information it is often impossible in critical cases to judge progress or direct treatment intelligently. With any serious degree of acidosis, estimation of the bicarbonate reserve should be made once daily. In acute danger, such analyses are sometimes demanded at frequent intervals, perhaps once every 4 hours, to indicate whether the response to treatment is favorable or whether a change should be made. At this stage, the greatest service of this test is to give warning of an increase of acidosis on fasting, often before clinical symptoms make this evident, and in time to avert the danger by giving food. As an arbitrary ground plan for applying the results of this test, the scheme in Table I may be suggested.

Nevertheless, clinical judgment and experience are important in deciding whether unfavorable progress calls for a reversal of treatment

or for more rigorous adherence to the same plan. There is ample evidence in the present series of cases that neither this nor any other single test can be followed blindly as an infallible guide. Irregularities are sometimes marked, even in absence of extraneous modifying factors. Thus, patient No. 63 showed the lowest CO₂ capacity in the entire series (12.3 per cent), yet recovered promptly, whereas other patients died although their bicarbonate reserve was by no means so low. Patient No. 35 developed malaise, nausea, and drowsiness on fasting, and the observers were convinced that unless fed he would have died in the typical intoxication. The CO₂ capacity was within normal limits even without alkali dosage. Probably it would have fallen at a later stage; but the significant facts are that the clinical symptoms alone gave warning in time to permit effective treatment, that

TABLE I.

Degree of acidosis.	Plasma CO ₂ .	Further drop of CO ₂ permitted before interrupting fast.
	<i>vol. per cent</i>	
—	Above 53.	To 45 volume per cent.
Mild.	53-40	Drop of 10 to 5 volume per cent.
Moderately severe.	40-31	" " 3 " 2 " " "
Severe.	Below 31.	Fast interrupted in 6 to 12 hrs. unless CO ₂ rises with fasting and alkali.

the intoxication symptoms increased when sodium bicarbonate produced an actual rise in the CO₂ curve, and that feeding cleared up the symptoms even though the CO₂ capacity was slightly lower on certain subsequent days than at the time of the intoxication. Such discrepancies and irregularities, spontaneous in origin, are much less numerous than those resulting from alkali therapy. Thus in case No. 30, a typical example of acidosis with fatal result on fasting, the plasma bicarbonate was forced up within normal limits by alkali dosage while well marked intoxication was present, and the last reading, with severe and hopeless intoxication existing, was 45 per cent, which falls within the limits of "mild" acidosis according to the above table. Patient No. 45 had before admission been kept saturated with huge doses of sodium bicarbonate. He entered almost in coma, typical except for absence of hyperpnea, notwithstanding the CO₂ capacity of 73.5 volume

per cent in his plasma. In full coma on September 9, the CO_2 capacity was 84.9 volume per cent, *i.e.* abnormally high, and higher than on other occasions without coma. Patient No. 71 was received in coma with the usual low plasma bicarbonate of 22.1 per cent. On the subsequent days he remained intoxicated and delirious, even when the plasma bicarbonate was forced as high as 50.2 per cent, which is near the normal level for a boy of 9 years. Thereafter it was never below 38.8 per cent, and on the day of death in coma was 48.5 per cent. Patients not in this series have also been seen, who died in coma notwithstanding normal CO_2 capacity of the plasma. These facts cast no reflection upon the accuracy of the analytical method, but merely illustrate that dearth of alkali is not the sole nor essential feature of the condition. Fasting is sometimes beneficial even when the blood alkalinity falls somewhat; but in particular, a high alkalinity is no assurance of safety in the presence of obvious clinical intoxication or a high and increasing concentration of acetone bodies in the blood.

(*h*) *Alkali Therapy.*—This subject is partly discussed in connection with the results of the treatment of coma, in Chapter VII. The possible benefits consist in relieving a dangerous dearth of alkali, and in facilitating the elimination of acetone bodies. The possible harm lies chiefly in the nausea which may result from oral administration and the sudden death which may follow within a few hours after excessive intravenous doses. It is conceivable that alkali may affect the toxic state for either good or ill in ways not now understood. Both beneficial and injurious effects are illustrated in the present series of cases.

Close observation also shows that, whether the differences are significant or accidental, the condition called diabetic coma does not present a uniform picture. Aside from the rather atypical fasting form, there are differences in the symptoms which usher in coma. At one extreme are patients with extreme dyspnea, gasping so that speaking and swallowing are difficult, yet with consciousness perfectly clear until near the end. Such air-hunger is accounted for largely though not entirely by acid intoxication, and alkali may perhaps save life. Of patients of this type, No. 63 was saved by alkali even after he had gone on into unconsciousness, when he might not have been

saved by simple fasting; the dyspnea of No. 39 was somewhat relieved by alkali, but nevertheless she went on into stupor and died. At the other extreme are cases characterized chiefly by malaise, drunkenness, and drowsiness, with hyperpnea little marked; and these prodromal symptoms may also be relieved by alkali, sometimes with surprising promptness. The great majority of cases represent a mixture falling between these two extremes.¹²

The older clinical literature seems to prove that many patients with continuous ketonuria were saved from both dyspnea and intoxication for considerable periods by alkali, and the onset of coma thus delayed. In the treatment of actual coma, alkali has been seldom successful, and the patients saved by it are few. Under all circumstances, its effect is necessarily temporary and palliative. The fact is well known that the death rate from coma was not appreciably altered by the introduction of the alkali treatment. If death was somewhat deferred, the patient died subsequently in coma nevertheless. Magnus-Levy recognized that this result could be prevented only by some method which would check the process of acetone body production. Fasting checks this process; accordingly the great majority of cases of acidosis can be treated by this means alone, and alkali holds no more than a minor adjuvant position. Its use has seemed valuable under two conditions. The first is in combating a long and stubborn acidosis, as in patient No. 23, both for relieving malaise due to acidosis and for avoiding more serious danger. Experience does not prove whether it is best given in smaller doses, 5 or 10 gm. daily, for longer periods, or in larger doses on occasional days when demanded by clinical or laboratory indications. Such a need is rather rare, and the indiscriminate or routine use of alkali is not to be recommended. Particularly prolonged administration, of 2 weeks or more continuously, is probably best avoided, for fear of harm in some patients. The second use of alkali has been for combating coma in certain cases as already mentioned. Under all circumstances, it must be understood that control of the metabolic condition by fasting or food is the essential means of treatment;

¹² This was written before reading the closely similar observations of Cambridge, *Am. Med.*, 1916, xxii, 363-373, who suggests that one form is due to loss of blood alkali, the other to loss of tissue alkali.

failure in this attempt must end fatally in spite of any dosage of alkali, and the crisis is not past until the production of acetone bodies is markedly and progressively diminishing.

In any of the three types of acidosis above described, continuously high or increasing ketonemia and intoxication lead sooner or later to a condition where the further administration of alkali is ineffectual. The reason for the failure is unknown, because the real nature of the intoxication is unknown. The possible irregularities in the ketonemia and the alkaline reserve are indicated by observations of Fitz¹³ upon three fatal cases of coma (Table II).

TABLE II.

Case No.	1st observation, in early coma.		Interval between 1st and 2nd observations.	Sodium bicarbonate by mouth in interval.	2nd observation shortly before death in coma.	
	CO ₂ capacity of plasma.	Total acetone bodies of plasma (as acetone) per 100 cc.			CO ₂ capacity of plasma.	Total acetone bodies of plasma (as acetone) per 100 cc.
	<i>vol. per cent</i>	<i>mg.</i>		<i>gm.</i>	<i>per cent</i>	<i>mg.</i>
—	18.9	71.2	36 hrs.	0	26.7	127
72	14.0	54.5	8 "	25	17.0	97.8
71	22.1	83.8	8 days	72	48.5	192.5

By reference to the history of case No. 71, it will further be seen that during 4 days before the final observation, the CO₂ capacity of the plasma ranged from 38.8 to 50.2 per cent, and the total acetone of the plasma between 212.5 and 368.4 mg. per 100 cc. Also, there was no constant relation between plasma alkali and plasma acetone. These cases afford additional illustrations of increasing intoxication and death notwithstanding rising alkaline reserve of the plasma. Still other examples might be gathered from the literature to show that the intoxication is by no means in proportion to the concentration of total acetone in the plasma. Hence the failure of alkali is not necessarily an insufficiency of diuresis resulting in retention of these acids or their salts. There is no evidence that alkali either increased or diminished the production or accumulation of acetone bodies at this stage. This point deserves further investigation. The sugges-

¹³ Fitz, R., Acetone Bodies in the Blood in Diabetes, *Tr. Assn. Am. Phys.*, 1917, xxxii, 155-158.

tion, especially of recent English authors,¹⁴ that the explanation lies in different relative proportions of acetoacetic and hydroxybutyric acids, the one being more toxic than the other, lacks proof at present. There is need of more clinical observations and animal experiments also on this question. In fact, nothing more than a descriptive status is really established even for the word "intoxication." Diabetic coma is a profound breakdown of metabolism. It may well be, in accord with Woodyatt's ideas, that the abnormality extends through the whole chain of intermediary compounds, that no one substance will be demonstrable in lethal quantity and toxicity, but that the general disorder of protoplasmic chemistry may be responsible for death. Alkali could necessarily have little influence here. Certainly the condition is complex. Ketonuria, ketonemia, lowered plasma alkalinity, and clinical symptoms are ordinarily associated in a relation regarded as typical. The abnormalities of kidney function with severe acidosis are notorious; they presumably involve variable excretion of acids and bases; they necessarily upset any calculations based on normal renal activity; and they may explain more or less of the exceptional behavior noted. Aside from the occasional spontaneous variations, it is obviously possible to distort the usual relations by artificial alteration of one feature, for example raising the blood alkali by administration of alkali, without altering the underlying process or the clinical result.

For practical purposes, sodium bicarbonate is the alkali of choice, on the basis of effectiveness and innocuousness. A salt of strongly alkaline reaction, such as sodium carbonate, deranges the stomach more readily, and its intravenous use involves greater danger of thrombosis in veins¹⁵ or, in case of leakage, necrosis about them. Stronger alkalis must be changed immediately into sodium bicarbonate in the circulation, by chemical laws and because an actually alkaline reaction of the blood would be incompatible with life. This fact does not necessarily conflict with Murlin's¹⁶ observation of a difference in the action of sodium carbonate and bicarbonate upon experi-

¹⁴ Cf. Hurtley, W. H., *Quart. J. Med.*, 1916, ix, 301-408. Kennaway, E. L. *Biochem. J.*, 1914, viii, 355-365.

¹⁵ Cf. Umber, *Deutsch. med. Woch.*, 1912, xxxviii, 1403.

¹⁶ Murlin, J. R., and Sweet, J. E., *J. Biol. Chem.*, 1916-17, xxviii, 261-288. Murlin, J. R., and Craver, L. F., *Ibid.*, 289-314.

mental animals; but no superiority of strong alkalis in the practical treatment of human cases has been established. Any special advantages in the use of other bases (potassium, calcium, magnesium) have also not as yet been demonstrated.

Sodium bicarbonate can be given by the four usual routes.

By Mouth.—This method is preferred when possible. The maximal dosage is generally 2 or 3 gm. an hour or 5 gm. every 2 hours. Few patients can take 100 gm. per day, and none can take this for many days in succession. If the taste is objectionable, it is probably best disguised by administering in carbonated water. The most serious objection to the oral method is the possible nausea, and the dosage should be regulated to avoid this. Diarrhea is also frequent. More or less edema, generally harmless, may result from large doses. Defective or sensitive kidneys may possibly suffer injury, and inhibition of diuresis is a possible serious consequence. On the whole, this method is the safest and with prudence seldom results in harm.

By Rectum.—The well known drop method is the best. In deep coma, retention and absorption are generally poor. In a less extreme stage, this method may be the safest and most convenient substitute or supplement for oral administration. A mixture of equal parts of physiological saline and 4 per cent sodium bicarbonate solution (making a 2 per cent bicarbonate) was recently given thus to a boy of 12 years for 4 days continuously, and as much as 35 gm. sodium bicarbonate and corresponding quantities of fluid were thus introduced without the least difficulty or irritation. There is a possible question whether, if the large bowel is filled with injection fluid, there may be any effect on peristalsis higher up which will aggravate vomiting or interfere with dosage by stomach. Otherwise there is probably no objection to giving alkali by rectum.

Intravenously.—The usual fluid for injection is 4 per cent sodium bicarbonate in water or salt solution. Followers of Martin Fischer favor hypertonic solutions, for withdrawing water from the tissues and for promoting diuresis. Intravenous alkali injections, instead of being among the first measures employed, should be resorted to only reluctantly and on urgent necessity. The possible danger of the familiar practice of injecting a liter of 4 per cent bicarbonate solution has already been mentioned. The occasional sudden reviving effect

is probably due to a circulatory influence of the bicarbonate or the fluid or both. It is almost always temporary, and perhaps carries in itself the danger of later collapse. There are times when not enough alkali can be given by stomach or rectum to prevent a dangerous fall in blood alkalinity. The intravenous method is then commonly used, but the quantities are probably most safely limited to about 250 cc. for adults, repeated at intervals of several hours if necessary. Presumably the Woodyatt apparatus for continuous uniform injection would be best of all. Intravenous alkali injections should be used to keep the blood alkali from falling too dangerously low, rather than to try to maintain it at a normal level, but sometimes remarkably large quantities are required even for the former purpose. The largest doses may be demanded especially in the severest intoxication, which is the very time when, owing to feeble circulation, the danger is greatest.

Since boiling changes bicarbonate into the carbonate, solutions may be prepared in one of the following three ways: (1) by boiling the solution, and then passing sterile CO₂ gas through it to change carbonate back to bicarbonate, until a pink color is no longer obtained in samples tested with phenolphthalein;¹⁷ (2) by making the solution without boiling, sterilizing it by filtration through porcelain; (3) by taking clean sodium bicarbonate, preferably from a freshly opened package of a chemically pure brand, with sterile apparatus into sterile water or salt solution, without further sterilization.¹⁷ This last and easiest method is safe enough for intravenous and perhaps even for subcutaneous use. Solid particles are removed by filtration through sterile cotton or filter paper if necessary. Solutions are warmed to body temperature before injection.

Subcutaneously.—Magnus-Levy¹⁷ called attention to the fact that sodium bicarbonate, as a neutral salt without marked irritating properties, can be given subcutaneously. The method is relatively little employed, because of the fear of infecting or damaging the susceptible tissues of a diabetic, as well as producing pain or discomfort. One feature of usefulness was demonstrated in the twelve year old boy

¹⁷ Magnus-Levy, A., Ueber subkutane Infusionen von Mononatriumkarbonat, *Therap. Monatsh.*, 1913, xxvii, 838-843. Also Joslin's text, 1917, 397.

above mentioned. On his last day of life, 35 gm. sodium bicarbonate given by rectum were only partly absorbed. 40 gm. given intravenously failed to check the fall of the alkaline reserve. The patient was sinking into unconsciousness, with Kussmaul breathing and the full picture of typical diabetic coma; CO₂ capacity of plasma 26.5 volume per cent. A total of 90 gm. sodium bicarbonate in 4 per cent solution was given subcutaneously between 7:30 p.m. and midnight. The hyperpnea was considerably diminished; there was no perceptible influence upon consciousness or the general condition for either good or ill. The slow increase of intoxication continued as before. Death occurred at 1:40 a.m., and blood taken immediately after showed a plasma bicarbonate reading of 68.1 volume per cent. A few authors heretofore have opposed the acid intoxication hypothesis by reporting death in coma with alkaline urine. Inability to give enough alkali has been a prevalent excuse for failure. There is no objection to placing enough bicarbonate beneath the skin to give the patient the benefit of any desired level of alkalinity; and with the aid of the recent improved methods of estimating the alkaline reserve, it is possible for any follower of the acid intoxication doctrine to convince himself that the patient's blood alkali can be kept at a fully normal level, but he dies in deep coma nevertheless.

B. INFECTIOUS AND SURGICAL COMPLICATIONS AND EMERGENCIES.

The methods employed in managing cases of this group are shown in the individual histories, and the collective results are presented in Chapter VII. The experience, though favorable on the whole, is so limited that discussion of the treatment must be based largely on the literature and on general principles. For the older literature, reference may be made to text-books and the papers of Umber,¹⁸ Kaposi,¹⁹ Kraus,²⁰ and Karewski,²¹ and for developments under the newer dietetic methods, to Joslin's text and Strouse's²² paper. Com-

¹⁸ Umber, *Deutsch. med. Woch.*, 1912, xxxviii, 1401-1403, 1433-1434.

¹⁹ Kaposi, H., *Ergebn. Chir.*, 1913, vi, 52-75 (128 references to literature).

²⁰ Kraus, F., *Deutsch. med. Woch.*, 1914, xl, 3-8 (with statements by Naunyn, von Noorden, and Minkowski).

²¹ Karewski, F., *Deutsch. med. Woch.*, 1914, xl, 8-13.

²² Strouse, S., *Med. Clin. Chicago*, 1916, ii, 37-52.

plete discussion of surgical complications, like complete treatment of a patient, demands the collaboration of physician and surgeon. The present brief suggestions will omit statistics, most surgical details and finer classifications, and will be limited to general outlines of practical procedure.

Certain broad dicta may be taken directly from former authors. First, every patient coming for treatment of any medical or surgical ailment should have the urine tested for sugar, whether diabetes is suspected or not. There is ample proof that this admonition is far from superfluous even today. Even with a negative test, Kaposi urges strict inquiry for diabetes in the family or past history, and attention to present or past obesity, suppurations, or other suspicious indications. Second, mildness of the diabetes and slightness of the complication or operation promise the best outcome and the least contraindication to surgical measures; but mild diabetes may turn suddenly severe with a complication or shock, and a complication may be aggravated by diabetes, so that unnecessary interference should be avoided in the presence of any active symptoms, and the prognosis should always be guarded. The more threatening the complication and the more critical the necessity of surgical intervention, the less is diabetes regarded as a contraindication. Third, the special dangers threatening the diabetic are peculiar susceptibility to infection, subnormal healing and repairing power, and acidosis. The last causes most deaths. The first two are largely overcome by aseptic and operative care. Fourth, the better the dietetic preparation, the less the danger. Since acidosis is the chief peril, the best preparation will include a maximum assimilation of carbohydrate; therefore formerly an oatmeal period was recommended (von Noorden, Addis, and others).²³ Fifth, the surgical technique of an emergency operation should be the simplest yet most effective possible, avoiding shock, traumatism or long anemia of the parts, elaborateness, and anything tending to lengthen the time of operation or dispose to subsequent sloughing or infection. Sixth, local or spinal anesthesia is considered safest from the standpoint of acidosis. Proper general anesthesia is usually well borne by well prepared

²³ Addis, T., *J. Am. Med. Assn.*, 1915, lxiv, 1130-1134.

patients. It should be as brief as possible. Psychic as well as physical distress should be guarded against. The anesthetic of choice is nitrous oxide and oxygen. Ether is more dangerous. Chloroform should never be used for diabetics. Seventh, postoperative care includes on the one hand the most skilled dieting, aiming particularly at carbohydrate assimilation, and on the other hand surgical precautions, such as exercise and other measures favoring circulation and general hygiene, and avoidance of tight dressings. Eighth, fatal coma or other disaster may occur from any sort of operation, in any grade of diabetes, after any form of preparation, any kind of anesthetic, and any postoperative care (Naunyn, Karewski, and others). Ninth, operative relief from tumors or other troubles sometimes has a beneficial influence upon the diabetes (Eising and others).²⁴ Tenth, the use of alkali stands on about the same basis as in uncomplicated cases. The frequent occurrence of acidosis with operation or anesthesia in non-diabetics has been brought into some prominence of late (Crile,²⁵ Bradner and Reimann,²⁶ Burnham,²⁷ Lincoln,²⁸ Morriss,²⁹ and others). The recent work of Henderson and Haggard³⁰ indicates that the lowering of the carbon dioxide capacity of the plasma does not represent a true acidosis. Accordingly, only the acetone body production can here be regarded as evidence of acidosis. The treatment has consisted in preliminary carbohydrate diet, and, in emergency, glucose and sodium bicarbonate, alone or separately, orally, rectally, subcutaneously, or intravenously. The glucose is unquestionably the more important for a non-diabetic. The value of alkali has been questioned. Naunyn strongly advocated saturating every diabetic with sodium bicarbonate before operation, and he has had the largest following. Undoubtedly the blood alkalinity can be raised by alkali dosage, but there is the open question whether artificially raising the blood alkalinity is

²⁴ Eising, E. H., *J. Am. Med. Assn.*, 1914, lxii, 1244-1245.

²⁵ Crile, G. W., *Ann. Surg.*, 1915, lxii, 257-263; *Am. Med.*, 1916, xxii, 447-451.

²⁶ Bradner, M. R., and Reimann, S. P., *Am. J. Med. Sc.*, 1915, cl, 727-733.

²⁷ Burnham, A. C., *Am. Med.*, 1916, xxii, 438-441.

²⁸ Lincoln, W. A., *Ann. Surg.*, 1917, lxxv, 135-141.

²⁹ Morriss, W. H., *J. Am. Med. Assn.*, 1917, lxxviii, 1391-1394.

³⁰ Henderson, Y., and Haggard, H. W., *J. Biol. Chem.*, 1918, xxxiii, 333-371.

necessarily synonymous with benefiting the patient. Alkali has not prevented the high mortality from postoperative acidosis in the past. Strouse has had good results in operations with alkali, and Joslin in operations without alkali. The practitioner's choice in individual cases will be governed by his attitude on the general subject.

Contrary to past practice, alcohol is at present not used in this hospital as a food at any stage in diabetic complications or the acidosis accompanying them.

Authors have divided complications into those for which the diabetes is wholly or partly responsible, and those independent of the diabetes. Therapeutic measures are sometimes influenced by theories as to the reason why diabetics are subject to so many characteristic complications and so lacking in resistance to damage of all kinds. Notions that excess of sugar directly injures tissues or provides a favorable medium for bacteria have been sufficiently discredited. It is also important to emphasize that though malnutrition predisposes to infection, the susceptibility of diabetics is something special and peculiar, since human beings or animals suffering from other conditions involving equal or greater inanition and cachexia are not afflicted in this manner or degree. As formerly pointed out,⁸¹ one general conception of diabetes is applicable also to all complications. The present treatment is built upon the idea, supported by considerable evidence in addition to the treatment, that diabetes is weakness of the general nutritive function, including both catabolism and anabolism. It is thoroughly in line with this point of view that every part of the diabetic body should manifest diminished power of maintaining normal function, of repairing the natural wear and tear, of healing wounds, and of resisting infectious invasions. Not only the grosser complications, but also retinitis, cataract, arteriosclerosis, neuritis, asthenia out of proportion to loss of flesh, and the multitude of other disorders listed in classical text-books, accord with this conception. Since the trouble is due to deficiency not of nutritive materials but of the nutritive function, relief should be expected from strengthening this function, even at the price of diminished food supply and body weight. Experience indicates that this result actually

⁸¹ Allen, *Am. J. Med. Sc.*, 1917, cliii, 313-371.

follows, and that there should be no hesitation to impose rational undernutrition for the purpose of raising resistance.

Complications and operations fall for practical management into those with which there is opportunity for preparation, and those affording no opportunity for preparation.

1. When There is Time for Preparation.

(a) *Prophylaxis.*—Just as the food tolerance is never fully restored in typical diabetes, so also the resistance is probably never entirely normal. It is possible, for example, that no dietetic treatment will ever bring the resistance to tuberculosis quite to normal, and that the incidence of this disease will accordingly always be higher among diabetics than among the general population. Also, if an infection does gain lodgment, there is always the danger that diabetes will be made worse and that resistance will collapse correspondingly. On the other hand, resistance is probably highest when a diabetic is kept as nearly as possible like a correspondingly undernourished non-diabetic. Reduction of diet to something like the Chittenden standard has never been shown to cause serious lowering of resistance. Below this scale, freedom from symptoms necessitates emaciation and weakness in proportion to the severity of the diabetes; but it has repeatedly been pointed out that feeding beyond the tolerance gives only a temporary and dearly bought benefit to weight and strength, and it seems evident that such an attempt actually lowers resistance at all stages. Three points of prophylactic advantage from efficient dietetic treatment can be set down as facts. First, the long list of complications which have been the chief torment of diabetic patients in the past are largely prevented; a pimple does not develop into a carbuncle; an abraded toe heals instead of becoming gangrenous, etc. Second, the aggravating influence of complications upon diabetes is thus either avoided or reduced to a minimum. Certain cases in the present series show the occasional possibility of attaining the ideal that a patient shall pass through a crisis of infection or operation without developing either glycosuria or acidosis; and in a larger proportion it is possible to avert acute death and also guard against any lasting injury to the diabetes. Third, health and

resistance are maintained either indefinitely or for the longest possible time, whereas overfeeding entails progressive decline in all respects and corresponding liability to and damage from complications.

(b) *Preparation for Emergency.*—This is generally synonymous with preparation for operation. The time available naturally varies with the surgical condition, but something like a tumor or a quiescent appendix may permit all necessary leisure and care. Active diabetes is first controlled in the usual manner. A carbohydrate period is important thereafter; and if acetone is persistent, it is probably best to continue the highest possible carbohydrate diet without fat until the Rothera reaction is negative if possible. The blood sugar and all other tests should also be brought to normal if circumstances permit. Meantime, protein will lower carbohydrate assimilation and may tend to prolong acidosis, but will support strength better than any other food. It may be called an ideal preparation which sends a patient to operation after a fat-free diet of 1.5 gm. protein per kilogram of weight and the highest feasible carbohydrate ration, with all laboratory tests normal. In case of sudden damage of assimilation from operation or anesthesia, this arrangement insures the greatest possible liability to glycosuria, which is generally easy to control, and the least possible liability to acidosis, which is the chief danger. Joslin and Strouse give examples of preparation along these lines. The latter, for example, prepared a woman with a fat-poor diet of eggs and 85 gm. carbohydrate, so that the urine was free from sugar for 15 days and from acetone for 5 days before operation. A combined hysterectomy, right salpingectomy, and oophorectomy, under nitrous oxide preceded by morphine and atropine, was then borne without incident other than one day of glycosuria. While diabetes necessarily involves operative danger, it is believed that these principles offer the best chance of safety.

(c) *Treatment with Subacute or Chronic Complications.*—As mentioned elsewhere, some complications, such as nephritis, require no departure from ordinary management. Others, such as infections or pregnancy, have interrelations with diabetes which are important in influencing both conditions. On the whole, the most serious medical complication is tuberculosis, and especially the conflict is sharp here between the overfeeding customary for one disease and the

underfeeding demanded by the other. Severe tuberculosis with severe diabetes makes an inevitably fatal prognosis. When either disease is mild, the chance is a little better but by no means good. When both are mild, treatment is more hopeful. A number of patients under observation by recognized tuberculosis specialists have improved strikingly when taken off the traditional high diet and placed on a lower diet which abolished their diabetic symptoms. It is believed that this plan, with the usual fresh air and other measures, promises the best results with this combination.

This belief is corroborated by the experience with surgical complications, which proves plainly that tissue vitality and resistance to infection are built up by treatment which controls the diabetes. The most numerous class of surgical troubles are furunculosis and gangrene. The best local treatment of both is palliative and conservative. Surgical authorities seem to agree that incision of boils should be avoided, unless absolutely demanded by spreading infection or toxic absorption. Gangrene has been the occasion for multitudes of needless operations and deaths in the past. Together with cataract, retinitis, neuritis, and less numerous ills, it furnishes the strongest reason for treating diabetes in the elderly as carefully as in the young; for notwithstanding the part attributed to arteriosclerosis or other causes, efficient dietetic treatment prevents such troubles almost without exception. Stetten and Lambert and Foster,³² and others have proved the advisability of treating gangrene conservatively when possible, with diet, measures to improve circulation, and simple local care. Even tissues appearing dead may revive to surprising degree. A line of demarcation becomes established, and operation is either avoided or reduced to a minimum. It is bad advice to operate early and high, where the tissues and vessels are sound; and patients should not be operated on without dietetic preparation. The only indications for abandoning expectant treatment and operating promptly are advancing infection or fever and intoxication, not checked by other measures and threatening danger either in themselves or in their influence upon the diabetes. Here the treatment demanded is that

³² Stetten, D. W., *J. Am. Med. Assn.*, 1913, lx, 1126-1133. Lambert, A. V. S., and Foster, N. B., *Ann. Surg.*, 1914, lix, 176-185.

for an emergency, as discussed below. Otherwise, even if operation is later necessary, the longest possible time is afforded for preparation. Death from amputation should then nearly always be avoidable. The worst result recorded after such preparation is that of Baldwin,³³ whose patient's urine quickly became free from sugar and acetone, and amputation under ether 3 weeks later was followed by death in coma within 2 days. Owing to lack of details, it is not possible to judge the fitness of the preparatory diet. Though such cases are generally rather mild, yet there is always the possibility of genuinely severe diabetes in an old person, or of continuous injury of assimilation by a chronic infection, so that either early or late operation may end in disaster. Complete laboratory tests are generally a reliable means of judging whether operation is safe or not.

2. When There Is Little or No Time for Preparation.

The most dangerous emergencies are the cases suddenly presenting themselves with serious infection coupled with intense diabetic symptoms. Some of the examples of exaggerated nitrogen loss, maximal D : N ratios, and uncontrollable acidosis belong in this class; *e.g.*, Joslin's³⁴ case No. 513. As the diabetes makes the infection worse and the infection makes the diabetes worse, it is frequently impossible to break the vicious circle, and a large proportion of such patients die. There probably is no constant rule of diet except to exclude fat. On the one hand, these patients are specially subject to fasting acidosis, so that feeding with carbohydrate or protein, either or both, may be necessary, perhaps for a majority. On the other hand, if past experience indicates correctly that ordinary coma responds better to fasting than to carbohydrate, there is a chance that the same may be true of some cases with infection, and that control of the diabetes by the quickest and most radical means possible may be the one hope of saving life.

As with uncomplicated cases, the plan in this hospital with infections has been to impose immediate fasting and then depend upon clinical and laboratory indications for guidance. Chapter VII and the

³³ Baldwin, J. F., *Am. J. Surg.*, 1916, xxx, 65.

³⁴ Joslin, E. P., *Treatment of Diabetes Mellitus*, 2nd edition, 1917, p. 353 ff.

case histories show the collective and individual experiences and results. Medical emergencies, even of such magnitude as lobar pneumonia, have for the most part been met successfully. Fasting has benefited some patients, while others have done well on low carbohydrate-protein diets. It is believed that the results on either plan are more favorable than are possible under any method based on the fallacy of overfeeding for the sake of strength.

Surgical complications offer one more element of hope if the surgical treatment can succeed. The decision between radical and conservative measures is often most difficult and doubtful. On the one hand, dietetic control may revolutionize the surgical state and the infection may come quickly to a standstill, when operation might be fatal. Thus the life of the carbuncle patient No. 27 was probably saved by immediate fasting. On the other hand, with mistaken delay either the diabetes or the surgical condition may quickly become hopeless, and what is demanded is the most prompt and radical surgical intervention. Strouse gives an example of success due to right judgment. A pregnant diabetic woman with threatening acidosis was placed first on a low vegetable diet, but progressed rapidly toward coma. Accordingly Cesarean section was performed under morphine and local anesthesia. Acidosis remained high for 2 days, then cleared rapidly, and the patient was soon out of danger. The results of radically terminating a complication are apt to be most brilliant when, as in this case, the diabetes is inherently mild and is only stirred to intensity by the complication or by wrong diet. Both complications and operations are extremely dangerous in severe cases with flagrant symptoms. As the Carrel-Dakin method has been so widely adopted by surgeons, it is only necessary to mention the great importance of effective wound sterilization, not only for saving gangrenous limbs, but also in carbuncles or other surgical infections, to put an end to toxic absorption with the least possible shock or delay. With advancing sepsis, a quick amputation of a limb or removal of an appendix or other focus, even in the presence of threatening acidosis, may save life in a minority of cases.

Postoperative care is adjusted to meet conditions. A well prepared patient, coming through operation symptom-free, may have his diet built up as in absence of complications, first with carbohydrate, then

with protein, finally with fat. In the presence of an emergency, the usual choice must be made between fasting and feeding for acidosis, following careful clinical and laboratory observations rather than any fixed rule. Nutrition and reparative power, emphasized by Jopson,³⁵ are doubtless best served by protein as usual. While acidosis is the chief danger, absence of glycosuria should be maintained or achieved as early as possible, even at the price of lowered nutrition.

All cases of this entire group demand the constant combined watchfulness of the best surgeon and the best diabetic specialist available. With this cooperation Joslin's statistics show the favorable results obtainable in some of the most desperate cases.

³⁵ Jopson, J. H., *Tr. College Phys. Philadelphia*, 1916, xxxviii, 255-257.

IV. Treatment Following Cessation of Glycosuria.

Here are to be considered (A) the carbohydrate tolerance test; (B) the maintenance diet; (C) the period of observation and instruction; and (D) the period of after-care.

A. CARBOHYDRATE TOLERANCE TEST.

After a patient becomes free from glycosuria, his fast is continued at least one day longer, so as to assure at least 24 hours of complete sugar-freedom before giving food. This plan also is based upon the idea of resting the weakened function. In mild cases, it is permissible to start the test when the patient is sugar-free, even without fasting. In severe cases with hyperglycemia a fast-day usually precedes a carbohydrate test, even though glycosuria is already absent. In the severest cases of all, when the patient is extremely weak and the tolerance is known to be trivial, the carbohydrate period is sometimes omitted and a period of gradually increasing protein substituted. It may be rather important to judge the severity correctly in this respect. Appearances may deceive the inexperienced, so that the benefits of the carbohydrate period are unnecessarily sacrificed in a patient actually possessing considerable reserve strength and tolerance. On the other hand, with genuinely extreme weakness there is the possibility of a fatal collapse of strength on the low vegetable ration, which would be prevented by protein. This danger is really serious only in children, because the collapse may come suddenly. Adults weaken so gradually that there is plenty of opportunity to avert collapse by substituting a low calory protein diet.

The standard program of the carbohydrate test has been to give 10 gm. carbohydrate the first day, and increase by 10 gm. daily until the limit is reached. The first trace of glycosuria does not necessarily represent the limit. When the first glycosuria appears, the practice has been to repeat on the following day the same quantity of carbohydrate which caused glycosuria. If the glycosuria disap-

pears, the regular increase of 10 gm. daily then continues, and occasionally the true tolerance is found to be several times the quantity on which the first accidental trace of glycosuria appeared. When glycosuria occurs on two successive days with a certain intake, the tolerance is considered to be 10 gm. less than this; *i.e.*, the highest quantity taken without glycosuria is regarded as the tolerance.

The test is ordinarily carried out with green vegetables, for purposes of uniformity, and because they are the most bulky and therefore most appreciated form of carbohydrate. The benefit of salts, vitamins, etc., in vegetables is a possible accessory advantage. On the first days, the hungry patient is naturally best pleased with the vegetables lowest in carbohydrate, which afford the greatest bulk. If the tolerance is high, the bulk soon becomes excessive. As far as possible, the patient's wishes are allowed to determine the choice of vegetables. While the approximate grouping into classes of 5 per cent, 10 per cent, 15 per cent, etc., is a convenient guide in selection, it is necessary especially in severe cases to reckon the carbohydrate of each vegetable as accurately as possible from the standard tables, if the test is to be at all exact. With a high tolerance, the lower class vegetables are gradually replaced by those of higher carbohydrate content, until finally, with the highest tolerance, bread and cereals may be reached, though preference is given to potatoes and garden vegetables as long as possible, in order that absorbable protein may interfere as little as possible with the pure carbohydrate tolerance. Fruits are also permitted during the carbohydrate test, beginning generally with grapefruit in the earlier stages and advancing to those richer in carbohydrate. The fruit never represents more than a rather low fraction of the total carbohydrate intake, and with this arrangement the fruit sugar has seemed to make no important difference as compared with starch in fixing the tolerance.

Modifications of the standard plan are used chiefly to suit varying degrees of severity. It will be observed that the scheme outlined is particularly adapted to severe cases with low tolerance. If the tolerance were 300 gm., an increase of 10 gm. per day would require a month for carrying out the test. The feasibility of prolonged vegetable diets is illustrated by cases Nos. 1 and 3, but they have no special virtue beyond the low calories, and exaggerated length of a car-

bohydrate test is generally undesirable. For this reason the increase in the milder cases is more than 10 gm. per day, sometimes as high as 50 gm. per day. Two points are to be borne in mind in regard to such modifications. First, the tolerance determined by a rapid test is by no means strictly comparable to that found in a slow test in the same or another patient, inasmuch as the slower increase, by more prolonged undernutrition, builds up a definitely higher assimilation. Second, too short a test sacrifices much of the benefit, and a week or two if possible is profitably spent as a carbohydrate period.

The purposes served by the test are diagnostic and therapeutic. Therefore it is repeated at 6 months or other intervals, as may seem convenient or desirable.

Diagnostic.—First, the carbohydrate test serves as a basis for reckoning the subsequent carbohydrate allowance. The assimilation is considerably higher for carbohydrate taken alone than in a mixed diet, but the test gives a standard basis of reckoning. Second, the use of a uniform test permits comparisons between patients and between the same patient at different times, for judging both the severity of the case and the progress under treatment.

Therapeutic.—First, most patients at the end of their fast have more or less acidosis. The vegetable period, which enables the highest possible assimilation of carbohydrate, is for this reason the quickest and most effective means of relieving acidosis. Ketonuria diminishes, and the plasma bicarbonate rises without alkali dosage. Individual peculiarities regarding acidosis may be indicated by the varying stubbornness with which it resists carbohydrate ingestion. Second, there is important benefit in the undernutrition, which at first is almost like fasting.

B. THE MAINTENANCE DIET.

When the limit of tolerance has been reached in the carbohydrate test, a single fast-day is given to clear up glycosuria. Then (or immediately after the initial fast, if for any reason the carbohydrate period is omitted) the building up of a maintenance diet is begun. A full diet is not begun suddenly, for fear of bringing back symptoms. As may be seen in the case histories, scarcely any two cases have

been managed identically; the régime has been individualized to suit individual needs. With acidosis, carbohydrate is kept as liberal as possible. For weakness, protein is raised rather rapidly to 1.5 or at least 1 gm. per kilogram of body weight. Fat is added last, the addition is made slowly, and the final allowance is kept within the tolerance as nearly as this can be determined. Under the special conditions, the fat ration is what essentially determines the body weight, but the latter has been allowed to fall until a maintenance diet can be assimilated without obvious diabetic symptoms.

A few cases in this series have been of a grade of severity indicated by the fact that, after cessation, glycosuria would return when the diet consisted solely of a few hundred grams of thrice cooked vegetables on certain days or of six or less eggs on other days. With such a trivial food tolerance, the diet is best limited to the small quantity of protein which can be taken without glycosuria, until the assimilation improves. For the most part, however, mixed diets have been given following the carbohydrate test, the increase being preferably limited to one class of food at a time, so as to observe the respective effects of the addition of carbohydrate, protein, or fat. The principles of the dietary plan were so clearly stated by Taylor³⁶ that his remarks are worth quoting at some length.

"It is impossible in a discussion of so large a subject as diabetes to do more than present briefly a few points. The clinician, even of the most advanced modern type, who views the work that for the past ten years has been devoted to the intermediary metabolism of diabetes ought not to obtain the notion that this matter comprehends the substance of the disease entirely, and that upon the elucidation of the intermediary metabolism now under investigation depends our knowledge of the pathogenesis of the disease. Certainly, the laboratory investigator has no such conception. If up to the present the laboratory investigations have laid special stress upon the intermediary metabolism, it is because it is the most suitable phase for investigation. Nearly all the studies deal with abnormalities in the catabolism of fat and sugar because these reactions lend themselves to investigation. But there is a broader view-point that every laboratory man must recognize, and which every clinician should understand, which may explain many of the divergent features of diabetes. The up-building processes of the body can never be dissociated from the pulling-down processes. There is no such thing as a disturbance in the burning of sugar without an effect upon the

³⁶ Taylor, A. E., *Tr. College Phys. Philadelphia*, 1916, xxxviii, 254-255.

anabolism of sugar in the tissues, and likewise no disturbance in the burning of fat without similar influence in the building-up process of fat. Fat and sugar are vital in the building up of metabolism. We have every reason to believe that when the body cannot burn sugar and fat it cannot utilize sugar and fat in constructive anabolism. Abnormalities in the utilization of sugar and fat in the building-up processes may be as important in the production of certain symptoms of diabetes dealing with resistance as are the abnormalities in the catabolism.

"I would, in the second place, draw attention to one point in connection with the current use of the Allen treatment, which is based upon a misconception. When the diabetic has been made sugar- and acid-free, how far shall he continue his diet? Shall his increase of food be controlled by the urinary signs or shall he adopt other criteria? It has not been demonstrated that it is necessary to give the usually stated 40 calories per kilo. Investigations have recently shown that a man of 70 kilos may live sixty days upon a diet of coarse bread, potatoes, cheese, and eggs, containing about 2000 calories, without loss of weight. If such a man should happen to have diabetes and were subjected to the Allen treatment, it would be an absurdity to attempt to feed him back to 40 calories per kilo. The man dealing with a patient should bear in mind that what he needs to feed to is not the normally high maximum of calories but the low minimum standard of calories."

As stated in the preliminary publications, in accordance with the principle underlying the entire treatment, the fact that a person is diabetic calls for restriction of his total diet, and, in proportion to the severity of the diabetes as indicated by the carbohydrate tolerance, the allowance of all three classes of foods should be diminished. With regard to the necessary influence of such restriction upon body weight, it was advised that every patient, no matter how mild the diabetes, be kept a few pounds, preferably at least 10 or 15 pounds and in obesity more, below his usual former weight. In proportion as the diabetes is more severe, the weight as well as the diet should be kept lower. Overtaxing the anabolic side of metabolism by attempts to make patients carry too much weight will, in accord with Taylor's expression, bring a return of active diabetes manifested chiefly by excretion of products of deficient catabolism; while lightening the anabolic burden by reduction of body mass makes its benefit evident in an improved catabolic function.

There is a further interrelation between reduction of weight and diet. It is known from earlier metabolic studies that undernutrition reduces the food requirement not only absolutely but also relatively;

i.e., not only are there fewer kilograms of weight, but also fewer calories are needed per kilogram. A recent illustration is afforded in the observation of Anderson and Lusk,³⁷ that a dog after fasting 13 days showed a diminution of 20 per cent in weight and of 28 per cent in heat production. A special point in the study by Allen and DuBois lay in establishing the influence of this principle upon diabetic metabolism. It was there shown that G. S. (patient No. 10 in the present series), starting with a basal metabolism 2 per cent above the average normal when severe diabetic symptoms were present, dropped to 21 per cent below normal on the eighth day of his fast. This calculation was based upon the DuBois height-weight formula; and as the weight was 31 per cent below normal, the reduction below the original normal metabolism was far more than 21 per cent. The reverse change was demonstrated in W. G. (patient No. 8 in the present series). "Starting at 26 per cent below normal on January 11, when glycosuria was absent, his metabolism rose, on increased diet and the return of active diabetes, to 20 per cent below normal on January 15 and to 11 per cent below normal on January 22." This patient was 42 per cent below his normal weight, so that the absolute reduction below his original normal energy exchange was far greater. These experiments carried out by DuBois established one essential point in this theory of treatment; *viz.*, that a relatively high metabolism accompanies active symptoms in the severely diabetic patient, and that the fasting and low diet which control these symptoms enable him to descend to the low metabolic level proper to him as an emaciated human being, so that his maintenance requirement falls as low as that of any other equally emaciated individual.

Lusk³⁸ summarized the case studied by Geyelin and DuBois as follows:

"When the patient was intensely diabetic, the number of calories produced per hour, as measured by the calorimeter, was 73.2. The weight of the patient was 56½ kilograms. The heat production was normal for that weight. Later, through the starvation, the weight fell from 56½ kilograms to 46 kilograms, and the man developed a high degree of tolerance for carbohydrate. The calories

³⁷ Anderson, R. J., and Lusk, G., *J. Biol. Chem.*, 1917, xxxii, 421-445.

³⁸ Lusk, G., *Tr. College Phys. Philadelphia*, 1916, xxxviii, 244-248.

produced per hour fell from 76.4 to 43, or was 35 per cent under the normal for the lower body weight. Thus he requires only about 60 per cent of the food that he had required previously when he was heavier and diabetic."

Patient No. 54 also was studied in the calorimeter by DuBois. The findings quoted in her case record show that the metabolism of this extremely emaciated woman was the lowest ever recorded, and "only 40 per cent of the original heat production was necessary for life."

The nitrogen output of this patient was not correspondingly reduced; and, though authors from Sivèn to Chittenden have demonstrated how low the protein metabolism of normal persons may be brought, it has been constantly borne in mind that protein is the most essential food and its reduction the most risky of all. It must be duly regulated, not only because it is a food and a source of both sugar and acetone, but also because its specific dynamic action is greater than that of any other food in increasing metabolism. As the body weight is low, 1.5 gm. per kilogram have been arbitrarily chosen as a standard allowance of protein. Freedom from glycosuria is possible on a higher protein ration with fat restriction than with unlimited fat. The new method therefore has the advantage over former ones in this respect, and is sufficiently elastic to allow such balance of the diet as may suit individual beliefs in favor of high or low protein.

It is worth mentioning that the calorimetric results quoted have been obtained with ingestion of little or no carbohydrate. Persons acquainted with the literature need not be reminded that the increase of nitrogen excretion or of total metabolism on withdrawing carbohydrate or replacing it with fat applies only to high fat rations or to a certain standard of metabolism; for by lowering the level of nutrition it is always possible to reduce both total and protein metabolism very low, even without carbohydrate. The slightly greater sparing power of carbohydrate is, however, one reason for retaining it in the diet, as noted below.

Patients with the emaciation and minimal diet corresponding to the severest diabetes are necessarily far below normal in strength. The above mentioned investigation of Anderson and Lusk is of special importance with regard to the muscular activity of such patients.

These authors proved that when a dog was reduced in weight by fasting, there was a saving of energy when the animal ran in a treadmill, because less energy was required to move the lighter body. But when the calculation was based upon the absolute work performed, the expenditure of energy was exactly the same before and after fasting; that is, the organism can economize in its basal metabolism, but the same absolute labor costs the same absolute energy, irrespective of the state of nutrition. In diabetes, however, there are additional factors, namely the non-utilization of much of the energy contained in high diets, and the preternatural weakness and lassitude due to the resulting intoxication. Williams³⁹ has carried out a unique investigation by dynamometer tests of patients under treatment, demonstrating directly an increase of muscular strength when the diet is reduced so as to bring it within the metabolic capacity.

The following are fair conclusions from the evidence at hand. Persons with mild diabetes are as a rule easily enabled to maintain themselves on mixed diets with moderate restrictions which reduce their weight but raise their efficiency and comfort practically to normal. Persons with moderate diabetes require more rigid restrictions, which bring them more or less below normal, but yet their diet is more agreeable and their comfort and usefulness maintained both higher and longer than on limitation of carbohydrate alone. Patients with severe diabetes necessarily face the hardest conditions. The investigations have shown the enormous load of useless and injurious metabolism carried by such patients with their active symptoms, and the striking reduction of this burden under treatment which controls symptoms. The low metabolism and efficiency of inanition remain. There may be a tendency to calculate diets which appear absolutely low, but yet are *luxus rations* for this state and injure assimilation accordingly. The sympathy of the inexperienced onlooker is strangely greater for weakness and emaciation held in check by a tight rein on diet, than for the worse and rapidly progressive condition which, on overfeeding, appears as the simple consequence of the disease. It is possible for any case under unskillful restrictions, and for a few cases even under the most expert care, to end in actual death from starva-

³⁹ Williams, J. R., *Arch. Int. Med.*, 1917, xx, 399-408.

tion; but Joslin's and the present statistics agree in showing that this is not one-tenth as frequent as other causes of death, notably coma. Had circumstances permitted, the present series of cases might have afforded unusual material for a study of undernutrition, and might also have established the lower limits of a maintenance diet, which at present are unknown. It can only be said empirically that with remarkably few exceptions the curve of falling weight and the curve of rising assimilation meet at a level on which life can be maintained. The best experience seems to agree that, when such treatment is properly carried out, the unavoidable hunger and disability are less distressing to all concerned than the troubles accompanying acidosis and complications under former methods.

C. THE PERIOD OF OBSERVATION AND INSTRUCTION.

Treatment can seldom be inaugurated or patients instructed as satisfactorily elsewhere as in a hospital with a well conducted metabolism ward. This statement applies not only to the critical cases, where the advantages are most evident, but even to the mildest ones.

For the physician, a hospital offers the best facilities for the two prime essentials of treatment, accurate diet and laboratory control. He is also spared much unnecessary labor and inconvenience if the organization is right.

For the patient, a hospital offers relief from work and worries, and both theoretical and practical education concerning diabetes. One test of treatment is found in the fact that under proper conditions a patient is benefited by contact with other patients. Any fears concerning his own initiation are relieved on acquaintance with others who have gone through the same or more. He sees and hears the actual consequences of following or breaking diet, and his choice is generally for fidelity. He falls naturally into the habits of his environment, and learns so much from his neighbors and the general atmosphere of the place that instruction is made very easy.

Much of the benefit of the early stage of treatment is often lost by undue brevity of the observation period. The extremely long hospital sojourn of most patients in the present series is accounted for partly by the severity of the cases, and partly by the requirements of

investigation. Few patients can remain in private institutions so long, but also comparatively few cases are so severe. It may seem that little is really being done after the first brief period of most active treatment, and that a longer stay imposes a cost in time and money which is unjustifiable, especially for poorer patients. It is unfortunate that poverty and necessity shorten the hospital period injuriously in so many cases, and that public institutions are generally so ill equipped to care properly for diabetics. Also much is accomplished by the classes, clinics, and social service work conducted for diabetics by some of the best institutions and specialists. But, as a rule, the ideal hospital experience for a mildly diabetic patient can seldom be less than 2 weeks, and for severe cases the time may extend into months.

For observation, this period is useful in order to determine the true food tolerance, so as to plan a diet which is neither too high, thus causing injury of assimilation and later relapse, nor too low, thus occasioning unnecessary privation and loss of weight. Laboratory tests, employed as described hereafter, are the chief means of judging progress. The patient should not be discharged until these tests give either normal results or adequate assurance of continued progress in the right direction.

For instruction, this period is used to equip the patient with a sufficient working knowledge of the care of his own case. Experience has shown that the simple essentials can readily be mastered by even the least educated persons, if they are willing and conscientious. Diets are readily calculated by the more intelligent patients, especially as the plan followed is so simple. Uneducated patients are sent out with fixed written menus, together with a list of absolute quantities of other foods which may be substituted for individual dishes on the standard menu. Before leaving, a patient generally spends most of his time for about a week in the diet kitchen, participating in the actual preparation of his own and others' diets. He is thus of some service, and at the same time acquires practice in cooking and calculation which guards against mistakes at home. Men, women, and children alike are generally put through this practical training; but when a relative, servant, or other individual will be largely concerned in the actual labor, this person is also given the

course of instruction. For testing the urine, the Benedict sugar method alone is sufficient, and can be learned by anybody. The tests, in severe cases or if the blood sugar is high, are best carried out upon the four separate urine specimens of each 24 hours, as done in the hospital. There is no harm in patients' learning as many laboratory reactions as they like, but the sugar test is really all they need to know, and they are more liable to become morbid over too many tests. Under proper conditions, only very rare patients are made nervous or hypochondriacal by performing their own sugar tests, so that these must be made for them by other persons. They must be equipped with definite knowledge of what to do if glycosuria appears. The best psychic state is generally assured when they know they are regularly and consistently sugar-free, and have confidence in their ability to control glycosuria if it appears.

D. THE AFTER-CARE.

The period of after-care properly extends over the remainder of the patient's life. For a considerable time at least, he should keep an accurate record of the facts pertaining to his case, most conveniently on a printed form supplied for the purpose. Such a record should include the naked weight, the exact diet, the urinary reactions, and the subjective health. No matter how thorough the instruction in hospital, questions and difficulties often arise, especially in the early period after returning home. The patient is encouraged to ask advice when needed, but particularly is ordered to report regularly at intervals ranging from one week in severe cases to several months in mild cases. Some reports may be made by letter, especially by patients at a distance, but it is necessary for intelligent supervision that the patient present himself in person at definite times. Occasional emergencies also arise, and the patient should have some knowledge of how to meet them. For example, many may profit by the advice that in case of any infection, they should immediately omit fat from the diet. But such an emergency should be reported without delay to the physician in charge, in order that he may superintend any further measures necessary.

When a patient reports in person, his naked weight and a urine and a blood sample are taken. The accuracy of his record is thus checked. If the blood sugar is normal, and the nitroprusside test is negative in urine (Rothera) and in blood plasma (Wishart), practically nothing else is needed. If all is not so favorable, such other analyses are performed as may be necessary to show whether there is danger or what is the direction of progress.

These occasional tests are the guide for such adjustments of diet as may be necessary from time to time. The severely diabetic patient requires rather close supervision for checking wrong tendencies in their incipiency and for the best results in general. The encouragement and moral support gained in personal contact are furthermore specially important in the severe cases, though a high proportion of milder cases without it will sooner or later go wrong. A case lost from sight is generally a failure. Milder diabetes should not involve invalidism or irksome dependence; but these persons, even while leading comfortable and useful lives, should keep in touch with their medical adviser, for experienced oversight of their condition and diet and for information concerning advances in treatment.

V. Ideals of Diet and Laboratory Control.

In the earliest preliminary outlines of this treatment, the plan was defined as an attempt to spare a weakened function by rest, and to this end it was proposed to make and keep every patient free from glycosuria and from obvious acidosis. This initial step appeared as a sufficiently radical, even hazardous, departure from the former management of severe cases; and it was hoped that there might be more or less improvement in such assimilative function as remained to these patients, corresponding to the gain in tolerance known to occur when the symptoms of milder diabetes were cleared up under the old treatment. The reality of such improvement in many of the most intense cases in their earlier stages is now a familiar fact, and is discussed in Chapter VII. Even in the first patient, however, the inability to gain in assimilation to any important degree was manifest, and other cases quickly confirmed the fact that prolonged severe diabetes was characterized under this plan by permanently low food tolerance, and that downward progress was merely delayed and not prevented. The obvious path for investigation was to determine whether the degree of functional rest represented by the crude tests originally selected is adequate for such extremely severe cases of diabetes as were intentionally selected for trial of the treatment; and this also would have answered the question whether or to what extent there is a genuinely spontaneous downward progress in diabetes of any type. At this earliest period, the question was discussed with Joslin whether it might not logically be required to abolish hyperglycemia rather than merely glycosuria, and whether it is possible to bring the blood sugar to normal in the severest cases. Under the conception of diabetes as a weakness of the total metabolism, it would have been necessary to carry out simultaneous studies of the carbohydrate, protein, and fat functions; to determine whether overstrain of any side of metabolism was present; whether such overstrain was demonstrably injurious; and whether the overstrain and injury could be obviated. Such studies upon a few cases would have given an

early answer to the essential question. In the first patients, it was not possible to perform even blood sugar analyses. With the expansion of laboratory facilities, the therapeutic problem became replaced by others; and in consequence, treatment was applied to a long series of patients over a long period of time with no advance over the original crude criteria. That is, negative sugar and ferric chloride reactions in the urine were maintained if possible, as originally recommended; but hyperglycemia, ketonemia, and the excretion of several grams of acetone bodies with increased urinary ammonia daily, as shown in the records, were allowed to continue without investigation of their possible consequences or the development of any further means to combat them.

This policy has been followed by disastrous results, both in the present series, and in the experience of others with the same method. Meanwhile, experiments upon partially depancreatized dogs have shown similar conditions. After suitable operation, a dog on a given diet may be free from glycosuria and yet have hyperglycemia. One of two things happens. Either the hyperglycemia passes off and the animal lives indefinitely, or hyperglycemia persists, with or without ketonuria, and the progressive decline duplicates that of corresponding human diabetics. This outcome in animals which are demonstrably free from spontaneous downward tendency furnishes decisive proof that this degree of functional overstrain may of itself produce this result.

This fact does not conflict with the observation of Mosenthal, Clausen, and Hiller⁴⁰ concerning the stubbornness of the tendency to hyperglycemia in severe diabetes. For practical reasons, it may sometimes be necessary to allow patients to go along with this level of blood sugar which assists their defective power of combustion, apparently by mass action. It is surprising how well many patients can do under such conditions, and for how long a time. But the downward progress which ultimately follows this overstrain cannot properly be called spontaneous. Also, the greater the genuine severity of the case, the more quickly and obviously does this continuous hyperglycemia bring disaster. It is believed that the utmost effort

⁴⁰ Mosenthal, H. O., Clausen, S. W., and Hiller, A., *Arch. Int. Med.*, 1918., xxi. 93-108.

should be made to maintain normal blood sugar at any stage; but above all, proper treatment demands that a case be so managed from the earliest diagnosis that the tendency to hyperglycemia shall be prevented or delayed as long as possible.

The conditions described above do not apply to dogs with pancreatic atrophy or to occasional human patients with organic disease obviously progressive in character and causing decline irrespective of diet. Time has not yet permitted answering the other half of the question; *viz.*, whether the great mass of typical diabetic patients are ultimately subject to downward progress even when all functional overstrain is relieved as far as ascertainable.

As shown in Chapter VII, results have been decidedly best when early cases of diabetes have been so treated as to keep them normal to all the chemical tests used. In resuming the therapeutic problem recently, difficulty was anticipated in a large proportion of more advanced cases, because the hyperglycemia is often very refractory to fasting. It has proved possible, however, to achieve a normal blood sugar in almost all cases on a plan prompted by the following reasoning.

Reduction of body mass has been a regular means of improving assimilation. But if it were desired only to relieve of his obesity one of the fat patients in the series, the best method would be neither plain fasting nor a haphazard mixed diet. The rational diet for obesity is one containing protein to protect body nitrogen and bulky vegetables to fill the stomach, while low in calories so as to compel combustion of body fat. An obese person can endure such a treatment, when on plain fasting he might become dangerously weakened before his weight was sufficiently reduced. The same considerations apply with greater force to weakened diabetics. By subjecting these emaciated patients to an obesity cure, their weight has been reduced sufficiently to conquer their hyperglycemia. This means, in practical application, that after the initial fast and carbohydrate test, if the blood sugar is still high, the patient receives a diet in which the only real food is protein, generally about 1 gm. per kilogram of body weight. Body nitrogen is spared and strength maintained better than on plain fasting, and the program is continued until the blood sugar falls to 0.1 per cent. The specimen laboratory chart facing

page 150 illustrates such a treatment, through the periods of the initial fast, the carbohydrate test, then the protein diet till the blood findings are normal, and finally the mixed maintenance diet. Rare cases are so severe that both hyperglycemia and ketonuria persist for weeks on this exclusive protein diet. Here it has been necessary to keep the patient for a week or two on a diet with negligible food values, *viz.* soup, bran, agar jelly, and thrice cooked vegetables, in order to obtain normal blood sugar, which may then continue on the above-protein diet. Protein is increased if possible to 1.5 gm. per kilogram of weight. The first food added to it is carbohydrate, and a patient, according to severity, is required to assimilate 5 to 20 gm. without hyperglycemia, and thus to be free from any trace of ketonuria, before proceeding to the gradual addition of fat. The limit of fat and calories in the maintenance diet is governed by laboratory tests. The importance and interpretation of these tests change in the later observation period from what they were at the inception of treatment, and a few remarks may be devoted to the three phases of metabolism involved.

Protein.—No direct tests of protein metabolism are required in the late observation period. Most important would be total nitrogen analyses in any case of doubt concerning the nitrogen balance, but on the protein allowance recommended the patient ordinarily comes into nitrogen equilibrium with simple clinical observation. Ammonia is always normal if acidosis is controlled as described. Unpublished analyses in this laboratory have shown that in the most intense active diabetes there is increase of amino-acids both in the urine, as reported in the literature, and in the blood; but this, like the exaggerated nitrogen catabolism, is regularly absent under the routine treatment. Sufficient warning of an overtaxed protein metabolism is afforded by hyperglycemia or ketonuria.

Carbohydrate.—With Benedict's method,⁴¹ it is now as easy to determine the sugar in blood as formerly the sugar in urine, and really simpler and more satisfactory to make the analysis than to send the blood to a laboratory. One hindrance to its use by practitioners has

⁴¹ Lewis, R. C., and Benedict, S. R., *J. Biol. Chem.*, 1915, xx, 61-72. Benedict, S. R., *ibid.*, 1918, xxxiv, 203-207. Bock, J. C., and Benedict, S. R., *ibid.*, 1918, xxxv, 227-230.

been the cost of a colorimeter, which has been met by the introduction of the Bock and Benedict⁴¹ instrument. Epstein's⁴² modification of the Benedict method, though not quite so accurate, is the simplest and cheapest of all and requires only a few drops of blood, obtainable from the ear or finger. A large number of physicians whose tests must be made in their own offices and who would never undertake a more elaborate method, will undoubtedly make use of this device, and will have no excuse for being without blood sugar analyses. Knowledge spreads rapidly among diabetic patients, and instead of objecting to the drawing of blood many of them doubtless will soon be demanding it.

If the blood sugar is kept normal, urine tests are almost superfluous. The patient has the agreeable knowledge that glycosuria is always absent, and his tests merely guard against errors in diet or any unforeseen change. The blood sugar is one of the most delicate indicators not only of the carbohydrate but of the total metabolism. Even though glycosuria be absent, a dangerous lack of control of the diabetes is indicated in those instances where the blood sugar actually rises after one or several days of fasting. It is sometimes but not necessarily associated with a correspondingly unfavorable change in the acidosis. The hyperglycemia after carbohydrate ingestion rises and falls relatively quickly. There is a more gradual rise and fall after protein. The absence of hyperglycemia after feeding pure fat, and the slowness of the rise of blood sugar on adding fat to a diet, are in accord with the accepted belief that fat is not converted directly into sugar; but the hyperglycemia is particularly lasting and stubborn. The limit of fat in a maintenance diet is reached when hyperglycemia results from its further addition to the ration of protein and carbohydrate which has been fixed as necessary. The ideal is that the blood sugar shall not be above 0.1 per cent fasting or above 0.15 per cent during digestion.⁴³

⁴² Epstein, A. A., *J. Am. Med. Assn.*, 1914, lxiii, 1667-1668. Instrument with instructions obtainable from Ernst Leitz, 30 East 18 Street, New York City.

⁴³ As this monograph goes to press, the first of a series of papers from the laboratory of S. R. Benedict, who has already contributed so preeminently in the field, are appearing in *The Journal of Biological Chemistry*, 1918, xxxiv, 195-262. The application of a newly perfected method, which determines quantitatively

Fat.—The two direct evidences of disordered fat metabolism are acidosis and lipemia, which will be considered separately.

Acidosis.—Quantitative tests are necessary precautions when acidosis exists; but as far as now known, there is no danger from diabetic acidosis if the nitroprusside test is negative in both urine and blood plasma.⁴⁴ It has proved possible to keep the reaction consistently negative in some of the severest cases of diabetes. A question is possible whether strictness to this degree is necessary: whether

the sugar even in normal urine, gives promise of results of the highest importance in the study of sugar tolerance and carbohydrate metabolism. The prediction may be ventured that such a refined method will reveal a pathological excretion of urinary sugar by diabetics with the familiar marked hyperglycemia. Investigation will have to show whether the urine becomes normal for sugar when the above requirements of normal blood sugar are fulfilled. It is to be emphasized that the essential progress and improvement of clinical results must lie in this direction of finer methods, earlier diagnosis, and stricter control of incipient abnormalities. Only by such means can the principle of treatment by sparing a weakened function be carried out successfully.

⁴⁴Legal (*Z. anal. Chem.*, 1883, xxii, 464) first observed that the nitroprusside reaction (originated by Weyl as a creatinine test) might serve as a test for acetone and acetoacetic acid. V. Arnold (*Centr. inn. Med.*, 1900, xxi, 417), by fine qualitative tests showed that acetone is excreted only in the severest grades of acidosis, while the substance present in ordinary so called acetonuria is acetoacetic acid. Embden and Schliep (*Centr. ges. Physiol. u. Path. Stoffwechs.*, 1907, ii, 289) found quantitatively no preformed acetone in the fresh urine in some cases of ketonuria, and in other cases it ranged about 1/10 to 1/4 of the total acetone bodies. Folin and Denis (*J. Biol. Chem.*, 1914, xviii, 267) stated that "acetone urines contain from two or three to nine or ten times as much acetoacetic acid as acetone." Rothera (*J. Physiol.*, 1908, xxxvii, 491) regarded his improvement of the nitroprusside test as a test for acetone; but W. H. Hurtley (*Lancet*, 1913 (1), 1160) proved that with pure materials the Rothera reaction is sensitive to acetoacetic acid in 1 to 400,000 dilution, but to acetone only in 1 to 20,000 solution. Kennaway (*Guy's Hosp. Rep.*, 1913, lxxvii, 161) confirmed the fact that the Rothera test is essentially an acetoacetic test which is at least 25 times as delicate as the Gerhardt ferric chloride reaction; and he suggested that the greater opportunity and ease of diffusion through the lungs as compared with the kidneys is the reason why most of the preformed acetone leaves the body through the former. There is no simple qualitative test for β -oxybutyric acid. To some extent the intensity of the acetoacetic reactions serves as a rough index of the quantity of both acids present, but there are wide departures from this rule in both directions.

normal persons with identical nutrition would not show slight ketonuria, and whether it may not be harmless. There is an opposite speculation whether a diet or metabolic state productive of ketonuria is not more or less harmful even to normal persons, and whether a diabetic may not be more susceptible to injury. The presence of β -oxybutyric acid out of proportion to the small acetone-acetoacetic fraction seems to characterize some of the long standing severe cases. Any considerable ketonuria in severe cases is associated sooner or later with hyperglycemia. When the blood sugar is low, faint nitroprusside reactions have been allowed to exist in some patients, without empiric evidence of harm. While ketonuria is most closely associated with the fat ration, it can result directly or indirectly from unwise addition of any kind of food to the diet. When acidosis in the strictest clinical definition is kept absent as described, the plasma bicarbonate is regularly high, generally above rather than below 65 per cent.

Lipemia.—The investigation of this subject is apparently of rapidly growing importance. It has long been known that some cases of diabetes are characterized by lipemia far in excess of anything found in any other condition. Some of the facts recently established⁴⁵ are that the blood fat may be several times the normal without noticeable turbidity; that the lipid relations, especially the high cholesterol, are in contrast to normal alimentary lipemia; that in severe diabetes the hyperlipemia is apparently as constant and characteristic as the hyperglycemia, and that it is largely associated with the fat intake and with other active diabetic symptoms. At present, the findings seem to support the conception of diabetes as a disorder of the total metabolism, and to furnish further evidence against the misleading practice of labelling phloridzin, adrenalin, or other forms of sugar excretion as “diabetes.” The question immediately arises whether excess of fat in the blood is not as truly indicative of overstrain and injury as excess of sugar. It is also essential to know whether the rigid program above outlined brings the lipoids as well as other blood constituents to normal. The work of Gray⁴⁵ shows actually low levels of blood fat in some severe cases under strict treatment. Many analyses are also under way in this hospital. It is

⁴⁵ Allen, *Am. J. Med. Sc.*, 1917, cliii, 313–371. Gray, *Boston Med. and Surg. J.*, 1918, clxxviii (references to Bloor and Joslin).

not yet certain whether fat determinations are necessary for guiding treatment at this stage. The blood sugar and nitroprusside tests may perhaps suffice.

It should be emphasized that comparison and clinical judgment are necessary in interpreting the significance of all laboratory tests. It is wholly erroneous to consider that hyperglycemia, ketonuria, or any other laboratory finding is in itself proof of a breaking strain upon metabolism, or that absence of such indications gives assurance that all is well. As in dogs, so in patients, hyperglycemia may gradually subside on right diet or may gradually develop on wrong diet. The same is true of ketonuria, and doubtless also of lipemia. Some patients in this series have been discharged with marked hyperglycemia and ferric chloride reactions present. These persisted for months, but yet the policy was safe, because it was recognized clinically that the cases were essentially mild diabetes, and that these symptoms would gradually clear up, without requiring that an elderly or weak person be subjected to more serious privations. Such liberties with a severe case, even though the remaining symptoms be slight, are risky; and they are disastrous with any case unless the diet is within the actual tolerance. It is highly important not to treat an incipient case of potentially great severity as if it were a genuinely mild case. Also, in some severe cases in this series, the blood sugar was sometimes brought to normal by withdrawal of carbohydrate, with a diet too high in fat and calories. More or less ketonuria was present, and doubtless the blood fat was high. Notwithstanding absence of hyperglycemia for weeks or months on carbohydrate-poor diet, such a case can be expected to go steadily downhill. The character of the case, comparisons of different tests, and the direction of progress are therefore important guides in treatment and prognosis. Too much emphasis upon any single test may be as misleading as the lack of tests; and though laboratory work should never be slighted, the experienced man with very simple means will administer far better and safer treatment than the tyro with a great laboratory at his disposal. The ideal treatment therefore begins with rather extensive laboratory study, but in the end comes down to a very few simple tests.

While discussing ideals, the fact should be plainly faced that the program above suggested is for very severe cases an excessively rig-

orous one. The patients of this extreme type are weakened by it; sometimes they must be temporarily kept in bed; and their physical and psychic depression becomes greatest at about the time the blood sugar becomes normal. No disaster has occurred under the method, and none of these patients has refused it. Strength returns when a maintenance diet is resumed; sometimes it seems as great as before, but more often the fall in both flesh and strength is noticeable. In view of the questionable prognosis in such extreme cases at best, the conservative physician will ask himself whether it is advisable to impose such privation, especially as inanition and the dangers of chance infections are obviously brought closer. In a few cases, moderate hyperglycemia and slight nitroprusside reactions without other symptoms have been permitted in the interests of strength and efficiency. Similar ideals have suggested themselves to a number of the best workers in this subject, on account of their similar mishaps with the less careful methods. As far as known, however, both the plan and execution of the above program are new. It has been applied because the patients wished to live, and because it was certain that they would die soon unless saved by radical measures. Their subjective comfort after the rigid treatment has been about the same as before. The downward progress formerly evident has in every instance been either arrested or delayed—the few months of experience do not permit answering which. It is not certain whether such a method is to be generally recommended in practice, and in any event there is no desire to urge it upon either physicians or patients. It is fairly certain that the rigid plan will prolong life and also maintain a fixed level of nutrition, if not indefinitely, at least considerably longer than laxer methods. If hyperglycemia, ketonuria, and other symptoms are allowed to persist, a definitely gloomy prognosis must be accepted, and the choice is essentially either death in coma or progressively more severe undernutrition, which becomes more extreme than required under the rigid plan and increases to death in starvation. The above qualifications apply, however, only to these cachectic patients with excessively severe diabetes. The greatest importance of the plan lies in its application to earlier cases, and for these it is strongly and unreservedly recommended. In the early stage it is shorter and easier to carry out, involves no extreme privation or

physical deterioration, and fulfills the purpose of relieving metabolic strain as far as present analytic methods can determine. It has thus far demonstrably prevented downward progress in several cases of the type which ordinarily progress downward, and it offers at least a chance of continued subjective health, whereas looser methods promise nothing but death.

When the blood sugar is normal, glycosuria from trivial carbohydrate ingestion does not occur. Accurate reckoning of the diet is just as essential; but yet if glycosuria results from slight fluctuations in the carbohydrate content of vegetables, or from adding a few hundred grams of thrice cooked vegetables, the patient is certainly too close to the verge of his tolerance and trouble will follow unless the condition is improved. There are the following reasons for giving carbohydrate as prominent a place in the diet as feasible. First, it gives the quickest and most harmless danger signal. Second, at least a small quantity is necessary to fulfill the ideal of freedom from ketonuria. Third, it spares protein more effectively than fat, and incidentally spares the total metabolism somewhat; and as shown by Zeller,⁴⁶ if the carbohydrate of the ration is equivalent to one-tenth of the fat calories, the sparing is as effective as though all the fat were replaced by carbohydrate. Fourth, by permitting a supply of fresh green vegetables, it makes a diet more agreeable and satisfying than a higher carbohydrate-free ration. Fifth, on general principles and for reasons partly unknown, a mixed diet is the only natural diet, and no diabetic will ever live long on any other. Caution is needed against the mistake committed by some, in giving so much carbohydrate that a living ration of protein and fat is made impossible. But as stated, the rule in this hospital recently has been to reduce the total diet sufficiently to enable any patient to assimilate at least 5 gm. of carbohydrate, and correspondingly more in the less extreme cases.

Various methods of treatment have been tried in the present series. At one extreme there has been reversion to the old practice of carbohydrate-poor diets of 40 calories per kilogram or more. At the other extreme are a few cases treated according to the rigid

⁴⁶ Zeller, H., *Arch. Physiol.*, 1914, 213-236.

program last outlined. The results shown are therefore not those of any one method. The results of different methods should be compared and the choice of treatment governed accordingly. The experience is believed to support the original principle that treatment should aim to spare a weakened total metabolism, and that in proportion as carbohydrate must be restricted, the total diet should also be kept low.

VI. Practical Management of Diets.

A. ORGANIZATION.

Many physicians and hospitals have found it possible to conduct diabetic treatment more or less successfully under adverse conditions. Foods may by special arrangements be served from the general kitchen if necessary. Though some patients in the present series, especially in observations requiring accuracy, have been isolated in individual rooms, others have been in open wards with patients suffering from other diseases. Their own fidelity, and the knowledge that glycosuria and fasting would follow an indiscretion, have maintained a high general average of good conduct.

The ideal arrangement, and the one which is being rapidly adopted by the best hospitals, is to organize a special diabetic or metabolic ward, with a separate diet kitchen in as convenient proximity to it as possible. The kitchen organization here, and the cooperation of Miss Emmeline Cleeland, the diet nurse, have contributed much to the success of the work.

The head of the kitchen may be either a specially qualified nurse or a trained dietitian who is not a nurse. Her time is best left free for duties of supervision. The physician has merely to order a diet in terms of protein, carbohydrate, and calories. The nurse then translates these figures into the actual foodstuffs, superintends the cooking, and is responsible for the accurate recording of everything pertaining to the diet. She maintains a sympathetic acquaintance with all patients, takes care that the selection and preparation of food suits their tastes as well as possible, and by smoothing small difficulties contributes greatly to lighten the lot of the patient and the labor of the physician. Under some circumstances it may be convenient for one nurse to have charge of both the kitchen and the ward, and to supervise also the qualitative testing and recording of the urine.

The assistant diet nurses vary in number with the number of patients and the degree of detail required. Labor is saved at the

expense of some slight inaccuracy by weighing certain foods after cooking, by estimating certain other foods, etc. Servants at lower wages can save both the nurses' time and some of the more disagreeable features of the work. In this hospital every kind of food has been weighed accurately raw, and cooked separately for each patient. With this arrangement, one assistant nurse for about eight patients has been needed. If the service is rotating, an assistant nurse should if possible spend at least three months in the kitchen continuously; otherwise both time and accuracy are sacrificed in teaching new nurses. At the end of the three months she should be familiar not only with the cooking but also with the duties of the head nurse.

B. EQUIPMENT.

The equipment is mostly that of an ordinary kitchen. A few special articles have been found useful, as follows:

Diet scales.—An accurate spring balance has been used for weighing the individual food portions. In construction it is similar to the ordinary letter scales. This model is manufactured by Chatillon and Company, 85 Cliff Street, New York. The price, formerly \$5.00, is now \$7.50. Each patient buys such a balance preparatory to returning home. The dial is movable, so that it can be set at zero after the dish for receiving food is placed on the weighing stage. The weight of the food can then be read directly in grams. The quickness and convenience of such an instrument is important for prolonged fidelity in weighing food, for few patients will trouble themselves through months and years with the tediousness of ordinary scales and weights.

Steamer.—A well known form of steam cooker has been used for cooking vegetables without loss of carbohydrate. The reservoir at the bottom contains water; the compartments above hold the vegetables. As the steamer is constructed on the unit system, few or many of the compartments may be used at any time as needed. By this means a number of different vegetables can be steamed simultaneously, and the more easily cooked ones can be removed before the others.

Slide Rule.—Nurses who are to calculate many diets can save time

and trouble in multiplication by learning to use a simple slide rule. A convenient one is the "Merchant's," obtainable from the Keuffel and Esser Company, 127 Fulton Street, New York City.

Adding Machine.—Additions have been performed with the Golden Gem Adding Machine, manufactured by the Automatic Adding Machine Company, 148 Duane Street, New York City. A small and inexpensive instrument of this sort aids not only in time-saving but also in accuracy.

Records.—A twofold record of diets has been kept. A more detailed separate diet chart shows each individual food item for each meal, together with the totals, as illustrated in the specimen diets hereafter. A statement of the totals for the day is also entered in the laboratory chart, in order that the relation between diet and laboratory findings may be evident at a glance.

One general form of laboratory chart has been used since the early organization of the work, with slight modifications as needed from time to time (Table III). It measures 30 by 90 cm., and folds so as to conform to the clinical charts. In the table two figures are given for carbohydrate, protein, and fat for each day. The upper figure (in bold face type) denotes calories, the lower figure (in ordinary type) grams. For convenience in entering on the chart, the two figures are written in the form of a fraction; the figure above the line (calories) is written in red ink, that below the line (grams) is written in black ink. Formerly there was a column for alcohol, but this has been dropped, and if alcohol is given on any rare occasion, it is written into the total calory column. There also was formerly a column for sodium bicarbonate, but as this is so seldom used, the column has been discontinued and any occasional doses of alkali entered in the "Remarks" column. Among foods, three columns are found under "Bacon," the abbreviations indicating the three forms in which it is served; first whole bacon; second crisp bacon, fried so as to reduce the fat content as low as possible; third the clear bacon fat, practically free from protein. These three forms serve different purposes, and yet the advantage of the bacon flavor is retained. The two columns under vegetables show the total weight respectively of carbohydrate-containing or thrice cooked kinds. The various "Remarks" columns give room for additional analyses or special notes, explanations, time of day, etc.

C. NOTES ON SPECIAL FEATURES OF THE MAINTENANCE DIET.

1. *Fast-Days*.—Occasional single days of fasting or greatly reduced diet have been prescribed in the after-treatment of all cases. They are taken at regular fixed periods, the length of the interval and the rigor of the program being proportioned to the severity of the diabetes. In the typical severe cases, a fast-day is taken once each week, the patients generally choosing Sunday for the purpose. In even the mildest cases, such a day is ordered at least once a month, more commonly once every 2 weeks. Individuals react differently. Some go about their usual affairs; others are comfortable in bed; others become weak and depressed. When discomfort persists even after habituation, and in any mild case when desirable, the ordeal is mitigated if possible. The addition of a few hundred grams of thrice cooked vegetables to the bran, soup, and coffee of an ordinary fast-day may give relief. Especially in milder cases, vegetable days are useful; not the old fashioned kind with fat and other additions, but only vegetables containing such carbohydrate as will not raise the blood sugar above 0.15 per cent and will leave it not above 0.1 per cent on the following morning. Protein and other foods necessarily diminish the benefit of a fast-day in proportion as they are allowed. Von Noorden's designation of fast-days as "metabolic Sundays" is suggestive. There is no evidence whether the same number of calories weekly will be borne any differently if distributed over 7 or 6 days. But as the body in other respects seems to function more efficiently by working 6 days and resting 1, it is possible that a similar principle may apply to metabolism; also, the patient may perhaps feel and work better if he takes the larger ration on 6 days and relaxes as completely as necessary on the 7th. The occasional relief from the metabolic burden may also be beneficial in even the mildest cases, in guarding against downward progress and in atoning for any chance indiscretions. Such days of special restriction are also a strong reminder of the existence of diabetes and the need of continuous precaution, so that they aid instead of hindering discipline. Regular fast-days are intended for prevention of symptoms. When fasting is compelled by the actual occurrence of glycosuria or hyperglycemia, the diet is wrong and must be changed.

2. *Water*.—There is no objection to mineral waters, but they are without special virtues and are unnecessary when good plain drinking water is available. Mineral springs and resorts should be rated solely according to the efficiency of their dietetic treatment, and in as far as curative influence is attributed to the water they constitute an unfavorable environment.

3. *Alcoholic Beverages*.—As stated, all alcohol habits are best discouraged, and as the calories of alcohol must strictly be counted in a limited diet, the patient will generally prefer more wholesome food. Light wines, as low as possible in both carbohydrate and calories, are probably best for those with whom alcoholic beverages are a habit too firmly fixed to be broken.

4. *Coffee or Tea*.—The use of weak tea or coffee, or Kaffee Hag, not more than three cups daily, has already been mentioned as permissible with fasting or any diet, except that a coffee habit has not been cultivated in persons not addicted to it. Joslin often substitutes a drink made of cocoa hulls.

5. *Milk*.—Sugar-free milk of satisfactory taste is prepared by D. Whiting and Sons, 570 Rutherford Avenue, Boston, Mass., and its keeping qualities are such that it can be shipped long distances. Little use has been made either of it or of home-made preparations of casein and washed cream (*i.e.* cream mixed with large volumes of water to remove lactose, and skimmed off after rising or centrifugation). Milk is important for children, but it is considered the best policy to regulate their total diet so as to create sufficient carbohydrate tolerance to enable them to take natural milk. Sugar-free milk would thus be needed only temporarily, or as part of the diet of diabetic infants.

6. *Soup*.—Thin soup made from bones or stock contains very little nutrition, but its warmth and flavor are highly gratifying, and it also supplies salts, and aids in serving bran biscuits, thrice cooked vegetables, and other articles having little taste. It has been allowed in quantities of 300 to 600 cc. daily, during fasting, carbohydrate tests, and all other diets. Sometimes beef tea, made from beef extract, has been used as a means of avoiding even the small quantities of protein of ordinary soup.

7. *Salt*.—Probably because of the rather monotonous and unsatisfying diet, patients with severe diabetes often crave surprising quantities of salt. Many of them develop edema on unrestricted salt intake. The susceptibility of individuals differs. Though no real harm has been seen from the edema, salt-free diet has sometimes temporarily been necessary to remove it, and for all severe cases sodium chloride is given in a weighed daily allowance like other items in the diet. The limit has commonly been 5 gm. daily; sometimes only 3 gm., occasionally as much as 8 gm. Numerous glass tubes containing such weighed quantities of salt are kept on hand in the diet kitchen. The nurse uses a part of the day's allowance for seasoning, and the rest is placed in a small salt shaker on the patient's tray, to be used at his discretion with one day's meals. The craving is generally not noticed when limitation of the supply prevents forming the abnormal habit.

8. *Meats*.—Meats are included in the diet according to their food value and the tastes and digestion of the patient. Eggs and vegetable proteins are available on the same basis. No indications of specific differences between proteins and no advantages in vegetarianism have been observed. For a low protein vegetarian diet, it would be necessary to use care in selecting the kinds of protein, to assure an adequate supply of all indispensable amino-acids.

9. *Fats*.—These are chosen on a similar basis of suitability. There is no need to pay attention to the content of higher or lower fatty acids from the standpoint of ketonuria. If anything, butter is preferable to olive oil.

10. *Raw and Steamed Vegetables*.—Since carbohydrate is desirable in the diet, it is obviously preferable to use vegetables without extraction when possible. Even ordinary boiling is a partial extraction. Therefore, for accurately retaining the food value, vegetables have been served either raw or steamed in the steamer above described. Additional mention may be made of canned vegetables, which are used either in this way or after thrice cooking if necessary. Canned or dried vegetables are important aids to the winter diet. Patients sometimes prepare their own supply in summer. The advantage of giving carbohydrate in the pleasant, varied, bulky, and satisfying form of vegetables, rather than in smaller quantities of

bread or cereals, is obvious. With green vegetables, eggs, butter, etc., there should be no fear of a lack of vitamins or other accessory substances in the diabetic diet.

11. *Thrice Cooked Vegetables.*—Whatever time a vegetable requires to cook is divided into three approximately equal periods, and the boiling water changed so as to make three extractions of carbohydrate. Each patient's portion is made ready for cooking as usual, weighed raw, and tied loosely in a single layer of cheese-cloth, and the portions for different patients thus boiled together in one large pot. The thrice cooked vegetables have been used to contribute bulk with negligible food value. They are so important for this purpose that the treatment would in some cases be almost impossible without them, and they add much comfort in other cases not quite so severe. The different kinds of vegetables vary in the degree to which they retain their flavor, but most are palatable and some are practically as appetizing as with ordinary cooking.

Their empirical use without analyses has entailed some uncertainty and inaccuracy in the present series. Such analyses before and after boiling or extraction have been made by Wardall.⁴⁷ There is always a question in interpreting such figures. The cellulose of which vegetables are largely composed is a carbohydrate, but indigestible. On the other hand, if starch and soluble carbohydrates are alone considered, there is a question whether other substances present may not become potential sugar-formers upon digestion. Furthermore it is possible that more or less starch inclosed within cellulose may not be utilizable. Phloridzinized animals could scarcely furnish fully conclusive results. Accordingly an empirical element remains, and numerous patients in the present series have had sufficiently severe diabetes that extracted vegetables could not be taken without limit. The empirical observations have closely agreed with Wardall's chemical proof that spinach, celery, and asparagus are the safest for this purpose. Cabbage, cauliflower, Brussels sprouts, and onions retain enough carbohydrate to cause glycosuria much more readily than the three first named. If only 1 per cent absorbable carbohydrate should remain, and if a kilogram of the vegetables should be given in a

⁴⁷ Wardall, R. A., *J. Am. Med. Assn.*, 1917, lxi, 1859-1862. See also Joslin's text, 2nd edition, p. 261.

day, it is clear that such carbohydrate content is important for a patient whose actual tolerance may be 5 gm. or less. As previously mentioned, this state of excessively low tolerance ought not to be allowed to persist; but nevertheless carbohydrate should always be reckoned as accurately as possible. There is no reason why patients whose tolerance is a little greater should not, at least for occasional variety, receive higher class vegetables which have been extracted to reduce their carbohydrate content; but analyses such as those of Wardall will be necessary before they can be used with accuracy. What can be done with fruits in this direction will also bear further investigation.

Besides a little carbohydrate, thrice cooked vegetables convey more or less salts, and may have some real importance in this respect. Blunt and Otis⁴⁸ found that spinach loses 50 per cent, string beans 43 per cent, navy beans 39 per cent, peas 36 per cent, and potatoes 22 per cent, respectively, of their iron in cooking. Salts of potassium and heavy metals are also furnished in utilizable form by such vegetables. Courtney, Fales, and Bartlett⁴⁹ investigated the salt content of vegetables boiled so thoroughly as to be comparable to the thrice cooked kind. Tables IV and V are reproductions of two of their tables.

This large loss of salts occurred in the first few minutes of boiling; for example, spinach boiled only 10 minutes had already lost 42.2 per cent of its ash; the very prolonged further boiling had relatively little effect. These authors confirm the well known marked predominance of bases over mineral acids in vegetables, and the assimilable character of these bases, which are probably in combination with organic acids. It is possible that the very high plasma bicarbonate (above rather than below 65 per cent) so often found in severe cases under rigid treatment may be attributable to the vegetable diet. With the customary liberal use of vegetables, diabetics should certainly suffer no lack as respects quantity, variety, or assimilability of the supply of mineral bases.

⁴⁸ Blunt, K., and Otis, F. A., *J. Home Economics*, 1917, ix, 213-218; *Chem. Abstr.*, 1917, xi, 2124.

⁴⁹ Courtney, A. M., Fales, H. L., and Bartlett, F. H., *Am. J. Dis. Child.*, 1917, xiv, 34-39.

For practical purposes, thrice cooked vegetables (generally spinach, celery, and asparagus) have been used in limited quantities without any food value being reckoned for them. The protein of green vege-

TABLE IV.

Content in Gm. of Solids of 100 Gm. of Vegetables Prepared by Boiling.

Vegetable.	Minutes boiled.	Solids.	Ash.	CaO	MgO	P ₂ O ₅	Cl	K ₂ O	Na ₂ O	H ₂ SO ₄	Fe ₂ O ₃	Total N.	N as protein.
Spinach..	90	8.30	1.172	0.305	0.035	0.123	0.036	0.238	0.068	0.034	0.0090	0.497	3.10
New Zealand spinach..	30	4.26	0.535	0.145	0.021	0.052	0.000	0.157	0.040	0.016	0.0154	0.236	1.48
Young... carrots	30	6.31	0.408	0.039	0.014	0.043	0.023	0.181	0.038	0.022	0.0070	0.108	0.67
Onions...	45	6.82	0.398	0.020	0.013	0.067	0.008	0.186	0.010	0.056	0.0026	0.189	1.18
String beans..	150	5.31	0.371	0.070	0.030	0.063	0.045	0.123	0.011	—	—	0.190	1.19
Asparagus....	30	4.59	0.370	0.038	0.021	0.101	0.024	0.174	0.001	0.025	Tr.	0.283	1.77
Potatoes.	30	20.51	—	—	—	—	—	—	—	—	—	—	—

TABLE V.

Percentage Lost in Water under Ordinary Boiling Conditions.

Vegetable.	Minutes boiled.	Solids.	Ash.	CaO	MgO	P ₂ O ₅	Cl	K ₂ O	Na ₂ O	H ₂ SO ₄	Fe ₂ O ₃	Total N.
Spinach.....	90	32.2	45.2	Tr.	61.5	48.2	71.1	64.8	61.1	57.2	28.2	23.1
New Zealand spinach....	30	41.3	72.2	3.6	81.0	70.2	100.0	81.9	77.8	78.7	50.8	22.3
Young carrots.....	30	37.5	47.8	28.4	41.6	34.6	57.1	47.3	48.8	49.9	Tr.	22.2
Onions.....	45	22.5	28.0	26.1	10.6	24.6	31.4	29.2	0	31.6	"	19.8
String beans.....	150	31.8	43.4	21.4	54.1	42.7	46.8	55.2	56.3	—	—	26.7
Asparagus.....	30	27.4	46.7	26.6	40.1	34.6	46.4	49.2	Tr.	52.1	Tr.	24.1
Potatoes.....	30	4.4	—	—	—	—	—	—	—	—	—	—

tables is known to be poorly absorbable.⁵⁰ Irrespective of any food content, diabetics should not be allowed to gorge themselves on these extracted vegetables. Those on reasonably liberal diets do not need them at all. The allowance for any patient is generally not more

⁵⁰ Rubner, M., *Berl. klin. Woch.*, 1916, No. 15.

than a kilogram per day, and less in proportion as ordinary vegetables can be used. Excessive quantities are a useless burden upon both the purse and the digestion.

12. *Fruits*.—Fruits are the best diabetic desserts, when they can be tolerated. Most patients can take at least grape-fruit. Within reasonable limits, there is no prejudice against fruits because of their carbohydrate being largely in the form of sugar. Neither is there a favorable bias because so much of the sugar is levulose, for in the long run the actual carbohydrate and total food values are probably the determining factors of a diet. Reference must be made to text-books for the proportions of different carbohydrates in fruits. The latest article that has chanced to come to notice is that of Eoff,⁵¹ showing that 52 to 75 per cent of the sugar in apple juice is levulose.

13. *Nuts*.—Some nuts resemble prepared diabetic foods in their low carbohydrate and high protein and fat content. They must be used with corresponding caution. No superior assimilation for nuts or other less common foods has been observed.

14. *Unusual Carbohydrates and Abnormal Modes of Administration*.—Notwithstanding more or less deceptive appearances of assimilation, little or no practical value is to be expected from caramel, pentose, 7-carbon sugars (hediosit), or other unusual food elements. Likewise no hope should be entertained of any special assimilability of glucose given by rectum or other abnormal way. It need only be noticed that no patient was ever saved from either starvation or coma by such means. Confusion will be avoided by recalling the faulty theory underlying such attempts. In acidosis, the only lasting benefit must come from relief of the metabolism which is breaking down, by reducing the diet especially in fat, and not from the introduction of strange compounds. In nutrition, the level of total diet and weight determined by the actual assimilative power is a limitation which cannot be cheated by artificial devices.

15. *Bran Bread or Biscuits*.—These are the only form of bread substitute used for the type of cases treated in this hospital. In milder cases bran can be used in various ways; for example, bread can be made of eggs, fat, and bran, or bran can be mixed with ordinary

⁵¹ Eoff, J. R., *J. Ind. and Eng. Chem.*, 1917, ix, 587-588.

flour to lower the carbohydrate and food value of the latter. But while severely diabetic patients crave some form of bread, they do not wish to devote any of their scanty protein or fat to this use. Accordingly the following recipe was developed for a bran-agar bread having no appreciable food value.

Bran Biscuits.

Bran, weighed dry.....	60 gm.
Agar-agar, powdered.....	6 "
Cold water.....	100 cc.

The bran is tied in cheese-cloth and hung under the cold water tap to wash (with stirring or kneading as required) until the water runs through clear. The agar is mixed in 100 cc. water (cold) and brought to the point of boiling. The agar solution (hot) is then added to the washed bran. The mixture is molded into three cakes and placed in a pan and when firm and cold baked until dry and crisp. Salt may be included in the recipe if desired. The biscuit or muffin shape may be chosen, but it has generally been preferred to make thin flat pieces like well browned toast. The toasting helps the flavor a little, and the dryness facilitates keeping.

The chief caution is necessary in the choice of bran. Ordinary bran flours or breakfast foods are high in carbohydrates. Some kinds of cheap bran contain middlings or other carbohydrate admixture. It is possible to buy purified bran, such as Kellogg's. But the bran ordinarily used for feeding cattle, which on inspection is seen to consist of coarse flakes of the outermost hull of the wheat, is obtainable very cheaply at feed stores, and is perfectly satisfactory when washed under the cold water tap for half an hour or more as above described.

Some patients like these tasteless bran rusks at once; others either accept or enjoy them after becoming used to them. They are best served hot, like toast, with butter, bacon fat, a fried egg, or even soup, to give them flavor. Besides contributing bulk, like the vegetables, the bran is still more active in favoring catharsis, and since its introduction the traditional constipation of diabetic patients has been almost unknown in this hospital. A few individuals cannot take the bran; in others sometimes indigestion or diarrhea limits the

amount. On general principles, an inert substance should not be taken to excess, and accordingly the allowance is generally no more than one or two of the above cakes at each meal.

Bran has never been responsible for glycosuria in this hospital, and is probably not digested to any important extent. The chemistry of bran, especially from the standpoint of digestion, is not thoroughly known. It is poor in cellulose (2 to 4 per cent in most analyses), and from its richness in protein and amides, phytin and other complex compounds, might supply the body with much nitrogen and phosphorus if digestible. Guareschi⁵² states that bran milled to an impalpable powder is 91 to 92 per cent digestible, and emphasizes its value for food and for vitamins. The fine milling therefore defeats the purpose for which bran is used in diabetes.

16. *Proprietary Foods*.—So called "diabetic" and "gluten" preparations have largely fallen into disrepute because of the rankly fraudulent character of so many of them. It is still very common for patients to announce that as soon as diabetes was discovered they began to eat gluten bread, with or without a doctor's orders; but knowledge on the subject is increasing, and it is becoming generally known that a physician should at least never order such a food without specifying a reliable brand.

The medical profession is indebted to Professor John P. Street for the most complete analyses of diabetic foods. The results are obtainable in the publications of the Connecticut Agricultural Experiment Station, especially the report for 1913, Part 1, with added analyses in the report for 1914, Part 5, and the report for 1915, Part 5. These data are the best basis for the choice of a diabetic preparation. With improved technical methods, the best brands have been brought to a high state of perfection from the standpoint of carbohydrate-freedom and agreeable taste. Without invidious distinctions, mention may be made of American made examples of the three principal classes of such foods; *viz.*, gluten flour, which is manufactured in high purity by Hermann Barker, Somerville, Mass.; casein flour and muffins, as prepared by Lister Brothers, 110 West 40th Street, New

⁵² Cf. Guareschi, I., *Ind. chim., min. e metal.*; 1917, iv, 97-103; *Chem. Abstr.*, 1917, xi, 2124. Holmes (Holmes, A. D., *U. S. Dept. Agric., Bull.* 751, 1919) has obtained a coefficient of digestibility of only 45 per cent for finely milled bran.

York City; and soy bean flour, one brand of which is made by the Cereo Company, Tappan, New York, while the most extensive use of soy beans by diabetics at present is in the form of the "Hepco" flour, dodgers, etc., made by the Waukeshia Health Products Company, Waukeshia, Wisconsin. For complete lists and analyses of such foods, reference must be made to Street's reports or Joslin's text-book.

The essential objection to all such bread substitutes is that in absence of carbohydrate, they have necessarily been composed of protein and fat, and thus have represented highly concentrated forms of food. Both physicians and patients have often viewed these breads as harmless, or even commendable by reason of their high protein and food value. The great amount of protein and calories that can be so easily and inadvertently consumed in this way is capable of tremendous damage. Janney⁵⁸ has pointed out that the potential carbohydrate represented in the protein often exceeds the total carbohydrate of ordinary bread. It is necessary to warn strongly against this indiscriminate misuse of even the best preparations, in which the manufacturer is not to blame. There is no objection to making up as large a proportion of the diet as desired from these flours, provided the total diet is accurately reckoned and restricted as usual. For cases of the grade of severity treated in this hospital, the use of such preparations has been abandoned, simply because the patients prefer to take their protein and fat in meat, eggs, bacon, butter, etc., rather than in flour or bread.

Because of the very limited quantity of these concentrated foods which can safely be included in any diet, and because of the dangerous ease with which patients can be tempted to overstep their real tolerance by taking only a small quantity in excess, the manufacturers of some of the better brands are moving in the direction of reducing the undesirably high food value by the introduction of some indigestible substitute for carbohydrate. A non-utilizable flour might be employed in three ways; first, to dilute ordinary flour for mild cases, so as to reduce the carbohydrate and food value of wheat, corn, or other bread; second, to dilute the special diabetic flours, so as to make them permissible more often and in larger quantities, while at the same:

⁵⁸ Janney, N. W., *Arch. Int. Med.*, 1916, xviii, 584-605.

time probably reducing their cost; third, for making an entirely non-nutritious bread substitute, perhaps finer and more agreeable than the bran bread. An extreme illustration of the feasibility of the use of a non-nutritious flour can be gained by making a batter with egg, spices, and impalpable talcum powder, and frying it crisp. This will appear more satisfying than the egg fried alone. While talcum is inert and harmless, it is scarcely to be recommended for eating, and a non-utilizable flour for practical use is most likely to be found in the vegetable kingdom, probably in some form of cellulose or other polysaccharide.⁵⁴ Ridicule or opposition may be aroused by suggestions of flour from cotton, peanut-shells, corn-pith, etc., and the technical difficulties also have thus far baffled manufacturers. The German experience in the recent war, that large quantities of wood flour may cause intestinal disturbance, was confirmed in one short test with diabetics; but the long experience with bran and shorter trials of other indigestible substances have shown that the prudent use of these is safe and practicable. Critics should bear in mind the following facts: first, it is generally conceded that the food of civilized man is overconcentrated, frequently excessive, and subject to improvement by an admixture of indigestible material, as in coarse vegetables; second, the diabetic flours which it is proposed to dilute are dry protein-fat powders representing an unnaturally concentrated form of food; third, diabetics must be more closely limited in their total food intake than normal persons, and yet they have the usual, even if not an excessive craving both for bread and for bulk.

D. GENERAL SCHEME AND SPECIMEN DIETS.

Two general plans are possible for diabetic diets. The one which has been customary in the past has aimed to give the patient substitutes as nearly as possible resembling the accustomed dishes which he must forego. Accordingly, diabetic cook-books have been filled

⁵⁴ Concerning some indigestible carbohydrates, see Mendel, L. B., *Centralbl. ges. Physiol. u. Path. Stoffwechs.*, 1908, iii, 641-654. Mendel, L. B., and Swartz, M. D., *Am. J. Med. Sc.*, 1910, cxxxix, 422-426. Swartz, M. D., *Tr. Connecticut Acad. Arts. and Sci.*, 1911, xvi, 247. Concerning the German experience with wood flour, see Salomon, H., *Wien. med. Woch.*, Dec. 15, 1917 (favorable), and Neumann, R. O., *Vrtiljschr. gerichtl. Med.*, 3rd edition, li, pt. ii, (unfavorable).

with composite recipes, carbohydrate-free puddings, saccharine sweetening, imitation milk, and a host of similar artifices. The most convenient way to manage such a diet accurately is to weigh out the day's allowance of eggs, fat, etc., in the morning and use for cooking the different meals as required. It may be urged that habits of food are hard to break, and that a diabetic should not be deprived of gustatory pleasure unnecessarily. It may be objected on the other hand that such diets tantalize and tempt more than they satisfy; that saccharine keeps alive the taste for sugar, that the liability to carelessness is increased, and that a patient does best to face squarely the fact of his diabetes and the necessary restrictions, and to resolve to eat to live rather than live to eat, especially since care in diet is the means whereby all the other pleasures and advantages of the world are opened to him in fullest measure.

It is generally believed that the plainest and simplest diets are the most wholesome for mankind in general. It has therefore been considered inadvisable to take such great pains to depart from such a diet for diabetics. Not only is simplicity highly important for accuracy, fidelity, convenience, economy, and healthful habits, but in the long run the simple diet has proved the most satisfying and the least irksome. The patient begins such a Spartan régime immediately after his initial fast in the hospital, when anything tastes good, and by the time he leaves the hospital his new habit of diet is established. With simple menus and a balanced ration, diabetics are free from abnormal cravings, and natural hunger on reduced diets is also easier to appease.

Simplicity does not mean unpleasantness to sight or taste. Here the skill of the diet nurse or cook comes into play. The refinement of the table service, even though not expensive, has its esthetic value. Salads and other simple dishes can be made attractive in appearance. A single egg can loom surprisingly large to the eye if beaten into a fluffy omelette or soufflé. Variety in cooking and combining the same foods varies them to the taste. Vegetables offer variety in soups, and the different ways of serving meat are well known. Eggs, bacon grease, meat, or the juice from meat give variety and taste to thrice cooked vegetables, and even to bran muffins. There is no inherent objection to condiments or spices, but these, except salt, have been little used, since the diabetic appetite generally needs no stimulation,

and the simple taste of plain foods is sufficiently appreciated. Coffee lovers generally learn readily to like their drink black, without saccharine. A little fruit is a sufficient dessert in most cases. The desire for cake, puddings, and other luxuries is discouraged by disuse. Exceptions have been made only in some extremely severe cases on minimal diets, since small treats mean so much to these patients. Agar jelly, ices, sherbets, etc., can be flavored with saccharine, coffee, wine, brandy, fruit juices, or sugar-free caramel (the quantities required being very small). Likewise agar with soup or beef extract makes an agreeable meat jelly. Such tricks often eke out a low diet or relieve a hard fast-day in the worst cases; but the better fed class of patients do not need them.

The physician who cannot calculate diets to suit his individual cases, but is dependent upon text-book menus, will not be able to substitute celery or spinach when one or the other is disliked, and will occasionally meet patients who know more about diets than he. Anybody who has a list of food values and can use the decimal system can easily make up the simple diets required by diabetics. The unwise complexity of dishes in the past has doubtless been largely responsible for the unfortunate helplessness of so many physicians in this regard. The use of the metric system is not a difficulty but a great convenience, and it can be learned in a few minutes by those unaccustomed to it. Though the energy value of carbohydrate and protein is 4.1 calories per gm., and of fat 9.3 calories per gm., it is sufficiently accurate for ordinary purposes to reckon them as 4 and 9 calories respectively.⁵⁵ One elementary example should make the method clear.

Suppose that a patient's weight is 50 kilograms, that his tolerance in the carbohydrate test was 180 gm., and that he is to be given a mixed diet containing one-sixth of this maximal carbohydrate tolerance, together with 1.5 gm. protein and 30 calories per kilogram.

⁵⁵ Food chemists are well aware of the technical considerations which make absolute exactness impossible in the ordinary reckoning of a diet. A practical point is that the number of calories obtained by multiplying the total grams of protein, carbohydrate, and fat by the proper factors, and the number found by adding up the calories given in food tables for the individual meats, vegetables, and other foods served, are seldom identical. Either method is permissible.

One-sixth of the carbohydrate tolerance of 180 gm. is 30 gm. Any desired vegetables are selected from food tables to make up this total of 30 gm. for the day, and divided between the meals at will. The protein, fat, and calories in the vegetables chosen must be reckoned, which will give a result such as shown in Table VI.

TABLE VI.

Food.		Carbohydrate.	Protein.	Fat.	
	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>	
Breakfast.					
Canned asparagus.....	150	4.2	2.3	0.2	
Dinner.					
Lettuce.....	50	1.7	0.7	0.2	
Celery.....	37	1.1	0.5		
Canned Brussels sprouts.....	148	5.0	2.2	0.1	
Raw tomato.....	142	5.5	1.1	0.5	
Supper.					
Lettuce.....	50	1.7	0.7	0.2	
Raw tomato.....	150	5.9	1.2	0.6	
Cauliflower.....	86	5.0	1.4	0.6	
Gm.		30.0	10.0	2.4	
Calories		120.0	41.0	22.3	183

TABLE VII.

Food.		Protein.	Fat.	
	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>	
Breakfast.				
Eggs.....	100	14.8	10.6	
Bacon.....	50	5.0	33.6	
Dinner.				
Roast chicken.....	57	18.3	2.5	
Cream cheese.....	25	6.5	7.9	
Supper.				
Eggs.....	100	14.8	10.6	
Bacon.....	50	5.0	33.6	
Gm.		64.6	98.8	
Calories		258.0	899.0	1157.0

Taking up next the protein allowance, this, at 1.5 gm. per kilogram for a weight of 50 kilograms, will amount to 75 gm. of protein. Since 10.4 gm. of protein is contained in the vegetables already chosen, this leaves 64.6 gm. yet to be supplied for the day (Table VII).

TABLE VIII.

Food.		Carbo- hydrate.	Protein.	Fat.
gm.	cc.	gm.	gm.	gm.
Breakfast.				
Eggs.....	100		14.8	10.6
Bacon.....	50		5.0	33.6
Canned asparagus.....	150	4.2	2.3	0.2
Butter.....	5			4.1
Bran biscuits (2).....				
Coffee.....		150		
Clear soup.....		150		
Dinner.				
Roast chicken.....	57		18.3	2.5
Butter.....	10			8.2
Lettuce.....	50	1.7	0.7	0.2
Celery.....	37	1.1	0.5	
Canned Brussels sprouts.....	148	5.0	2.2	0.1
Raw tomato.....	142	5.5	1.1	0.5
Cream cheese.....	25		6.5	7.9
Bran biscuits (2).....				
Kaffee Hag.....		150		
Clear soup.....		150		
Supper.				
Eggs.....	100		14.8	10.6
Bacon.....	50		5.0	33.6
Butter.....	9			7.4
Lettuce.....	50	1.7	0.7	0.2
Raw tomato.....	150	5.9	1.2	0.6
Cauliflower.....	86	5.0	1.4	0.6
Bran biscuits (2).....				
Kaffee Hag.....		150		
Clear soup.....		150		
Gm.....		30.0	75.0	120.6
Calories.....		120.0	300.0	1085.0
				1505

A ration of 30 calories per kilogram for a weight of 50 kilograms means 1500 calories for the day. Since the foods chosen for carbohydrate and those chosen for protein together represent $180 + 1157 =$

1337 calories, this leaves 163 calories yet to be supplied in the form of fat. It is now necessary to divide the 163 calories by 9, thus showing 18 gm. as the quantity of fat needed. This could be supplied by 18 gm. of olive oil, or 24 gm. of butter, or the equivalent in any other fat. The total diet for the day is shown in Table VIII.

The specimen diets in Tables IX to XV are given as suggestions. In them, the factors 4.1 and 9.3 are used, as customary in this hospital.

TABLE IX.

Carbohydrate Tolerance Test.
A Day's Diet with 30 Gm. Carbohydrate.

Food.	Food.		Protein.	Fat.	Carbo-	
	gm.	cc.	gm.	gm.	hydrate.	
Breakfast.						
Canned asparagus.....	150		2.3	0.2	4.2	
Coffee.....		150				
Clear soup.....		150				
Dinner.						
Lettuce.....	25		0.4	0.1	0.9	
Celery.....	75		1.0		2.2	
Canned Brussels sprouts.....	150		2.2	0.1	5.1	
Canned okra.....	65		0.4	0.05	2.3	
Clear soup.....		150				
Kaffee Hag.....		150				
Supper.						
Lettuce.....	25		0.4	0.1	0.9	
Raw tomato.....	150		1.2	0.6	5.9	
Spinach.....	200		4.2	1.0	6.2	
Canned okra.....	66		0.5	0.05	2.4	
Clear soup.....		150				
Kaffee Hag.....		150				
m.....			12.5	2.2	30.0	
Calories.....			51.0	20.0	123.0	194

TABLE X.
Carbohydrate Tolerance Test.
A Day's Diet with 100 Gm. Carbohydrate.

Food.		Protein.	Fat.	Carbo- hydrate.	
	gm.	cc.	gm.	gm.	
Breakfast.					
Canned asparagus.....	150		2.3	0.2	4.2
Beets.....	208		3.2	0.2	20.0
Celery.....	50		0.7	0.05	1.5
Clear soup.....		150			
Coffee.....		150			
Dinner.					
Lettuce.....	100		1.3	0.4	3.3
Raw tomato.....	203		1.6	0.8	7.9
Carrots.....	218		2.3	0.8	20.0
Cabbage.....	172		3.5	0.6	10.0
Clear soup.....		150			
Canned okra.....	90		0.7	0.1	3.2
Celery.....	50		0.6	0.05	1.5
Kaffee Hag.....		150			
Supper.					
Lettuce.....	50		1.5	0.2	1.7
Celery.....	100		1.4	0.1	3.0
Turnips.....	230		3.2	0.4	20.0
Clear soup.....		150			
Canned okra.....	90		0.6	0.1	3.2
Raw tomato.....	54		0.4	0.2	2.1
Kaffee Hag.....		150			
Gm.			23.3	4.3	101.6
Calories.....			95.5	45.6	416.6
					557.7

TABLE XI.

Carbohydrate Tolerance Test.

A Day's Diet with 250 Gm. Carbohydrate.

Food.			Protein.	Fat.	Carbo-	
	gm.	cc.	gm.	gm.	hydrate.	
Breakfast.						
Orange.....	104		0.8	0.6	10.0	
Canned peas.....	204		7.2	0.4	20.0	
Carrots.....	218		2.3	0.8	20.0	
Rice.....	39		3.0	0.1	30.0	
Coffee.....		150				
Clear soup.....		150				
Dinner.						
Grapefruit.....	200				10.0	
Lettuce.....	100		1.3	0.4	3.3	
Canned asparagus.....	150		2.3	0.2	4.2	
Potato.....	168		2.0	0.1	30.0	
Canned lima beans.....	205		8.2	0.6	30.0	
Turnips.....	230		3.2	0.4	20.0	
Kaffee Hag.....		150				
Clear soup.....		150				
Supper.						
Apple.....	120		0.6	0.6	20.0	
Lettuce.....	100		1.3	0.4	3.3	
Raw tomato.....	64		0.5	0.2	2.5	
Parsnips.....	122		2.0	0.6	19.6	
Onions.....	303		5.1	1.2	30.0	
Kaffee Hag.....		150				
Clear soup.....		150				
Gm			39.8	6.6	252.9	
Calories			159.1	61.4	1025.0	1246

TABLE XII.

Exclusive Protein Diet, as Sometimes Used for Bringing Down Blood Sugar.

Food.			Protein.	Fat	
	gm.	cc.	gm.	gm.	
Breakfast.					
Egg white.....	162		20.0	0.3	
Celery T. C.*.....	200				
Spinach "	100				
Coffee.....		150			
Clear soup.....		150			
Bran biscuits (2).....					
Dinner.					
Flounder.....	216		30.0	1.2	
Sauerkraut T. C.....	200				
Brussels sprouts T. C.....	200				
Bran biscuits (2).....					
Coffee.....		150			
Soup.....		150			
Supper.					
Roast chicken.....	78		25.0	3.4	
Cauliflower T. C.....	200				
Asparagus "	100				
Bran biscuits (2).....					
Kaffee Hag.....		150			
Soup.....		150			
Gm.....			75.0	4.9	
Calories.....			307.0	45.0	352

* T. C. indicates thrice cooked.

TABLE XIII.

Example of a Low Maintenance Diet for a Case of Extreme Severity; Body Weight 30 to 40 Kilograms.

Food.		Protein.		Fat.	Carbo- hydrate.
		gm.	gm.	gm.	gm.
Breakfast.					
Eggs.....	100	14.9	10.6		
Bacon.....	50	5.0	33.6		
Butter.....	7		5.8		
Celery T. C.....	200				
Bran biscuits (2).....					
Coffee.....					150
Clear soup.....					150
Dinner.					
Flounder.....	72	10.0	0.4		
Butter.....	7		5.8		
Lettuce.....	25	0.4	0.1		0.9
Raw tomato.....	34	0.2	0.1		1.3
Cauliflower T. C.....	200				
Asparagus “.....	200				
Bran biscuits (2).....					
Kaffee Hag.....					150
Clear soup.....					150
Sup per.					
Eggs.....	100	14.9	10.6		
Cream cheese.....	13	3.3	4.1		
Butter.....	7		5.8		
Lettuce.....	25	0.4	0.1		0.9
Canned asparagus.....	71	1.0			2.0
Spinach T. C.....	200				
Cabbage “.....	200				
Bran biscuits (2).....					
Kaffee Hag.....					150
Clear soup.....					150
Gm.....		50.1	77.0	5.1	
Calories.....		205.0	716.1	21.0	942

TABLE XIV.

Specimen Diet of a Child Aged 3 or 4 Years (Patient No. 73), with Extremely Severe Diabetes; Weight 9 Kilograms.

Food.		Protein.	Fat.	Carbo- hydrate.
	gm.	cc.	gm.	gm.
7:30 a.m.				
Egg.....	50		7.4	5.3
Milk.....	25		0.8	1.0
Butter.....	7			5.8
Asparagus T. C.....	75			
Clear soup.....		100		
Bran biscuit (1).....				
11:00 a.m.				
Egg.....	50		7.4	5.3
Milk.....	25		0.8	1.0
Canned asparagus.....	107		1.6	0.1
Butter.....	6			4.9
Clear soup.....		100		
1:00 p.m.				
Milk.....	50		1.6	2.0
Butter.....	6			4.9
Raw tomato.....	60		0.5	0.2
Clear soup.....		100		2.3
Bran biscuit (1).....				
3:00 p.m.				
Milk.....	25		0.8	1.0
Clear soup.....		100		1.3
5:30 p.m.				
Egg.....	50		7.4	5.3
Milk.....	25		0.8	1.0
Butter.....	7			5.8
Celery.....	75		1.0	
Bran biscuit (1).....				2.2
Clear soup.....		100		
Gm.....			30.1	43.6
Calories.....			125.0	405.0
				15.2
				62.3
				591

TABLE XV.

Example of a Maintenance Diet, Showing the Substitutions Indicated for Patients Who Cannot Perform Calculations for Themselves.

Protein 90 gm. Carbohydrate 50 gm. Calories 2000.

Food.		Protein.	Fat.	Carbohydrate.	Substitutes.
gm.	cc.	gm.	gm.	gm.	
Breakfast.					
Eggs.....	100	14.8	10.6		
Bacon.....	50	5.0	33.6		
Butter.....	13		10.7		
Canned asparagus.	150	2.3	0.2	4.2	Fresh asparagus 124 gm. (in place of canned).
Bran biscuit (2)...					
Coffee.....	150				
Clear soup.....	150				
Dinner.					
Roast beef.	96	22.3	1.5		Roast chicken 69 gm. less butter 2 gm. } (in Flounder 160 gm. } place of Veal 79 gm. } roast Roast Lamb 113 gm. less butter 15 gm. } beef).
Butter.....	20		16.5		
Lettuce.....	25	0.4	0.1	0.8	
Raw tomato.....	150	1.2	0.6	5.9	Radishes 25 gm. (in place of lettuce).
Canned Brussels sprouts	295	4.4	0.3	10.0	Beets 61 gm. (in place of tomato).
Cauliflower.	100	1.6	0.8	6.0	Carrots 109 gm. (in place of Brussels sprouts).
Cream cheese.....	19	4.9	6.0		Celery 200 gm. (in place of cauliflower).
Bran biscuits (2) ..	150				
Kaffee Hag.....	150				
Clear soup.....					
Supper.					
Eggs.	100	14.8	10.6		
Bacon.	50	5.0	33.6		
Butter.....	20		16.5		
Lettuce.....	25	0.4	0.1	0.8	
Celery.....	75	1.0		2.2	Dill pickle 82 gm. (in place of celery).
Spinach.....	323	6.7	1.6	10.0	String beans 107 gm. (in place of spinach).
Cabbage.....	172	3.5	0.6	10.0	Turnips 115 gm. (in place of cabbage).
Cream cheese.....	19	4.9	6.0		Sauerkraut 228 gm. (in place of cabbage).
Bran biscuits (2)..					
Kaffee Hag.....	150				
Clear soup.....	150				
Gm.....		93.2	149.9	50.0	
Calories.....		369.0	1394.1	205.0	1968

CARBOHYDRATE

CALORIES

41

36.9

32.6

28.7

24.6

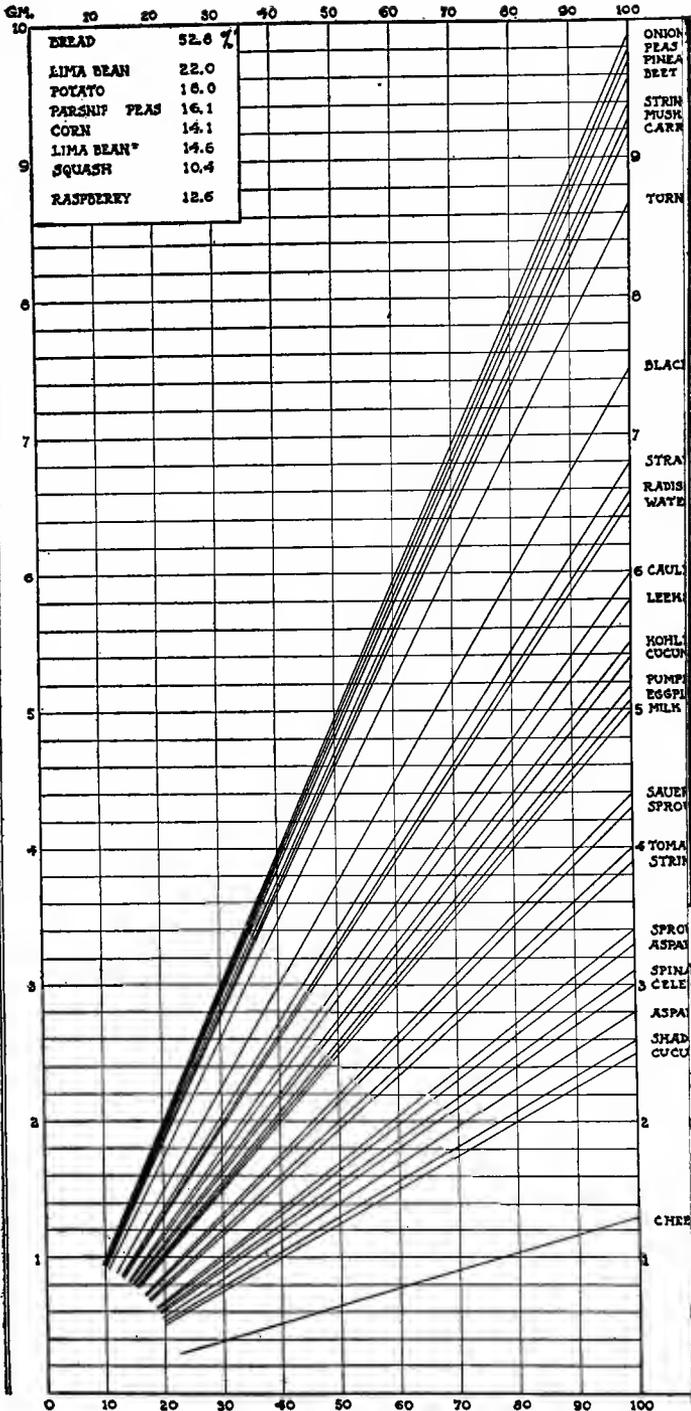
20.5

16.4

12.3

8.2

4.1



- ONION
- PEAS
- PINEA
- BETT
- STRN
- PUSH
- CARR
- TORN
- BLAC
- STRA
- RADIS
- WATE
- 6 CAUL
- LEEK
- HOLL
- COGUR
- PUMPI
- EGGPL
- 5 MILK
- SAUER
- SPROT
- 4 TOMA
- STRN
- SPRO
- ASPA
- 3 CELI
- SPINA
- ASPA
- SHAD
- CUCU
- CHEE

FOODSTUFFS IN GM.

E. FOOD TABLES.

The accompanying graphic charts illustrate a short method for approximating food values, which can be made both more convenient and more accurate if enlarged and used for wall charts. The abscissæ represent grams of foodstuffs; the ordinates show both grams and calories of carbohydrate, protein, and fat respectively. Thus, taking the number 50 at the bottom of the carbohydrate chart, and following the line up to where it cuts the line for sauerkraut, it is seen at a glance that 50 gm. of sauerkraut contain 2 gm. or 8.2 calories of carbohydrate. Conversely, if it is desired to select food containing 5 gm., of carbohydrate, one may start at the number 5 on the left of the chart and by following it across may see that this quantity is represented in about 51 gm. of onions, about 67 gm. of blackberries, about 100 gm. of either grapefruit or milk, etc. The same method is used in finding protein and fat values in the other charts.

The food values in Tables XVI to XIX are taken almost entirely from the tables of Bryant and Atwater, *Bulletin 28, Department of Agriculture, Bureau of Experiment Stations*, Washington, D. C. Similar tables, along with analyses of cooked foods, etc., are given in the book on "Food Values," by Edwin A. Locke, Appleton and Company, 1914.

Abundant data for diabetic needs are contained in Joslin's textbook. The list given in Chart 1 and Tables XVI to XIX is not extensive, but yet contains nearly everything found necessary for the diets in this hospital. Copies are supplied to patients for reckoning their diets at home.

TABLE XVI.

*Meat and Fish.**

Edible portion.	Protein.	Fat.	Carbohy- drate.
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Meats.			
Bacon.....	10.0	67.2	0
Beef, sirloin, very lean.....	20.5	6.4	0
“ round “ “	20.8	5.8	0
Chicken.....	22.8	1.8	0
Ham, very lean.....	20.2	20.8	0
Pork, tenderloin.....	19.5	14.4	0
“ loin.....	19.7	19.0	0
Lamb.....	19.1	12.4	0
Veal.....	21.0	3.6	0
Fresh fish.			
Sea bass.....	18.8	0.5	0
Blue fish.....	19.0	1.2	0
Cod, fresh.....	15.8	0.4	0
Flounder.....	13.9	0.6	0
Halibut.....	18.3	5.2	0
Salmon.....	20.6	12.8	0
Shad roe.....	20.9	3.8	2.6
“ whole.....	18.6	9.5	0

*Uncooked values.

TABLE XVII.

Vegetables, in Order of Their Carbohydrate Content from Lowest to Highest.

Edible portion.	Protein.	Fat.	Carbohydrate.
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
*Mushrooms (range 2 to 18 per cent).....	(3.5)	(0.4)	(6.0)
Cucumbers, fresh.....	0.8	0.2	2.5
Asparagus, canned.....	1.5	0.1	2.8
Celery, fresh.....	1.4	0.1	3.0
Spinach ".....	2.1	0.5	3.1
Asparagus ".....	1.8	0.2	3.3
Lettuce ".....	1.3	0.4	3.3
Brussels sprouts, canned.....	1.5	0.1	3.4
Rhubarb, fresh.....	0.6	0.7	3.6
Tomatoes ".....	0.8	0.4	3.9
" "canned.....	1.2	0.2	4.0
Brussels sprouts, fresh.....	4.7	1.1	4.3
Sauerkraut.....	1.5	0.8	4.4
Artichokes, canned.....	0.8	0.2	5.0
Leeks.....	1.2	0.5	5.8
Eggplant, fresh.....	1.2	0.3	5.1
Pumpkin ".....	1.0	0.1	5.2
Cucumber pickles.....	0.5	0.5	5.4
Kohlrabi, fresh.....	2.0	0.1	5.5
Cabbage.....	2.1	0.4	5.8
Cauliflower.....	1.6	0.8	6.0
Radishes.....	1.4	0.1	6.6
Turnips.....	1.4	0.2	8.7
Carrots.....	1.4	0.4	9.2
Beans, string, fresh.....	2.2	0.4	9.4
Beets, fresh.....	1.6	0.1	9.6
Peas, green, canned.....	3.6	0.2	9.8
Onions, fresh.....	1.7	0.4	9.9
Squash ".....	1.6	0.6	10.4
Lima beans, canned.....	4.0	0.3	14.0
Corn, green, fresh.....	2.8	1.1	14.1
Peas " ".....	4.4	0.5	16.1
Parsnip, fresh.....	1.7	0.6	16.1
Artichoke ".....	2.6	0.2	16.7
Potatoes.....	2.1	0.1	18.0
Lima beans ".....	7.1	0.7	22.0

* Wardall, (*J. Am. Med. Assn.*, 1917, lxi, 1859-1862) pointed out that the carbohydrate of ordinary mushrooms is in some non-extractable form, and the nitrogen according to Mendel's analyses is likewise in non-protein, non-utilizable compounds. The figures in the above table are therefore placed in parentheses to indicate their misleading nature. It would appear that ordinary mushrooms may be reckoned as having no appreciable food value, and that they therefore may be a welcome feature of the diabetic diet.

TABLE XVIII.

Fruits, In Order of Their Carbohydrate Content, from Lowest to Highest.

Edible portion.	Protein.	Fat.	Carbohydrate.
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Grapefruit.....			5.0
Watermelon.....	0.3	0.1	6.5
Strawberries.....	1.0	0.1	6.8
Blackberries.....	0.9	0.2	7.5
Muskmelon.....	0.6	—	9.3
Peaches.....	0.7	0.1	9.4
Pineapple.....	0.4	0.3	9.7
Orange.....	0.8	0.6	9.7
Lemon juice.....	—	—	9.8
Cranberries.....	0.5	0.7	10.1
Raspberries.....	1.0	1.0	12.6
Grapes.....	1.0	1.3	13.3
Apricots.....	1.1	—	13.4
Pears.....	0.6	0.8	14.2
Apples.....	0.5	0.5	16.6

TABLE XIX.

Dairy Products.

Edible portion.	Protein.	Fat.	Carbohydrate.
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Eggs.....	14.9	10.6	
Butter.....		82.4	
Whole milk.....	3.3	4.0	5.0
Buttermilk.....	3.0	0.5	4.8
Whiting's milk*.....	5.97	7.36	
Cream, average.....	2.5	18.5	4.5
Cheese.			
Dutch.....	37.1	17.7	
Cheddar.....	28.2	32.0	
Cheshire.....	26.9	31.6	
Cream.....	25.9	31.7	
American, pale.....	28.8	36.2	
" red.....	29.6	38.3	
Limburger.....	23.0	29.4	0.4
Boudon.....	15.4	21.7	0.7
Swiss.....	27.6	34.9	1.3
Brie.....	15.9	21.0	1.4
Neufchâtel.....	18.7	27.4	1.5
Roquefort.....	22.6	29.5	1.8

* D. Whiting and Sons, 570 Rutherford Avenue, Boston, Mass.

CHAPTER III.

Case Records.

Seventy-six cases have been selected for publication, for reasons stated in Chapter VII. Graphic charts have been chosen as the clearest and most compact means of presenting the large mass of clinical and chemical data. With a little attention to the key shown on all the charts, it is believed that they will be found simple and self-explanatory. The curves of ammonia, total acetone, and total acidity of the urine have been plotted as cubic centimeters of decinormal solution, for the sake of chemical calculations and comparisons. This plan will doubtless prove somewhat confusing to many clinicians, but the tables and summaries in the case histories express the results in grams. The written history of each case is supposed to be followed in conjunction with the graphic chart, and reference from one to the other will be necessary to make both plain.

Table I is a general summary of the entire series. The data mostly tell their own story. Further details, of the age incidence, complications, results of treatment, etc., are shown in Chapter VII. The etiologic relations are discussed in Chapter VIII.

CASE NO. 1.

Female, unmarried, age 28 yrs. American; no occupation. Admitted Feb. 24, 1914.

Family History.—Grandparents lived to healthy old age. Father living, aged 58, has arterial hypertension, neuralgia, and tendency to melancholia. Mother died at birth of this patient. An uncle died of tuberculosis. One full brother of patient died at 16 of appendicitis. One half-sister aged 22 has nephritis, consequent upon scarlatina.

Past History.—No childhood diseases except measles and one dysenteric attack. Normal menstruation began at 13. Patient graduated from university at 20. She has had a nervous, overactive life with late hours and irregular eating. Was considered remarkable among her family and friends for the amount of candy and sweets she consumed. Normal weight 115 to 120 pounds. July, 1912, patient's fiancé died of accidental poisoning. Patient became melancholic and kept

more to herself, while eating still more candy than usual. She and her parents were inclined to attribute onset of diabetes to grief.

Present Illness.—In Jan., 1913, abnormal thirst was first noted. In Mar., pruritus vulvæ. In May, menstruation stopped and remained absent. Hair fell out and is still thin. July, 1913, diagnosis of diabetes was made and routine diet prescribed, which was taken in huge quantities owing to polyphagia. Symptoms persisted and increased till Jan. 4, 1914, when she began treatment at a well known diabetic sanitarium. Qualitative and quantitative restriction of the diet, oat cures, vegetable days, etc., failed to clear up the condition. She was then transferred to this hospital, and arrived tired but not dangerously exhausted after a journey of 32 hours.

Physical Examination.—Height 165.6 cm. Weight 40.1 kg. Marked emaciation, face flushed and slightly puffy, drowsy and slightly alcoholic expression. No enlargement of tonsils or lymph glands. Blood pressure 103 systolic, 80 diastolic. Examination otherwise negative.

Treatment.—This was the first patient for the proposed treatment, and she was closer to coma than was desired for a first trial. Accordingly the attempt was made to be conservative. She was put to bed and a light supper ordered of two eggs, a slice of toast, and a cup of milk-cocoa. Breakfast the next morning included oatmeal; the rest of the diet was light and included vegetables and potato in limited quantities. Notice should be taken that the blank food space in the graphic chart for Feb. 24 to 25 does not represent fasting, but exact reckoning of the diet was impossible because cooking and other arrangements were not in readiness. At the same time liquids were forced to 6 or 7 liters per day, and alkali was given as stated under acidosis below. As coma was imminent, there was no choice but to take the chance of beginning the proposed treatment. Therefore Feb. 27 was a vegetable day with 45 gm. carbohydrate and 530 calories. Feb. 28 was a fast-day with nothing but 200 calories of whisky. Marked improvement was evident in the urine, which became alkaline, but there was a large bicarbonate edema as illustrated by the weight curve, and weakness and drowsiness continued. Then, in order to guard against any supposed dangers of fasting, 20 gm. oatmeal were permitted on Mar. 1, increased to 52.5 gm. on Mar. 2. By this time glycosuria and coma symptoms were entirely cleared up, and alkali was diminished. On Mar. 3 the diet consisted of soy beans and green vegetables. On Mar. 4 the diet was greatly reduced, consisting only of 90 gm. banana, 20 gm. oatmeal, 10 gm. potato, and 10 gm. cream. The patient was extremely weak, therefore the attempt was made to build her up by a routine diabetic diet, in the hope that she might be strengthened for later undernutrition treatment. No gain of weight or strength was achieved, but glycosuria returned and the persisting acidosis was greatly increased, as shown in the graphic record. It was again reduced by undernutrition, and brought to a minimum by a fast-day on Mar. 23. A carbohydrate period was then instituted to clear up the tendency to acidosis if possible, and the opportunity was taken to compare the assimilation of oatmeal

and pure starch. On Mar. 24, 40 gm. Kahlbaum's soluble starch were the only nourishment given, and 80 gm. on each of the succeeding days, in ten doses of 8 gm. each. On Mar. 29 a change was made to oatmeal, reducing the quantity of carbohydrate slightly as an allowance for the oat protein. Nevertheless a glycosuria of 1.39 gm. appeared on Mar. 31, proving the absence of any superiority of assimilation of the oatmeal over the soluble starch. The resulting traces of glycosuria were cleared up by a fast-day on Apr. 1. Acidosis now being entirely absent, another attempt was made to overcome the persistent weakness by as high a diet as possible without glycosuria. Though the attempt was made to balance protein, fat, and carbohydrate to this end, the graphic record shows that acidosis returned promptly, and glycosuria resulted on Apr. 12. This was cleared up by a fast-day on Apr. 14. The attempt was then made to build up strength by still higher diet and to diminish acidosis by increasing carbohydrate, even at the cost of glycosuria, with the idea that glycosuria could later be checked by brief fasting. Acidosis was not controlled, and weight and strength were not gained, and on Apr. 25 this attempt was abandoned. From this date to May 1, pure protein-fat diet was attempted, but both glycosuria and acidosis were present. At this time a more rigid program of undernutrition was begun. It will be seen that the calories during May averaged less than 1000 daily, a maximum of carbohydrate was introduced, and frequent fast-days were employed. The weight diminished very slightly. The complaints of weakness were about the same. Most of this period from May 1 to the end of July was vegetarian, chiefly nuts and green vegetables, of which the patient was fond. On June 30 an enormous fat intake was permitted experimentally, as mentioned under acidosis. No special virtue of the vegetarian régime was perceptible. Glycosuria and acidosis were practically absent during the undernutrition of the month of May; both returned with the higher caloric diet of June and July. This period was terminated because of the increasing weakness of the patient, due particularly to the low protein. In the period July 10 to 14 a test was made with raw pancreas feeding as described in Chapter IV.

Most of the month of Aug. was occupied with pure protein-fat diet of between 1000 and 1100 calories, and about 30 gm. protein. The patient was relieved of the fast-days, of which she had been complaining bitterly. Glycosuria was mostly absent, but acidosis was persistent. In Sept. the calories were increased, partly by use of alcohol, and a few fast-days mitigated by vegetables or alcohol were employed. Weight and strength were not thereby improved, and both glycosuria and acidosis were troublesome. Oct. was a period of marked undernutrition, the calories being mostly about 900 daily, carbohydrate-free, except for two tests in which respectively 60 and 58.8 gm. carbohydrate resulted in glycosuria, when added to this caloric intake. In Nov. and Dec. the carbohydrate-free diet was pushed to the upper limit of tolerance, so that traces of glycosuria and ketonuria kept recurring and were checked by occasional fast-days. The attempt thus to build up weight and strength failed as usual. The patient was dismissed

on Dec. 20 with instructions to continue diet as during Dec. and to take a fast-day once each week.

Acidosis.—The excretion of acetone bodies in the first few days was evidently very high, but the analyses were lost. Notwithstanding the alkali dosage, the urine was strongly acid, and the ammonia nitrogen was 1.7 gm. on Feb. 25 and 1.93 gm. on Feb. 26. Each day the patient took 2.4 gm. potassium citrate, small quantities of light magnesia, and calcium carbonate in quantities equal to the sodium bicarbonate. It was thus hoped to provide a balance of salts, and perhaps also to neutralize some acid with a non-irritating substance such as chalk. The sodium bicarbonate dosage was as follows: Feb. 25, 20 gm.; Feb. 26, 32 gm.; Feb. 27, 72 gm.; Feb. 28, 48 gm.; Mar. 1 to 7, 40 gm. daily; Mar. 8 to 20, 20 gm. daily. All alkali was stopped at this time. No effect upon the carbohydrate tolerance was evident.

As mentioned, acidosis was brought under control by the initial undernutrition period. With the high diets (Mar. 10 to 15) it returned very markedly, the ammonia nitrogen rising slightly above 1 gm. notwithstanding the alkali dosage, and the ketonuria reaching 28.7 gm. (as β -oxybutyric) on Mar. 15. With a single fast-day (Mar. 16) the ammonia nitrogen fell to 0.63 gm. and the acetone bodies to 9.57 gm. With reduced diet the acidosis diminished further, and was entirely abolished by the carbohydrate period, Mar. 24 to 31, the ammonia and acetone figures falling to normal, and the ferric chloride reaction turning entirely negative. Milder acidosis returned with the beginning of mixed diet after Apr. 2, and it was proved that carbohydrate, even to the point of causing glycosuria, could not keep acidosis absent. Especially in the period Apr. 19 to 24 the carbohydrate was gradually increased to 90 gm., with a total diet as high as 2800 calories (over 75 calories per kg. on 37 kg. weight). The highest glycosuria resulting was 7.26 gm. on Apr. 24. This program was adopted on the principle frequently stated in the literature, that 90 gm. carbohydrate intake is worth a glycosuria of 7 gm. The attempt was to build up weight and strength with the high diet, while keeping acidosis in check by a favorable carbohydrate balance. Acidosis, however, remained present as stated, and the peculiar weakness and malaise characteristic of severely diabetic patients with even moderate acidosis persisted likewise. Carbohydrate had to be discontinued in order to check the steady increase of glycosuria. Thus the diets of Apr. 29 to 30 consisted of 61 gm. protein and 200 gm. fat. Both protein and fat were then diminished, until on May 1 the diet was 53 gm. protein and 177 gm. fat. This would correspond to an orthodox diabetic diet of about 1.5 gm. protein and 37 calories per kg. Nevertheless slight glycosuria and heavy ferric chloride reactions persisted, and the ammonia nitrogen by May 1 was up to 1.2 gm. May 2 was a fast-day with 34 gm. butter, this quantity of fat being almost negligible for either good or ill. The glycosuria ceased before the close of the 24 hours, the ferric chloride reaction diminished to a trace, and the ammonia nitrogen fell to 0.6 gm. Thus 1 day of undernutrition accomplished what had been impossible on full diets either rich or poor in carbohydrate.

For the next 3 months a vegetarian régime was tried, as described under "weight and nutrition" below. Because of the low protein and fat, a relatively high carbohydrate tolerance was exhibited, which was also assisted by the very frequent fast-days. In this way both glycosuria and acidosis were almost continuously absent for a month. The hope of a gain in tolerance was disappointed, however, as demonstrated by the prompt return of both glycosuria and ketonuria when a moderate increase of diet was attempted in June and July.

On June 30 an enormous fat intake was allowed experimentally for a single day, followed by a series of lower diets, as shown in Table II.

TABLE II.

Date.	Diet.				Urine.				
	Protein.	Fat.	Carbo- hydrate.	Calories.	Volume.	Sugar.	Total nitrogen.	NH ₃ -N	Acetone bodies (as β -oxy- butyric).
<i>1914</i>	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>		<i>cc.</i>	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>
June 27	43.1	104.7	87.0	1403	2320	+	4.02	0.35	0.78
" 28	40.0	104.8	85.9	1415	3188	3.31	4.38	0.41	1.66
" 29	0.5	123.9	3.4	1270*	1858	0	2.17	0.35	0.62
" 30	83.6	448.6	72.4	4456	2128	+	4.55	0.92	4.67
July 1	74.7	292.8	51.0	2707	2629	4.12	11.38	1.34	8.57
" 2	57.4	185.7	64.0	2013	1422	7.11	4.54	0.91	3.21
" 3	57.6	202.0	68.3	2107	1852	14.63	6.22	2.00	5.64
" 4	41.0	112.0	39.0	1295	1411	4.06	6.28	1.50	2.73
" 5	0.2	0.2	1.8	290†	1506	0	4.14	0.80	0.47
" 6	36.3	109.8	72.6	1315	1528	0	6.17	0.38	1.11
" 7	55.1	101.2	68.2	1420	1630	0	7.02	0.43	0.48

* Butter 150 gm., strawberries 50 gm., alcohol 25 gm.

† Alcohol 40 gm.

The relation between combustion of food fat and body fat is here illustrated. The huge ration of June 30 did not produce any explosive increase of acidosis. The acetone bodies showed a rise on the same day, but a more marked one the following day, while the ammonia nitrogen did not reach its summit until July 3. It is evident that what happened was not the conversion of any large proportion of the fat on June 30 into acetone bodies, but rather an injury of fat assimilation produced by this excess and continued by reason of the fat rations (lower but still excessive) of July 1 to 3. On the fast-day of July 5, storage or depot fat was necessarily burned, yet the ammonia nitrogen was approximately the same as on June 30. On July 6, with a limited fat intake, the effect of carbohydrate was evident in producing a lower ammonia nitrogen excretion than on the fast-day. The entire observation is against the idea of a difference between food fat and

body fat in combustion, and indicates rather an overtaking of fat metabolism by excessive intake and improvement of assimilation by relief from the strain.

On the carbohydrate-free diet beginning in Aug., strong ferric chloride reactions and unduly high ammonia excretion were the rule. Temporary control of both glycosuria and acidosis was achieved with the low diets (about 900 calories) in early Oct. Thereafter it will be noted that the ferric chloride reactions were sometimes negative and never more than slight, even on carbohydrate-free diet, the general diabetic condition being now under better control. The continuance of slight acidosis, however, throughout so much of the period of treatment represents one of the serious mistakes in the management of this case.

Weight and Nutrition.—Weight at admission 40.1 kg., at discharge 35.2 kg.; *i.e.*, a loss of 4.9 kg. The initial gain in weight, up to 43.5 kg. on Feb. 28, represented a marked bicarbonate edema, simultaneous with the turning alkaline of the urine. Slighter edema was present on certain occasions later, notably Aug. 15 and Nov. 7, being due apparently to sodium chloride and removed by diminishing the salt intake.

On Mar. 21 the large fluid intake began to be restricted. The patient had been accustomed to large quantities of water for some months past and complained of thirst when the allowance was diminished by order; within a few days this complaint disappeared and the thirst remained normal thereafter.

Vegetarian diet was tried for a period of nearly 3 months, chiefly because of the claims in some quarters concerning differences in the glycosuric effect of different proteins, and the bare possibility that meat protein might at least stimulate a greater flow of gastric juice and correspondingly of pancreatic juice, and thus perhaps depress the internal function of the pancreas by stimulating its external function. Undernutrition was employed at the same time to create the most favorable conditions, and acidosis was kept absent by such quantities of carbohydrate as seemed within the tolerance. Butter was regularly allowed, eggs rather frequently, and a little bacon and bacon fat sometimes, but for much of the time the ration was vegetarian in the strictest sense, composed entirely of vegetables, fruits, nuts, soy beans, and occasional gluten preparations. There was no gain of tolerance, and no advantages of a vegetarian diet or evidence of specific differences between proteins were observed.

Neither food nor feces was analyzed. The former was calculated as usual from the Atwater-Benedict tables. On this basis the following reckoning can be made for the period from Mar. 16 to Nov. 30, for which the records of both food and urine are complete. Also, the total period of 260 days is divisible into two nearly equal portions, namely, 136 days up to July 31, during which the diet was largely and sometimes wholly vegetarian and contained considerable carbohydrate, and 124 days after July 31, in which the protein was of animal origin and the diet was almost continuously carbohydrate-free. The results for the various periods may be compared as shown in Table III.

TABLE III.

	Total calories in diet.	Average calories per day.	Average calories per kg. per day.	Total protein in diet.	Average protein per day.	Average protein per kg. per day.	Total nitrogen in diet (protein \div 6.25).	Average nitrogen in diet per day.	Total nitrogen in diet per kg.	Total nitrogen in urine.	Total nitrogen unaccounted for.	
			gm.	gm.	gm.	gm.	gm.	gm.	gm.	gm.	gm. per cent	
Total period 260 days.....	315,372	1,213	33	11,766.4	45.2	1.23	1,882.6	7.24	0.19	1,669.97	212.63	11.29
"Animal" period.....	149,256	1,204	33	6,620.0	53.4	1.44	1,059.2	8.54	0.23	958.99	100.21	9.45
"Vegetable" period.....	166,116	1,221	33	5,146.3	37.9	1.02	823.4	6.05	0.16	710.98	112.40	13.65

The patient lost 5 kg. weight in 9 months. If it be assumed that 90 per cent of a weight change is ascribable to fat, in this instance the loss of nitrogenous "tissue" would not exceed 500 gm. Using Voit's figure of 3.4 per cent N, the possible loss of body nitrogen would then be 17 gm. If it be urged that in an emaciated person the wasting of "tissue" in proportion to fat is higher, the above comparison of intake and output shows that the patient must have been nearly in equilibrium. At worst, the nitrogen deficit must have been small, and it may be assumed that the diet fulfilled the purpose of protecting body protein from any extreme loss while maintaining prolonged undernutrition.

Two deductions seem justified. (1) Digestion and absorption of protein were, as would be expected, distinctly better during the "animal" period, but the utilization of vegetable proteins, including the times when the diet was exclusively vegetable, was reasonably satisfactory. (2) Though the nitrogen intake was lower in the "vegetable" period, it must be called low also in the "animal" period, and it is evident that there is no serious obstacle to maintaining equilibrium on strict carbohydrate-free diet with a low protein ration. It is to be borne in mind that the energy intake is a question not of food ingested but of food absorbed. If it be permissible to assume that the same proportion of total calories as of nitrogen was lost in the feces, *viz.* 11.29 per cent, subtraction of this number from the 33 calories ingested daily would leave an average of between 29 and 30 calories absorbed daily per kg. of body weight. Accordingly, it would appear that this patient lived for 260 days on an average of 0.173 gm. N and 30 calories per kg. Work and exposure to cold were both far less than in ordinary individuals. On the other hand, the rather tall, very emaciated figure presented a disproportionate surface. Losses in sugar and acetone bodies were slight. On the whole, the figures obtained correspond satisfactorily to the known laws of metabolism in normal persons.

Subsequent History.—On Jan. 14, 1915, the patient reported by telephone that she was feeling well and had cleared up occasional traces of glycosuria by fast-days. On Jan. 20 she reported increasing difficulty in remaining sugar-free, and was instructed to return to the hospital if difficulty continued. Nothing more was heard until Apr. 1, when a letter stated that she had returned to her home in Indiana. On Apr. 26 a response to a letter of inquiry showed that the cause of her silence and removal was her adoption of Christian Science. Occasional later reports showed that she was eating everything at will, including much candy, and gradually losing strength. Death occurred from simple weakness the first of Oct. 1915, the terminal collapse being brought on by taking a dose of Epsom salts.

Remarks.—The patient, when received, was undoubtedly close to coma. She appeared then as having diabetes of extreme severity. The results obtained seemed highly favorable. In the light of later experience this treatment was very bad.

Part of the fault lay with the patient, who had always eaten injudiciously

and was the most unruly of the entire series for dietary control. The high diets, the persistence of glycosuria and ketonuria through considerable periods, and the changes in program from time to time were in some measure forced by the necessity of appeasing the patient's demands and meeting her psychic needs. She insisted not only upon nourishment but also taste and satiety, and slight privations brought on hysterical tears and melancholy which seemed serious as a possible influence upon the diabetes, though, as a matter of fact, no particular influence of psychic upsets upon the food tolerance was observed. She was given unusual leeway as being the first patient.

The cause of the final disaster was also instructive. It is noteworthy that although a very careful limitation of diet both quantitatively and qualitatively had resulted in threatened coma at the time of admission, subsequently on absolutely unrestricted diet no symptoms of acidosis were described, evidently because the patient lived so largely on carbohydrate, and the polyuria aided in the elimination of acetone bodies. Although the patient was young and the kind that typically dies in coma, death occurred from simple wasting and asthenia.

The chief difficulty consisted in inexperience with the treatment. The cautious manner of beginning treatment, and the partial, irregular, and inadequate character of the measures employed belonged to this stage of uncertainty and orientation. It showed the viciousness of some of the accepted methods in the management of diabetes. The same patient admitted at a later time could have been treated far better; and the case, though severe, was mild in comparison with some of the later ones. A bold initial fast, followed by testing of the tolerance for different classes of food and arrangement of a diet accordingly, would have brought far quicker and better results.

The actual accomplishment was that the patient was kept alive in the hospital from Feb. 24 to Dec. 20, with a loss of 5 kg. (one-eighth of her weight at entrance), and about a corresponding diminution of strength. Glycosuria and acidosis were kept entirely absent at certain times, and were controlled within small quantities at all times. Actual food tolerance was slightly less at the end than in the earlier part of treatment, and the progress was slowly but distinctly downward. The bungling and inadequate treatment furnished abundant reason for this slight downward progress in 10 months, and no "spontaneous" cause need be assumed. Methods and results of this sort have been common with a large proportion of practitioners who have undertaken to apply the fasting therapy. The record of this patient stands as a useful example of how a case should not be treated.

CASE NO. 2.

Female, unmarried, age 17 yrs. Italian, sewing machine operator. Admitted Apr. 13, 1914.

Family History.—Grandparents healthy as far as known. Father a day laborer and short of stature; weight about 200 pounds. Mother short, normal figure,

was agreeable to this Italian patient. In other words, the fast was not broken (as usual) by carbohydrate alone, but fat was introduced to make a total of 2000 calories. Also on the following days, diets low and relatively high in fat were compared, and on Apr. 30 a day of 100 gm. olive oil was given instead of a regular fast-day, according to the practice of some authorities. The results are discussed elsewhere (Chapter VI). They illustrate the harmfulness of attempts to use fat in this manner. In the first few days of May a rather low diet was given, with absence of glycosuria. The succeeding period represents a low calory diet, with as much carbohydrate as possible and frequently repeated fast-days for the purpose of overcoming the persistent ferric chloride reaction. On June 11 an enormous fat diet was given (137 gm. protein, 34 gm. carbohydrate, 6672 calories = 167 calories per kg.). A slight rise in the ammonia followed, but the patient's appetite was spoiled so she could take only a low diet for several days. On June 17 a less extreme fat diet was begun, which nevertheless represented not far from 100 calories per kg. of body weight. The results are discussed in Chapter VI. The onset of glycosuria and the marked rise of acidosis are the striking features. July 5 was a fast-day with alcohol. Thereafter a low diet was given, relatively rich in carbohydrate. Under this program both glycosuria and acidosis cleared up and were kept absent.

The patient was discharged Aug. 14, symptom-free and feeling well and strong. The hospital stay was uneventful except for occasional headaches for which no cause was found.

Acidosis.—Although there were no signs of coma, the analyses in the first few days indicated that trouble would have resulted before long on the restricted diet. On Apr. 14 to 15 no alkali was given, and the urine contained 2.4 to 2.7 gm. ammonia nitrogen and 4.2 to 7.0 gm. acetone bodies (as β -oxybutyric). Apr. 16 to 20, 20 gm. sodium bicarbonate were given daily, and 10 gm. on Apr. 21, after which alkali was stopped. The rise of ketonuria, up to 12.1 gm. β -oxybutyric acid on Apr. 18, was to be expected, but at the same time the ammonia, instead of falling, remained little changed, and actually rose to 3.1 gm. ammonia nitrogen on Apr. 18. With diminished fat and increased carbohydrate intake on Apr. 19 there was a drop in both ammonia and total nitrogen, but the steepest fall of the ammonia occurred on fasting. Thereafter the three principal peaks of the ammonia curve (Apr. 23, May 2, and June 19 to July 3) are clearly associated with the fat content of the diet. It is evident from the graphic chart that acidosis was not checked by liberal quantities of carbohydrate and protein, nor by a favorable carbohydrate balance, but on the contrary rose and fell according to the ingestion of fat. For about the last month in the hospital acidosis was entirely absent on a diet moderate in protein, relatively abundant in carbohydrate, and low in fat.

Weight and Nutrition.—Weight at admission 42.6 kg., at discharge 40 kg.; *i.e.*, a loss of 2.6 kg. The variations and excesses in diet were experimental. The diet at discharge was approximately 56 gm. protein, 120 gm. carbohydrate,

and 1400 calories (1.4 gm. protein and 35 calories per kg., reduced slightly by occasional fast-days). The patient's figure and strength at discharge appeared normal. The diet was planned as one on which she could work. She was instructed not to gain weight, and it was proposed to give her instructions thereafter chiefly on the basis of her body weight.

Remarks.—Aside from the intentional experimental variations, the treatment was fairly efficient and the result good. The reduction in weight and the arrangement of the final diet, restricted in total calories, adequate in protein and rather liberal in carbohydrate, was about what was needed for a relatively mild case, such as this one by this time had proved itself to be. By comparison of the diets of Apr. 14, 15, 18, and 19 with those of Aug. 9 and 11, it will be seen that the calories are about the same, while the carbohydrate, counting also that derivable from protein, is higher in the latter period. Along with this, the sharp contrast as respects glycosuria and ketonuria shows a decided upward progress in this 17 year old girl during these 4 months.

Subsequent History.—After discharge on Aug. 14, the patient followed diet and remained sugar-free for about a month at home. Owing to poverty it was almost impossible for her to obtain the necessary food, and she gradually began to take the diet of the rest of the family. Sugar reappeared, followed by other symptoms. She was readmitted Nov. 30, 1914, complaining of polydipsia, polyuria, and for the last few days loss of appetite and drowsiness.

Second Admission.—A 4 day fast was instituted, glycosuria ceasing on the 3rd day. On Dec. 4, green vegetables containing 20.5 gm. carbohydrate were taken without glycosuria. Another fast-day was then given as a therapeutic measure, and a mixed diet of eggs, butter, steak, and vegetables gradually begun. Slight glycosuria appeared within a few days. Beginning Dec. 16, the diet was almost constantly carbohydrate-free and unduly high in calories. Ketonuria was present most of the time up to July 24. Then, after a fast-day, a carbohydrate test was given in the form of green vegetables as usual. Beginning with 10 gm. carbohydrate on July 26, an increase of 10 gm. daily was made. Aug. 4, on 100 gm. carbohydrate, she showed a trace of sugar, which disappeared the next day when the same carbohydrate was given. The true limit was reached on Aug. 8 with 130 gm. carbohydrate. Accordingly, 120 gm., which had been tolerated the previous day, were accepted as her tolerance. The acidosis was thus cleared up (compare with increase of acidosis when fat was given in Apr., 1914). It returned in small amount on the subsequent carbohydrate-free diet, then diminished, so that after Sept. 7 it was absent. Another carbohydrate tolerance test was made beginning Oct. 11, and the limit was found to be practically the same as in Aug. Small quantities of carbohydrate were added to the diet in Nov., but discontinued on account of glycosuria. Beginning Dec. 13, a third carbohydrate tolerance test showed unchanged assimilation, and cleared up the slight ketonuria which had again developed on protein-fat diet. Carbohydrate was again included in a diet somewhat lower in calories, but was discontinued on account of persistent

slight glycosuria. Strenuous exercise was a feature of the treatment during this period in the hospital. The observations are discussed in Chapter V. The patient was discharged Feb. 2, appearing healthy and well nourished and feeling strong and capable of hard work.

Acidosis.—The ammonia excretion was constantly higher than that of normal persons; perhaps not higher than some normal persons would show on the same diet. No determinations were made during the carbohydrate tests, when lower values might have been found. A fall of the ammonia on fast-days and a rise on carbohydrate-free diet is shown by portions of the curve in Apr., May, and June; this is doubtless due in part to corresponding variations in total nitrogen excretion, but also illustrates the difference between fasting and protein-fat diet. Beginning Dec. 5, it is evident that a fast-day, followed by a reduction of fat in the diet while keeping protein the same, resulted in a drop in ammonia excretion. The carbon dioxide-combining power of the plasma remained in the neighborhood of normal without alkali dosage, but nevertheless showed a tendency to sink somewhat below the low normal limit. This was one of the patients who showed a fall in blood bicarbonate on fasting, as seen particularly after the fast-days of May 1 and Sept. 12. Certain other fluctuations in this curve are discussed in Chapter V in connection with exercise.

Blood Sugar.—This was mostly about 0.2 per cent. A rise is seen at the close of the carbohydrate tolerance test in Oct. Analyses were not made during the other carbohydrate tests. The normal values from Apr. 30 to May 11, and on Sept. 22 and 23, showed that a reduction was possible by suitable low calory diet, and the failure to insist upon such a level was one of the faults of the treatment.

Weight and Nutrition.—In general the lowest diets are those of Aug. and Oct. and the dismissal diet about the 1st of Feb. These amounted to 1300 to 1500 calories, which for a body weight of 40 kg. would equal 35 calories or more per kg. At other times this diet was increased by fat to as much as 3500 calories, or some 60 calories per kg. Two modifying features come into account. One is the number of fast-days, which serve to diminish the average intake somewhat below this figure. Second, the patient was kept most of the time on very heavy exercise, so that the caloric requirement was increased. The patient entered weighing 45.6 kg.; namely, a gain of some 5 kg. since her former discharge, with a corresponding loss of tolerance. She was dismissed weighing 39 kg.; *i.e.*, with a loss of 6.6 kg. in 14 months in the hospital. To this extent the treatment was one of undernutrition.

Remarks.—It was above noted that during 4 months in hospital, at the first admission, progress was upward. The patient was at home about 3½ months and broke diet in the latter portion of this period. The downward progress is plainly evident. After her second admission she frequently showed sugar on carbohydrate-free diet. Also her limit of tolerance for carbohydrate alone, in the green vegetable tests of Aug., Oct., and Dec., 1915, was almost exactly the quantity which could be included in her regular mixed diet in Aug., 1914, without any

appearance of glycosuria. It is thus clearly confirmed that a marked and lasting injury of assimilation can be produced by a few months of unregulated diet. On the other hand, the former carbohydrate tolerance tests of Aug., Oct., and Dec., 1915, covered a period of 5 months, and conclusively proved the absence of any perceptible downward progress during that time. Also the weight remained essentially the same, so that no disturbing factor was thus introduced. Moreover, comparison of the tolerance at the beginning and end of the second hospital period shows that glycosuria appeared on Dec. 14, 1914, on a diet of 60 gm. protein, 42 gm. carbohydrate, and 981 calories. If all these earlier occurrences of slight glycosuria be ignored, it is still evident that on repeated occasions in Jan., Feb., and thereafter, glycosuria was present on carbohydrate-free diets of some 1700 calories. In contrast to this, it is seen that from Dec. 27, 1915, to Jan. 1, 1916, a diet of 1760 calories with 10 to 30 gm. carbohydrate was tolerated without glycosuria, and the protein in this diet was fully as high as in the above mentioned carbohydrate-free periods. Glycosuria appeared only on Jan. 6, toward the close of another week on the 30 gm. carbohydrate allowance. It was thus present on Jan. 11, but cleared up on withdrawing carbohydrate from the diet. A slight gain in food tolerance is thus evident during these 14 months in hospital, and this upward tendency is the more remarkable in view of the improper treatment, with its long periods of overfeeding and almost continuous marked hyperglycemia. The essential criticism of the treatment in this period is that by pernicious protein-fat overfeeding (up to 60 calories per kg.) it held back the tendency to improvement, and ultimately sacrificed $6\frac{1}{2}$ kg. weight for only the slight gain of assimilation above mentioned. An excellent physical condition was maintained throughout, and the patient was discharged seemingly in splendid health. The failure of the plan of feeding for immediate weight and strength is well demonstrated by this prolonged trial. The transitory well-being is too dearly bought at the price indicated by the laboratory findings. Proper management would have imposed a rigid low diet from the outset and insisted upon continuously normal urine and blood. A sharper initial fall of weight would have resulted. A small quantity of carbohydrate could have been included in such a low calorie diet. Under such a program there is little doubt that the patient could have been discharged in fully as good physical condition and on fully as high a total diet as was actually the case; and the diet could have been balanced properly with carbohydrate, and the entire condition from the standpoint of the diabetes would have been far more favorable.

Subsequent History.—After discharge on Feb. 2, 1916, diet was followed until Mar. 8, when the patient began to take two slices of bread daily in addition to the weighed diet, because of a strong craving for carbohydrate. Sugar had been absent before, but then reappeared and continued. She was doing 5 hours work on the sewing machine at home and 2 hours housework daily, and in addition walked two miles two or three times a week. A fast-day was taken once a week up to the 1st of Mar.

Third Admission.—Mar. 20, 1916. Weight 39.4 kg. Nutrition and strength still appeared very good. Fasting was imposed Mar. 21 to 23 inclusive, then low protein-fat diet, gradually increasing from 1000 to 1200 up to 1800 calories, with protein ranging from 40 or 50 up to 60 or 70 gm. daily. The patient was again discharged on July 12 at her own request, still appearing in excellent condition. Headaches had been somewhat relieved after prescription of glasses by an oculist.

Acidosis.—It is of interest that heavy acidosis was brought on by the addition of two slices of bread to the weighed diet on which both glycosuria and acidosis had been absent. Fasting was begun on the day following admission (Mar. 21). The patient was depressed, dizzy, and significantly unwell. The finding of 33.4 per cent plasma bicarbonate showed the reason. Sodium bicarbonate was then given in 3 doses of 10 gm. each. Within half an hour after the first dose the clinical effect was striking. The headache, dizziness, depression, and malaise vanished, and were replaced by comfort and cheerfulness. It is possible that fasting alone would have been badly borne, as the tendency to a fall in blood alkalinity on fasting was previously noted in this patient. No more alkali was given. The CO₂ capacity was found normal on the day after the bicarbonate dosage, but fell to 46 per cent on the succeeding day (Mar. 23). On this day also glycosuria ceased. Mar. 24 to 27, a trial was made of carbohydrate-free diet, which frequently relieves fasting acidosis. On Mar. 24 nothing but 21 gm. protein was fed, the diet being coffee, soup, and veal. The blood bicarbonate rose a trifle. On Mar. 25 the diet contained 40 gm. protein and 800 calories. Thereafter protein was increased and fat diminished, so that on Mar. 27 the diet was 70 gm. protein and 600 calories. The net result of these low protein-fat rations was that by the morning of Mar. 26 the blood bicarbonate had risen to 52.8 per cent. On Mar. 28, the diet was sharply reduced to 16 gm. protein and 10 gm. carbohydrate. The blood alkalinity fell sharply as on a fast-day; *i.e.*, to 40 per cent on the morning of Mar. 29. Beginning Mar. 29, the diet was limited to green vegetables. On this, by the morning of Mar. 31, the CO₂ capacity had risen to 44 per cent, though the carbohydrate intake had amounted to only 30 gm. on Mar. 30. By Apr. 7, the plasma alkalinity had risen to within normal limits on low protein-fat diet. Thereafter it remained generally at a low normal level. No reason is known for the low reading of 45.6 per cent on June 27, unless it were the increased fat intake. By July 7, it had returned to normal without the aid of alkali, possibly with the aid of the small allowance of carbohydrate. The other tests were not parallel with the plasma bicarbonate. The ammonia nitrogen at first fell from 3.4 gm. on Mar. 20 to 1.94 gm. on Mar. 22, then remained nearly stationary to Mar. 27, thus corresponding to the plasma bicarbonate. But when the plasma bicarbonate fell at the beginning of the vegetable period, the ammonia fell also. Later, on protein-fat diet, the ammonia was a more sensitive indicator of acidosis than the plasma bicarbonate, being unduly high (Apr. 14; June 6 to 8) at times when the plasma bicarbonate was approximately normal.

The ferric chloride reaction became negative early in the vegetable period, at the very time when the plasma bicarbonate fell. It remained negative thereafter.

Blood Sugar.—The fall during the initial period of fasting and undernutrition is evident from the graphic record. Subsequently it rose, and remained much of the time in the neighborhood of 0.2 per cent. The decline to a nearly normal value shortly before discharge is in conformity with the other improvement.

Weight and Nutrition.—Weight at admission 39.3 kg.; *i.e.*, the same as at the previous discharge. Weight at discharge 35.2 kg. Nearly 4 months of treatment thus represented undernutrition to the extent of 4.1 kg. This undernutrition was imposed especially at the beginning of this hospital period. From Apr. 18 to discharge there was an actual gain of 1 kg. During most of the time one egg was allowed on fast-days, but beginning with July the fast-days were made absolute. The daily allowance of 70 gm. protein, 10 to 15 gm. carbohydrate, and 1800 calories was thus reduced to an average of 60 gm. protein and 1540 calories (1.7 gm. protein and 44 calories per kg.).

Remarks.—The carbohydrate tolerance test Mar. 28 to Apr. 4 showed an assimilation not above 60 gm. carbohydrate. Glycosuria also appeared subsequently on protein-fat diets lower than those previously tolerated. Very decided downward progress was thus clearly demonstrated in consequence of violations of diet, during less than 2 months at home, the violations being said to have been limited to less than 1 month. Susceptibility of this case to rapid downward progress on dietary overstrain is thus proved. On the other hand, in nearly 4 months of hospital sojourn this time, the progress was demonstrably upward. From Apr. 18 onward, as mentioned, there was a gain of 1 kg. weight, and at the same time the patient became able to remain free from glycosuria and ketonuria on diets decidedly higher in protein, fat, and carbohydrate than those on which glycosuria repeatedly occurred earlier in the period. The tendency of the blood sugar likewise was downward. Furthermore this improvement occurred in spite of grossly excessive diets, the tendency to spontaneous upward progress being thus all the more remarkable. In extenuation of the diet only two excuses can be offered. One is that the patient was taking heavy exercise, and it had not yet been learned that this does not atone for excessive diet. The other is that it was known that the patient at home would not adhere to any diet which kept her at all hungry or uncomfortable. Accordingly she was allowed this diet, on which her progress seemed at least temporarily favorable, in preference to a more beneficial diet which would be more liable to be violated.

Fourth Admission.—Sept. 11, 1916. (No graphic chart.) Patient returned to hospital with the usual history of having broken diet. Heavy sugar and ferric chloride reactions were now present on her former diet. A 4 day fast was necessary. A carbohydrate test with green vegetables in the usual manner showed a tolerance of 50 gm. A carbohydrate-free diet was then begun, with 40 gm. protein and 600 calories. The experiment was then performed of keeping this protein the same while gradually increasing fat to make a total of 1300 calories (see

Chapter VI). The result was glycosuria, while the ferric chloride reaction remained negative. Thereafter with less fat (900 to 1200 total calories) and the same protein, glycosuria was absent, but returned when the protein was increased to 50 to 65 gm. She was discharged on Dec. 4, 1916, still in fair subjective health.

Acidosis.—The CO₂ capacity of the plasma at first was 35.5 per cent. Weakness and malaise, making her unfit for work, were the only clinical symptoms of acidosis. With 4 days of fasting, the CO₂ capacity rose to 53.3 per cent. After 2 days respectively of 10 and 20 gm. carbohydrate, it was 59.5 per cent, and at the close of the carbohydrate test (Sept. 22) 58 per cent. This reaction to fasting is noteworthy in a patient who on previous admissions had shown such decided falls in blood bicarbonate on fasting. Likewise the heavy ferric chloride reaction diminished on fasting and cleared up during the vegetable period. The ammonia nitrogen, which was 3.3 gm. on the prescribed diet, dropped to 2 gm. at the close of fasting, and to 0.43 gm. on the fast-day (Sept. 23) following the vegetable period. Thereafter on protein-fat diets the plasma bicarbonate remained at a high normal level (59.8 to 68.8 per cent) and the ferric chloride reaction continued negative. The ammonia nitrogen ranged from 0.8 to 1.5 gm., and was thus the most delicate index of acidosis.

Blood Sugar.—This was 0.218 per cent in whole blood and 0.238 per cent in plasma on the first day of fasting (Sept. 13), 0.192 per cent in plasma on the last day of fasting (Sept. 16). It was never brought lower than 0.122 per cent in whole blood and 0.147 per cent in plasma. The last analysis, with sugar-free urine, showed 0.202 per cent plasma sugar.

Weight and Nutrition.—Weight at admission 41 kg., part of which was edema. Weight at discharge 34.3 kg. The final weight was thus only about 1 kg. less than at the previous discharge, but otherwise the condition was much worse. The carbohydrate test above mentioned indicated a loss of only 10 gm. tolerance. A truer index is afforded by the fact that traces of glycosuria now tended to appear on relatively low carbohydrate-free diet. In contrast to the 70 gm. protein, 10 to 15 gm. carbohydrate, and 1800 calories tolerated at the former discharge, the diet at discharge this time had to be limited to 45 gm. protein and 1200 calories (1.3 gm. protein and 35 calories per kg., reduced by the weekly fast-days to 1.1 gm. protein and 30 calories average). Moreover, marked hyperglycemia was continuous on this diet as stated, and glycosuria appeared upon very slight increase of either protein or fat. The patient had again demonstrated how rapidly she could progress downward with improper diet in the short period of 2 months at home. At this discharge she was distinctly weaker than ever before, though still comfortable and able to do housework. The treatment had not been radical, but she had been fed during the whole of this hospital period to the limit of her tolerance in order to keep up her weight and strength.

Subsequent History.—A note received from the family Mar. 14, 1917, stated that the patient died at 2:30 a.m. that day. She had again broken diet because of the

unfavorable environment, and the diabetes took its natural rapid course. She refused the petitions of her family that she return to the hospital.

Remarks.—The patient had been kept alive and almost uninterruptedly comfortable for 3 years under treatment. In view of her state of intelligence, will power, and environment, this was probably as much as could have been accomplished unless she had been kept continuously in an institution. The chief scientific interest in the case lies in its demonstration of rapid downward progress with dietary indiscretions, and complete absence of downward progress and distinct tendency to upward progress even under treatment which never was radical enough to remove the continuous evidences of slight metabolic overstrain.

CASE NO. 3.

Female, unmarried, age 26 yrs. American; no occupation. Admitted May 23, 1914.

Family History.—Father was never strong, and died when patient was 5 years old. Autopsy is said to have revealed numerous intestinal ulcers. His parents lived to healthy old age. Patient's mother is alive and well; her father died at age of 28 of tuberculosis said to have resulted from a career of dissipation; also her brother died of tuberculosis, and her sister with acute melancholia. Patient has one brother aged 32 who suffers from nervousness and indigestion. No diabetes or other family diseases known.

Past History.—Healthy life in excellent hygienic conditions, but numerous infections. Measles, mumps, chicken-pox in early childhood. Typhoid at 8. Tonsillitis at 16 with recurrent attacks in following years until right tonsil was removed 3 years ago. Only a little sore throat since then. 5 years ago "colitis" for 10 days; fever, vomiting, and dull aching pain in upper abdomen, considerable bloody diarrhea, no jaundice. Several slight attacks of grippe, the last about 3 years ago. 4 years ago, "intercostal rheumatism;" in bed about a week, no herpes. Quiet life; no overstudy, but considerable social activities in recent years, and some exhaustion after attending several dances in the same week. Not nervous. Worry and loss of sleep for some time following unhappy love affair 4 years ago, but this has entirely passed off. Moderate appetite, but she has eaten even more candy than the average girl.

Present Illness.—Jan. 12, 1914, after having been in apparently perfect health, patient woke up with malaise and slight abdominal pain. The attack subsided with fasting and bed-rest, but on account of slight tenderness and rigidity, laparotomy was performed on Jan. 14, revealing obliterative appendicitis and blood clots about right ovary, treated by removal of appendix and one ovary. Incision healed *per primam*, but 15 days after operation phlebitis occurred, first in left leg, then in right. Left leg has required bandaging until recently. Urine was reported normal in hospital, but it is doubtful if tests for sugar were made. Weakness and weariness felt at this time were attributed to convalescence, and the patient went to summer resorts to recuperate. Polyphagia, polydipsia, and

polyuria began, and most of her luxuriant hair fell out. The normal weight of 120 pounds diminished to 109 pounds. 2 weeks before admission, diabetes was diagnosed. The laboratory reports showed 8.3 per cent sugar and heavy ferric chloride reaction. A diet was prescribed containing considerable starch. Since then, rapid dimming of vision has been noticed. Menstruation has continued.

TABLE IV.

Date.	Diet.					Urine.			
	Protein.	Fat.	Carbo- hydrate.	Alcohol.	Calories.	Volume.	Sugar.	NH ₃ -N	Acetone bodies (as β-oxy- butyric).
1914	gm.	gm.	gm.	gm.		cc.	gm.	gm.	gm.
May 24	82.8	127.5	127.7	7.5	1854	2010	47.2	1.39	2.27
" 25	126.5	175.0	272	4.0	3259	2470	68.0	1.06	2.31
" 26	Fast-day.			35.0	245	910	4.2	0.88	0.88
" 27	"			25.0	175	644	0	1.00	1.63
" 28	4.2	0.8	25	—	122	825	0	1.15	1.93
" 29	10.9	2.5	60	—	302	934	0	1.23	0.64
" 30	37.0	9.5	162	—	848	1700	7.99	1.31	2.08
" 31	11.6	2.7	52	—	421	1362	4.22	0.34	1.05
June 1	7.0	1.2	22	—	125	1106	0	0.38	0.21
" 2	6.2	1.4	16	—	99	957	0	0.46	0.45
" 3	10.8	3.7	37	—	222	866	—	0.54	0.41
" 4	24.7	10.1	98	—	568	1008	0	0.53	0.37
" 5	Fast-day.			30.0	210	1758	0	0.35	0.74
" 6	14.0	1.8	98	—	474	774	—	0.55	0.80
" 7	Fast-day.			30.0	210	1325	0	0.32	0.35
" 8	14.0	1.7	85	—	419	727	0	0.67	0.88
" 9	31.7	6.4	144	—	779	2009	4.31	0.74	0.69
" 10	40.1	13.6	147	—	893	2278	4.57	0.43	0.48
" 11	43.7	15.1	150	—	932	2728	4.19	0.55	0.55
" 12	1.6	—	7.8	25.0	220	2054	0	0.35	0.41
" 13	43.2	10.4	113	—	735	1969	0	0.41	0.23
" 14	40.1	11.7	124	—	778	2060	0	0.27	0.33
" 15	38.5	7.8	136	—	787	1878	0	0.26	0.31

Physical Examination.—Height 161.3 cm. Patient appears rather juvenile for her age; still well nourished, and with look of perfect health. Mouth and teeth in good condition. Right tonsil missing, left appears normal. No enlarged lymph nodes. Reflexes normal. Examination otherwise negative.

Treatment.—(No graphic chart.) An observation diet was first permitted similar to what the patient had been taking. The initial treatment is shown in Table IV.

The most disturbing symptom was the blurred vision. The patient compared it to the effect of atropine. In the early days in hospital she became unable to read even with glasses. An oculist found no organic change, and vision rapidly cleared in parallel with the urine. After an uneventful period of hospital observation without return of any symptoms, the patient was discharged on July 24.

Acidosis.—This was never heavy, and was easily controlled by reason of the high carbohydrate tolerance. The only alkali used was 20 and 15 gm. sodium bicarbonate respectively on the first 2 days in hospital.

Weight and Nutrition.—Weight at admission 46.5 kg., at discharge 43.4 kg. The apparent reduction of weight was thus 3.1 kg., but actually must have been somewhat more, as the dried tissues recovered their normal water content during undernutrition after cessation of glycosuria. The treatment was characterized by low protein, low calory diets, as liberal as possible in carbohydrate. At first such diets were exclusively vegetable. Glycosuria at first resulted from 140 gm. carbohydrate, but by June 16, 171 gm. carbohydrate were taken without glycosuria. One egg was then added to the diet; and after June 22, 200 to 225 gm. carbohydrate could be taken daily without glycosuria. As a precaution, however, the allowance was diminished to 150 gm. The diet prescribed at discharge represented approximately 70 to 80 gm. protein (largely vegetable), 150 gm. carbohydrate, and 1200 to 1500 calories (1.5 to 1.75 gm. protein and 26 to 33 calories per kg., without fast-days). As the patient was about 9 kg. below normal weight, this allowance was considered prudent; and she was permitted to estimate her diet instead of weighing it, on condition that she be guided by her body weight and not allow herself to gain much flesh. She was still sufficiently well nourished to look and feel entirely healthy. The degree of undernutrition in hospital, and the extent to which fat was excluded and carbohydrate emphasized in the diet, can be shown by the following table.

	Total.	Average per day.
Calories in diet for 61 days.....	61,287	1005
Protein " " " 61 "	2,788.7 gm.	45.7 gm.
Fat " " " 61 "	2,073.1 "	34.0 "
Carbohydrate " " " 61 "	7,121.0 "	117.0 "
Nitrogen in diet for 61 days (Protein ÷ 6.25).....	446.0 gm.	7.3 gm.
" " " " 49 " (" ÷ 6.25).....	278.6 "	5.68 "
" in urine " 49 "	266.5 "	5.44 "
" " " per kg. per day (average 44 kg.)		0.125 "

It should be borne in mind that the diet was strictly vegetarian, chiefly green vegetables, except for a single egg daily after June 16. A considerable proportion of the protein was therefore non-absorbable, so that the close correspondence

between food and urine nitrogen must be attributed not to unusually good utilization of food, but rather to loss of body nitrogen. Protein restriction to this degree was doubtless unnecessary, but the rigid undernutrition was a commendable feature.

Subsequent History.—The patient led a thoroughly normal and comfortable life, but managed her diet so as to permit a gradual gain in weight. Occasional traces of glycosuria returned, and these and the gain in weight were not checked by moderate exercise which was advised. Presumably eating was increased in proportion to the exercise. During the 2 years outside the hospital the patient had been married and divorced, and though the glycosuria was attributed partly to worry, it probably was essentially of dietetic origin. The predominant difficulty consisted in traveling and hotel life, where vegetables were often cooked with starch and even sugar. Though feeling perfectly well, she reentered the hospital for observation on request.

Second Admission.—June 6, 1916. Weight 49.2 kg. The urine showed a trace of sugar which cleared up readily without fasting. The carbohydrate tolerance was not accurately tested, but was evidently somewhat lower than before.

The patient was dismissed June 20, weighing 48.1 kg., on a diet of 60 gm. protein, 50 gm. carbohydrate, and 1500 calories, with fortnightly fast-days. The first blood sugar analyses were made during this period, and showed a tendency to slight hyperglycemia.

Subsequent History.—The patient remained free from glycosuria while keeping house for herself. She then traveled again and gained moderately in weight. The traces of glycosuria which finally returned were again due to unintentional irregularities in diet in hotel life.

Third Admission.—Apr. 16, 1917. Weight 46.4 kg. Heavy glycosuria, slight ferric chloride reaction, ammonia nitrogen 1.96 gm., blood sugar 0.317 per cent, CO₂ capacity 46 vol. per cent. Glycosuria continued on the diet formerly prescribed, but ceased with a single fast-day, Apr. 22. A carbohydrate test thereafter showed a tolerance of only 50 gm. The acidosis meanwhile cleared up. A carbohydrate-free diet was then instituted, with 65 gm. protein and 1200 calories. On this there was an excretion of 0.8 to 1 gm. ammonia nitrogen daily. The last blood examination on May 23 still showed hyperglycemia of 0.176 per cent. The patient was discharged May 30, 1917, weighing 45.8 kg., on the diet above mentioned (1.4 gm. protein and 26 calories per kg.). She was to return to the hospital within a few months for observation to determine whether these measures were adequate.

Remarks.—One feature of interest is the possible origin of the diabetes from an infection or operation. Possibly this was no more than an exciting cause. At any rate, the diabetes was permanent. The case was of the most acute type and the progress very rapid, so that physicians had given a prognosis of only a few months of life. The actual result has been an approximately normal exist-

ence for 3½ years to date. The principal trouble has been that the life was too nearly normal. Though the patient was strictly faithful in her intentions, she led a rather strenuous life and exceeded her diet quantitatively in such manner that the weight was not held down to the desired degree of undernutrition. The greatest difficulty has been the prolonged life in hotels, where undue quantities of carbohydrate were eaten unintentionally. Such causes of injury are very serious in a case inherently so severe and so susceptible to harmful influences. In addition, there is the fact that the tendency to hyperglycemia was not detected and checked in its incipency. These various causes suffice to account for the clearly perceptible downward progress. Comparison between the great rapidity of such progress before beginning treatment, and its slowness during more than 3 years of still imperfect treatment, casts doubt upon the existence of any "spontaneous" cause. The patient is still comfortable and looks the picture of health. The more rigorous dietary restrictions now necessary will reduce her considerably in weight and strength, and it remains to be seen whether they will succeed in arresting the downward tendency.

CASE NO. 4.

Male, age 12 yrs. American; no occupation. Admitted June 22, 1914.

Family History.—Mother is well. Two of her grandparents died supposedly of Bright's disease, at age above 60. Her father died supposedly of typhoid at 62. Her mother died of cancer of the stomach at about the same age. Her only brother and sister are living and well. Father's grandparents died in old age. Father's mother died of heart trouble at above 70 years. His father died after 60 with some form of nervous and mental trouble along with glaucoma. An uncle of the father died at the age of 6 years of diabetes. Two brothers of the father died, one in Europe at the age of 21, supposedly from overstudy, the other of some nervous or mental trouble in a sanitarium. The father is the only survivor of his family and is neurotic. Patient's parents married when the mother was 19; she had two children 13 months apart and had typhoid when the first baby was 1 month old; no miscarriages. The first child developed diabetes at the age of 2½ years and died from it at 4 years.

Past History.—Patient had normal birth. Mother's milk disagreed and baby was raised on artificial food. At the age of 2 months, history of swelling of both sides of neck; incisions on the two sides said to have liberated enough pus to fill a drinking glass; no return of anything of the sort. The baby was healthy and fat, but not abnormally obese. Several attacks of bronchitis in infancy, "rheumatism" in the legs for 4 days when 4 years old, measles at 5, chicken-pox at 6, several attacks of tonsillitis thereafter, but no complaint of tonsils in recent years. In general a bright, healthy, active boy. He attended school for 2 years, thereafter was taught by governess at home. Candy was forbidden from fear of diabetes, otherwise an ordinary diet was taken with ordinary quantities of starch.

Present Illness.—Polyuria and polyphagia began at the age of 5, and diabetes was immediately diagnosed by family physician. Diet was restricted by withdrawal of sugars and most starches, substituting gluten bread, but through more than a year of such treatment patient never became sugar-free. A diabetic specialist was then consulted and glycosuria was kept absent for several weeks. Acidosis was found about this time, and a small amount of carbohydrate was then allowed. He remained under careful treatment up to the age of 9, but felt so badly and lost so much weight on carbohydrate-free diet that a change seemed necessary. He was then given liquid diet, taking two or three quarts of milk a day, but glycosuria became so heavy that strict diet was resumed within a few days. One such period has been tried since; otherwise a moderately restricted diet in weighed quantities has been taken. The usual oat cures, preceded and followed by vegetable days with eggs have been used repeatedly, but no fast-days. The patient's highest weight was 70 pounds at the age of 10. Up to the age of 11 the urine had been free from albumin so far as observed. At that time both glycosuria and acidosis became worse, and urine showed considerable albumin and casts. Nephritis has been present ever since, with more or less edema most of the time. Vision began to be blurred several years ago and was not aided by glasses. About a year ago there began to be a mist before his eyes, which has increased to nearly total blindness. The hair has been falling out since about the same time. Teeth have not decayed, but have failed to develop; two canines appeared about a year ago and barely protruded beyond the gums. Constipation is complained of, also attacks of vomiting. Coma has been seriously threatened on two occasions and has been averted by the free use of carbohydrate and alkali. A number of different climates and mineral springs have been tried without result. Neuritic pains in the legs are also complained of, and on two occasions recently slight superficial injuries have produced long-standing ulcers, one of which is barely healed. The gums are said to bleed whenever the teeth are washed. The patient has been bed-fast for a month or more on account of weakness, but recently has been sitting up and dressed for a few hours daily.

Physical Examination.—Height 140 cm., weight 23.8 kg. Extreme emaciation and weakness. Hair cream-colored, long, silky, thin. Eyelids droop with look of exhaustion; intraocular tension diminished. Pupils react to both light and distance, but tests of vision show that only marked changes in illumination are perceived and only large objects dimly distinguished. Vision better at periphery than at center of fields. Ears and nose normal. Mouth shows above mentioned condition of teeth, well kept, but tongue moderately coated. Palate and fauces narrow; only slight tonsillar enlargement. Palpable glands in neck, very small. A few sudamina especially on sides of neck. Otherwise skin is dry and slightly scaly. Knee jerks barely obtainable, other reflexes normal. General examination otherwise negative.

Treatment.—On June 23 and 24 diet was permitted according to description of

what had previously been taken. Fasting was begun with some misgivings on account of the extreme weakness, and whisky was administered in the small quantities which the patient could take without complaint of discomfort. By June 27 the strength seemed greater rather than less. Nevertheless as a precaution, since fasting had not heretofore been imposed upon any patient as dangerously weakened as this, it seemed conservative on this day to allow 155 gm. olive oil with a trifle of vegetables as a relish. Alcohol was given the next day, and on the following days olive oil was again added. Green vegetables were then added, representing carbohydrate as follows: July 1, 6 gm.; July 2, 12 gm.; July 3, 15 gm. A change was then made to protein-fat diet, increasing up to 61.6 gm. protein and 1530 calories on July 13. Pancreas was fed at this time as noted below. This diet was tolerated as far as glycosuria was concerned. The bare traces of glycosuria limited to certain portions of the day, which appeared so entirely unaccountable at that time, were explained subsequently as due to surreptitious eating, in this instance probably of a sweetened tooth-paste. On account of these traces of glycosuria and the persistent acidosis, an absolute fast was imposed notwithstanding weakness, and continued for 5 days, being followed by the alcohol day of July 19, and then by a limited protein-fat diet, always below 900 calories. By the end of this period, Aug. 7, the strength was far better than at any previous time. The patient was up and dressed most of every day, walked about the hospital, and on Aug. 7 was strong enough for an automobile ride. Beginning Aug. 9, a period of very low diet consisting largely of alcohol and green vegetables was instituted, particularly for the purpose of clearing up acidosis, until on Aug. 17 one egg was added to the whisky and vegetables. The diet was increased by one egg daily, till on Aug. 20 four eggs were given. After a fast-day with alcohol on Aug. 24 and a vegetable day on Aug. 25, protein-fat diet was begun and rapidly increased to 1600 to 1700 calories, with as much as 50 to 60 gm. protein. Glycosuria was stopped by the fast-days (with alcohol) of Sept. 5 and 6, but returned promptly with resumption of the high diet. It also persisted during the 2 alcohol days, Sept. 16 and 17, and the low protein-fat diet of 500 calories or less of the latter part of Sept. and the first of Oct., but cleared up when a diet was subsequently given composed of little more than alcohol and olive oil. The patient became very weak in consequence of this undernutrition. On Oct. 19 he woke up weak, but with normal consciousness. While he was eating breakfast consciousness gradually failed, and within less than an hour he was entirely unconscious. Pulse and respiration showed no special change. Tube feeding was instituted, a total of nine eggs and 30 cc. whisky being given in divided doses. Saline solution was given intravenously at intervals, and three doses of 10 gm. levulose each in 200 cc. solution were given subcutaneously. Benefit was only temporary, and death occurred after very gradual decline on Oct. 20, with continued unconsciousness but no other signs of diabetic coma and with urine negative for both sugar and acetone bodies.

Acidosis.—The patient entered with a daily excretion of approximately 18 gm.

total acetone bodies (as β -oxybutyric) and 2.5 gm. ammonia; these were brought gradually to an almost normal level. A slightly high ammonia and occasional traces of ferric chloride reaction persisted. Radical treatment of the acidosis was difficult because of the extreme weakness of the patient.

The results of attempting to maintain strength by the use of fat are shown in Table V.

Oil days instead of fast-days were tried at the outset as shown, because of their use by former workers and because of the patient's weakness. The first and

TABLE V.

Date.	Diet.					Weight.	Sodium bicarbonate.	Calcium carbonate.	Urine.				
	Protein.	Fat.	Carbohydrate.	Alcohol.	Calories.				Volume.	Sugar.	Total nitrogen.	NH ₃ -N	Total acetone bodies (as β -oxybutyric.)
1914	gm.	gm.	gm.	gm.		kg.	gm.		cc.	gm.	gm.	gm.	gm.
June 23	70.5	101	4.15	—	1623	23.8	—	—	3174	42.51	11.59	1.65	8.00
" 24	91.5	177	103.3	—	2319	23.2	—	—	2772	32.60	10.64	3.44	15.59
" 25	—	—	—	16.5	116	23.2	3	—	2953	12.96	6.67	2.75	9.22
" 26	—	—	—	19.5	137	22.3	—	—	2361	6.85	5.15	2.60	7.67
" 27	6.9	248	11.9	1.2	1578	22.4	—	—	2028	16.30	5.17	2.33	17.81
" 28	2.3	2.3	1.9	25.5	189	21.2	20	—	2074	8.90	5.68	2.70	8.95
" 29	—	50.0	—	26.0	632	22.0	—	5	2238	1.17	3.18	1.80	2.99
" 30	—	80.0	—	22.0	874	21.6	—	20	2483	0	3.50	1.79	4.77
July 1	2.1	102.6	5.8	20.0	1125	21.6	—	20	2153	+	3.61	2.37?	3.25
" 2	5.3	110.0	12.7	10.0	1201	21.0	—	5	1589	0.66	3.18	2.07	2.10
" 3	4.5	12.5	15.3	22.5	353	21.4	—	—	1324	3.92	2.70	1.32	4.35
" 4	7.6	38.0	—	21.2	532	21.6	—	—	1501	+	3.33	1.08	7.03
" 5	15.4	12.1	—	11.2	625	21.2	—	—	1340	0.80	3.08	2.20	8.19
" 6	15.4	52.1	—	17.5	669	21.6	—	—	1574	0.97	2.44	1.65	4.35
" 7	22.6	58.1	—	17.5	731	21.4	—	—	2855	0.36+	5.47	1.62	7.45
" 8	22.6	58.1	—	17.5	731	21.8	—	20	1736	+	2.83	1.15	7.23
" 9	22.6	58.1	—	17.5	731	22.6	—	—	2453	+	3.48	1.52	5.80
" 10	22.6	58.1	—	17.5	731	22.8	—	—	2749	+	3.33	1.48	5.87
" 11	30.8	82.2	—	17.5	1012	23.2	—	—	2769	+	3.75	1.47	11.66
" 12	30.8	82.2	—	17.5	1012	23.4	—	20	2467	+	4.29	1.26	6.26
" 13	61.6	124.4	—	17.5	1531	23.2	—	18	2768	+	7.94	1.55	6.28
" 14	Fast-day.			—	—	23.5	—	—	1031	+	3.25	0.59	3.37
" 15	"	"	"	1.5	—	23.0	—	—	1082	0.46	2.49	0.62	4.92
" 16	"	"	"	—	—	22.6	—	—	1225	0.22	2.47	0.70	3.24
" 17	"	"	"	—	—	22.0	—	—	1263	0	2.70	0.69	0.79
" 18	"	"	"	—	—	21.6	—	—	1130	0	1.92	0.28	1.46
" 19	"	"	"	12.0	—	21.6	—	—	1322	0	1.98	0.27	1.09

largest of such fat rations, on June 27, caused the acetone body excretion to rise suddenly from 7.67 to 17.81 gm. The next day, without fat, there was an equally sudden fall to 8.95 gm. The influence of smaller quantities of fat on subsequent days was less clearly distinguishable, but the general effect was an elevation of the ammonia and acetone body output, as shown especially by the fall with fasting after July 13. It is thus evident that even moderate quantities of ingested fat keep up acidosis, presumably by maintaining a higher fat metabolism than on fasting. Also, strength is not improved by such use of fat. On the contrary, acidosis tends to produce more marked asthenia than undernutrition.

The occasional alkali dosage is shown in Table V. Perhaps the reason for the absence of increase of ammonia excretion with the high fat intake of June 27, is that the ammonia formation was already at the maximum possible in this patient at this level of total nitrogen excretion. Possibly the lack of neutralizing substance was responsible for the marked clinical symptoms of acidosis (hyperpnea, prostration, small rapid pulse) which came on promptly toward the close of that day. It therefore seemed advisable to give 20 gm. sodium bicarbonate on the next day. Calcium carbonate might theoretically neutralize acid in the stomach and perhaps to some extent in the intestine. It is not known whether it served any practical usefulness in this or other cases where it has been tried. No other alkali was given except toward the close of the history; then on 6 days (Oct. 8 to 13) without symptoms suggesting acidosis and merely with a vague idea of guarding against salt starvation, the following mixture was given daily: sodium bicarbonate, calcium carbonate, magnesium oxide, each 2 gm., potassium bicarbonate, 1 gm. The giving or withholding of such mixtures has had no perceptible influence upon this or other patients. Vegetables presumably furnish sufficient quantity and variety of bases.

Tolerance.—This was exceedingly low, but an exact estimate of it is prevented by slips in the diet. At the outset, the barely perceptible traces of glycosuria in the early days of July seemed perplexing. Later, unaccountable glycosuria was encountered on certain days without clear relation to the known food intake. It had seemed that a blind boy isolated in a hospital room and so weak that he could scarcely leave his bed would not be able to obtain food surreptitiously when only trustworthy persons were admitted. It turned out that his supposed helplessness was the very thing that gave him opportunities which other persons lacked. Even on a diet which satisfied his appetite according to his own statement, as at the end of Aug. and the first of Sept., the attempt to evade the strict watch kept over him appealed to him as a sort of game or battle of wits, so that he even took things for which he had no real desire. Among these unusual things eaten were tooth-paste and bird-seed, the latter being obtained from the cage of a canary which he had asked for. Also his mother and his governess on visiting him sometimes brought lunch, which was kept in a closet supposedly without his knowledge; nevertheless, in the short intervals when he was unwatched, he managed to find it and remove such articles as might not be

missed. These facts were obtained by confession after long and plausible denials. The experience illustrates what great care is necessary if records of diabetic patients are to be vouched for as correct.

Weight and Nutrition.—Weight at admission 23.8 kg., at discharge 18.1 kg. One feature is the successful carrying through of two periods of inanition in a dangerously weak, small boy. The olive oil, as mentioned, probably did more harm than good. The whisky may have been of some slight aid, but there was no plain clinical evidence. The 6 days of almost complete fasting beginning July 14 were borne without signs of collapse, even though the weakness was such as to cause concern before any fasting was imposed. The diet of some 700 to 800 calories, protein, fat, and alcohol, in the latter part of July and the first part of Aug., was theoretically sufficient for maintenance, but was barely tolerated. Even though some of the glycosuria may have been due to slight errors in diet, the recurring traces of ketonuria show that this intake was excessive. The period of carbohydrate and alcohol beginning Aug. 9 cleared up the ketonuria, but did not avail to prevent its prompt return when a high carbohydrate-free diet was next attempted. The diet of 1600 to 1700 calories at this time was very high for this body weight; there was in fact a slight gain of weight and strength, but as usual the increasing glycosuria and ketonuria forced a cessation of this plan, and the end-result, as is invariably the case, was harmful instead of beneficial. The subsequent undernutrition beginning Sept. 16 was improperly planned, because the persistent glycosuria apparently indicated a remarkable absence of assimilation, whereas the real trouble was the unusual ingenuity of the patient in obtaining forbidden food.

Pancreas Feeding.—This patient developed a liking for raw pancreas, so that he spontaneously asked for it. It was therefore of interest to study the effect of a diet in which pancreas protein was the sole possible source of sugar; *i.e.*, a diet composed of nothing but pancreas, olive oil, and alcohol. This was the character of the diet beginning July 4; on that day 50 gm. of fresh pancreas were given as the only protein. The next day this was increased to 100 gm., which continued to July 7, when it was raised to 150 gm. This continued to July 11, when it was increased to 200 gm. On July 13 the quantity was increased to 400 gm. The traces of glycosuria were not cleared up either by pancreas or by fasting until the patient's trick of eating a small quantity of tooth-paste each morning was detected, whereupon on July 17 the traces of sugar ceased promptly. It is therefore evident that pancreas feeding did not avail to establish an assimilation for even the trivial quantity of sugar contained in a very few grams of tooth-paste. On July 20, after fasting, the first diet given consisted of 80 gm. fresh beef pancreas with whisky and olive oil. On July 21 the pancreas was increased to 120 gm. On July 22 it was only 96 gm. by mistake, on July 23, 120 gm. On July 24 and 25 the identical diet was given, with substitution of raw beef for pancreas. On July 26 and 27 the same quantity of beef was given, cooked before eating. On July 28 and 29, 120 gm. of raw pancreas were again substituted. The occasional glycosuria up to this time was irregular and probably due to surreptitious eating.

This diet was apparently near the verge of tolerance. After a fast-day on July 30 the same diet was given, of 120 gm. pancreas with addition of one egg; this diet continued to Aug. 8. A regular and persistent glycosuria was the result, evidently due to the fact that this diet was slightly in excess of the tolerance. It would therefore appear that fresh pancreas was not able to increase the patient's protein tolerance to the extent of one egg, since he was mostly sugar-free on pancreas or raw or cooked beef without the egg, and excreted small quantities of sugar on raw pancreas with addition of the egg. There was also no perceptible influence upon acidosis. Another pancreas feeding experiment was tried, beginning Sept. 10, with similar result (see Chapter IV).

Remarks.—This 12 year old patient, admitted after 7 years of downward progress, delayed but not stopped by the most competent care obtainable, with retinitis and profound emaciation and weakness, may be said to have been in the hopeless stage of his disease. It is of interest that both albumin and casts cleared up under treatment; they may therefore be attributed to the diabetes or perhaps to the acidosis, since true nephritis does not thus disappear. The weight was reduced by 5.8 kg. in the 4 months of treatment. The improvement in strength was evident to all concerned and considerable encouragement was felt at one time. The essential difficulty lay in the stealing of food; on account of this deception the treatment was improperly managed in several respects. The undernutrition period of the closing month was what brought on death, which may be attributed to inanition.

It seems unprofitable to speculate how long or in what condition this patient might have lived if he could have been treated by undernutrition from the first diagnosis of diabetes. What is certain, however, is that diabetic retinitis has never yet been known to develop under thorough treatment by this method; and anyone making use of high diets for the sake of supposed comfort must be prepared to assume responsibility for occasional blindness and similar troubles.

CASE NO. 5.

Male, married, age 34 yrs. American; customs inspector. Admitted July 15, 1914.

Family History.—Entirely negative for heritable or metabolic disease.

Past History.—Generally healthy life. Measles, tonsillitis, and adenoids in childhood. Neisser infection at 22. No history or indications of syphilis. Nervous and easily excitable since boyhood. Indigestion and constipation began at about 22 and have grown worse up to the present, probably aggravated by irregular eating since entering customs service at 23. There is a feeling of hunger with nausea between meals, temporarily relieved by eating; no pain, no vomiting, little eructation. No alcohol up to 25, then began to drink beer and other liquors, occasionally to slight excess; during the past 4 months has lost all appetite for liquor. Smokes two or three cigars a day.

Present Illness.—In July, 1913, while at work, patient experienced a sudden feeling of dizziness, then compression about chest, followed by vomiting, colic,

and diarrhea. After a doctor had given him calomel and salts at home, on diagnosis of "auto-intoxication," he had hot fever during that night, but felt well the next day and returned to work. Urine was not examined. From that time on he felt constantly thirsty and steadily lost weight and strength. About Sept. 1 the same doctor was consulted again and found 4 per cent glycosuria. Patient followed the routine restricted diet prescribed, but was sugar-free only twice for about a week; this sugar-freedom was obtained by rigid exclusion of carbohydrate. Acetone appeared, so a small quantity of carbohydrate was allowed, with resulting glycosuria. Occasional vegetable days have been employed. Lately a quart of milk daily has been added, and diet has been unrestricted on 1 day each week. On vacation in the country, July of this year, he took ordinary mixed diet for 1 week, and experienced an acute attack similar to the initial seizure 1 year previously. At present he follows the diet with restricted carbohydrate; feels nervous and weary, no polyphagia, slight polydipsia and polyuria; no dryness of skin, but on the contrary troublesome sweats. Normal weight has been 175 to 180 pounds; recently it has fallen to 144 pounds.

Physical Examination.—Height 173.8 cm. Weight 60.4 kg. Body well formed, but lean. Neurasthenic manner, expression indicating weakness and weariness. Skin very moist, noticeable pallor. Slight enlargement of tonsils. Knee jerks entirely absent. Other reflexes normal. Examination otherwise negative.

Treatment.—On the day of admission and the 2 following days, patient was allowed to choose a diet resembling his habitual one. Then 2 plain fast-days were given, followed by 3 alcohol days. The result, as shown in the graphic chart, was a clearing up of glycosuria but persistence of the ferric chloride reaction. Green vegetables were then added (July 23 to 27) and the latter reaction thus cleared up. After a single fast-day with alcohol on July 28, the patient proved able to tolerate a diet as high as 1100 calories with about 50 gm. protein and 70 to 75 gm. carbohydrate. This was undernutrition, representing, for a body weight of about 60 kg., about 0.9 gm. protein and less than 20 calories per kg. Alcohol was discontinued on Aug. 5, as it was unnecessary and the formation of a habit was undesirable. Beginning Aug. 11, an experimental period was begun to show the effect of increasing calories, particularly in the form of fat (see below). Thereafter, it was intended to place the patient upon a proper living ration preparatory to dismissal; but on Nov. 9 he suddenly requested discharge to accept a particularly favorable business opportunity. He was therefore allowed to go with approximate instructions regarding diet, following the plan of not weighing his food but judging portions by the eye, and guiding himself by his urinary tests and particularly by his weight. The diet ordered consisted of protein, fat, and about 100 gm. carbohydrate in green vegetables. The entire treatment was not one of undernutrition, because he left weighing approximately 1 kg. more than on admission to hospital. The relative mildness of the diabetes had not called for the most rigorous measures, and the patient was already far under normal weight. He was instructed never to allow himself to gain weight above 160 pounds.

Sept. 24	170	579	100	6495	105.5	61.6	2035	150.88	+++	13.84	1.44	—	302.8	101.6		+10.2	-50
" 25	155	612	92	6705	109.0	61.8	3375	168.75	++++	19.58	2.37	—	36.5	—		+2.3	-77
" 26	155	612	91	6697	109.0	61.4	3165	202.81	++++	17.47	1.58	8.050	—	—		+6.3	-112
" 27	Fast-day				—	62.2	3020	36.30	+++	12.56	2.42	9.570	—	—	2.98	0.99	-13.6
" 28	"				—			0	++	10.88	1.77	0.450	163.9	58.8		-11.9	—
" 29																	
" 30																	
Oct. 1																	

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TABLE VII.

Date.	Diet.					Weight.	Urine.				Nitrogen bal- ance.	Carbohydrate balance.
	Protein.	Fat.	Carbohy- drate.	Total cal- ories.	Calories per kg.		Volume.	Sugar.	FeCl ₃ reaction.	Total ni- trogen.		
1914	gm.	gm.	gm.			kg.	cc.	gm.	gm.			
Sept. 29	26.4	7.3	82.0	511	8.7	58.8	1375	+	+++	8.06	-4.13	+82.0
" 30	26.3	7.2	82.2	511	8.5	60.0	1975	0	+++	10.51	-6.69	+82.2
Oct. 1	26.2	5.9	75.6	471	7.7	60.8	3035	0	+++	6.80	-2.89	+75.6
" 2	25.7	7.3	80.9	513	8.4	60.6	2900	+	++	5.92	-2.10	+80.9
" 3	26.1	7.4	80.4	504	8.3	60.6	2995	0	+++	8.69	-8.98	+80.4
" 4	24.4	6.6	82.5	499	8.3	60.0	2715	0	+	7.06	-3.43	+82.5
" 5	32.5	13.0	80.0	582	9.6	60.2	3380	0	+	9.06	-4.22	+80.0
" 6	40.1	16.8	73.2	620	10.3	60.0	3195	0	0	8.56	-2.69	+73.2
" 7	44.9	57.8	80.1	983	16.3	60.0	2315	+	0	-	-	+80.1
" 8	45.5	51.6	84.3	1010	16.5	61.0	2590	0	0	8.38	-1.61	+84.3
" 9	46.1	51.7	82.3	1006	14.7	61.4	3205	0	0	8.46	-1.58	+82.3
" 10	45.5	51.6	84.3	1010	16.4	61.6	2615	0	+	7.95	-1.17	+84.3
" 11	51.5	56.3	82.6	1072	17.3	62.0	2795	0	0	-	-	+82.6
" 12	58.7	61.8	77.0	1129	18.1	62.4	2960	0	0	8.88	-0.14	+77.0
" 13	65.2	96.0	82.0	1495	23.6	62.2	2822	0	+	8.81	+0.98	+82.0
" 14	69.1	128.5	82.1	1814	29.1	62.4	3150	0	0	9.45	+0.83	+82.1
" 15	75.2	163.2	82.1	2161	34.4	62.8	3145	0	0	9.12	+2.05	+82.1
" 16	75.5	187.3	82.4	2392	38.1	62.8	2895	0	0	7.30	+3.84	+82.4
" 17	81	189	105	2518	39.9	63.0	4280	0	0	9.93	+2.11	+105.0
" 18	92	196	104	2621	41.6	63.0	3380	0	0	8.92	+4.76	+104.0
" 19	104	195	99	2643	41.9	63.0	3270	0	0	10.20	+5.27	+99.0
" 20	103	194	103	2647	41.7	63.4	3960	0	0	11.56	+3.78	+103.0
" 21	104	195	103	2661	42.0	63.4	3160	0	0	10.49	+4.99	+103.0
" 22	110	203	124	2851	45.0	63.4	4070	0	+	-	+5.38	+124.0
" 23	114	197	121	2646	41.7	63.4	3680	0	0	11.48	+5.49	+121.0
" 24	114	220	118	2999	47.0	63.8	4254	0	0	15.31	+1.64	+118.0
" 25	114	228	120	3073	48.4	63.4	4085	0	0	15.36	+1.61	+120.0
" 26	113	219	119	2829	44.7	63.2	4487	0	0	14.36	+2.47	+119.0
" 27	115	221	123	3128	50.0	62.8	3590	0	+	-	-	+123.0
" 28	112	227	118	3053	48.3	63.2	3810	0	0	-	-	+118.0
" 29	114	228	120	3074	48.8	63.0	3554	0	+	-	-	+120.0
" 30	81	222	39	2556	-	-	1605	0	0	-	-	+39.0
" 31	78	368	51	3950	-	-	930	0	+++	-	-	+51.0
Nov. 1	108	193	92	2610	39.4	62.2	3770	0	0	-	-	+92.0
" 2	148	292	92	3676	59.8	61.4	3205	0	+	-	-	+92.0
" 3	165	483	104	5595	90.8	61.6	2865	+	++	-	-	+104.0
" 4	165	482	99	5563	89.4	62.2	2600	+	+	-	-	+99.0
" 5	112	351	93	4099	65.9	62.2	3090	0	+	-	-	+93.0
" 6	Alcohol 20 gm.			140		61.6	2690	0	0	-	-	-
" 7	155	221	119	3177	53.6	59.2	2240	0	0	-	-	+119.0
" 8	114	220	120	3002	48.8	61.4	3880	0	0	-	-	+120.0
" 9	114	220	120	3002	49.0	61.2	1710	0	0	-	-	+120.0

Overfeeding Experiments.—The patient was peculiarly adapted to experiments with excessive diets, for though he had never suffered from true diabetic polyphagia, he was habitually a very heavy eater. Also his constipation was invincible, notwithstanding the most enormous fat diets. He took these diets with relish and without increase of his slight dyspeptic complaints. As indicated in the laboratory chart, the stools were small, hard, and infrequent, and carmine for demarcation was always retained for several days. With the return of diabetic symptoms in each instance the patient felt so much worse that he was glad to resume a rational diet even at the price of slight continual hunger. The experiments were of practical usefulness in convincing him of the inadvisability of trying to satisfy his appetite, and with this object lesson he has remained faithful to treatment from that time to the present.

Nitrogen Balance.—The most surprising feature is the remarkable nitrogen retention, comparable to that described in normal persons by Lüthje and in diabetics by Falta and coworkers. It is to be recalled that the patient was moderately emaciated from diabetes and had then been subjected to fasting and low diet, which had reduced his nitrogen excretion to a low level. Also the diet in this experiment was liberal in protein, and starting at 64.5 calories per kg. increased to 109 calories per kg.—an extreme surplus for a man at rest in a hospital ward. With the rapid gain in weight it is not surprising that considerable nitrogen was stored, but it is remarkable that the low output of 6 to 8 gm. daily was maintained up to the sudden increase on Sept. 13, the day before the onset of glycosuria, and simultaneously with the appearance of the first decided ferric chloride reaction. The retention then continued, but to a diminishing extent, notwithstanding the steady increase in total calories. The diminution of storage may probably be attributed to the active diabetic symptoms. Notwithstanding the large quantity of nitrogen stored, the fasting and low diet following Sept. 27 quickly brought a return to the same low nitrogen output as before. Analyses are not complete for the second period of overfeeding, but the data available fully confirm the results in the first period.

Influence of Body Weight.—The weight was built up in two feeding periods on different diets. Diabetic symptoms were present at the higher weight in each instance. The attainment of a higher weight in the second as compared with the first period of overfeeding may have been aided by the mildness of the symptoms on the second diet. This difference makes it clear that weight was not the sole factor in bringing back symptoms, but the kind and quantity of the different elements of the diet is necessarily an important factor.

Influence of the Diet.—Both glycosuria and acidosis were brought on by increase of the diet, particularly in fat. The influence of the three elements may be considered as follows.

1. Carbohydrate.—The glycosuria cannot be attributed merely to carbohydrate, because the increase of carbohydrate in the first overfeeding period was not great, and the quantity on certain days, such as Sept. 23, 25, and 26 with

heavy glycosuria was actually less than on earlier days without glycosuria. Also in the second overfeeding period the carbohydrate was regularly higher than in the first one, yet glycosuria was trivial in comparison with the first period. On the other hand, carbohydrate was not effectual in preventing acidosis, so that it would have been impossible, even in this relatively mild case, to control acidosis by feeding carbohydrate along with a high fat diet. A fallacy of the carbohydrate balance plan is also illustrated; for in the period Sept. 11 to 19 this balance was as high as before, yet the beginning ferric chloride reactions and the higher average acetone excretion, though so slight as to be often ignored, were actually significant of the damage already done by fat and soon to be more manifest.

2. *Protein*.—Protein was increased at the time of glycosuria and acidosis in the overfeeding period. Such increase did not prevent acidosis. The generally higher protein may be regarded as one cause of the heavy glycosuria in the first overfeeding period, as compared with the slight glycosuria in the second. On the other hand, protein can scarcely be credited as the sole cause of the glycosuria, since the latter was out of proportion to the increase of protein in the first overfeeding period, and also on certain days of the second period (*e.g.* Nov. 3 and 4), with slight glycosuria, both protein and carbohydrate were higher than on certain days in the first period (*e.g.* Sept. 20, 23, 25, and 26) with very heavy glycosuria.

3. *Fat*.—The principal increase in the diet was in the form of fat, and to this may be attributed most of the gain in weight and return of all diabetic symptoms. The fat diet was much higher in the first than in the second overfeeding period, and the excessive caloric intake in this form may be considered the most important factor in the production of both glycosuria and acidosis. Periods of fasting and lower diet quickly cleared up both the laboratory and the clinical symptoms.

4. *Calorimetry*.—This patient was studied by Dr. Eugene DuBois in the respiration calorimeter of the Russell Sage Institute of Pathology on Oct. 30 and 31 and Nov. 5, with a view to observing any possible anomalies in the disposal of the huge rations, particularly of fat. No departures from the normal were demonstrated either in the basal metabolism or in that following a heavy fat meal.¹

Subsequent History.—The patient remained at work in excellent condition, until he reported at the hospital on Dec. 28 weighing 160 pounds, glycosuria having come on with the increase in weight without change in the prescribed diet. Fasting and reduced diet at home brought him down to 157 pounds, but a trace of sugar returned on Jan. 10. He was therefore instructed to keep his weight thereafter below 155 pounds. He then remained continuously sugar-free until he reported at the hospital on Mar. 21 with the following history. On account of his slight indigestion he had consulted a well known stomach specialist of New York, who told him that he must omit most of his vegetables and take two white

¹ Cf. Allen, F. M., and Du Bois, E. F., *Arch. Int. Med.*, 1916, xvii, 1010-1059.

rolls daily. The patient objected that this would bring back his glycosuria, but the physician responded that he had better have glycosuria and feel better. The patient therefore took the white rolls for a short time, and promptly showed heavy glycosuria. He then on his own judgment stopped the rolls, cleared up the glycosuria by fasting, and reported at the hospital because his tolerance had been lowered and he now showed traces of sugar on the diet on which he was formerly sugar-free. A reduction of his green vegetables was therefore ordered, and he was instructed not to exceed his existing weight, which was then 150 pounds. At this weight he was reasonably well nourished and fully able to work, and his troubles were all classified as neurasthenic.

On Apr. 2 and again on Apr. 9, the patient reported, showing both sugar and ferric chloride reactions and weighing 149 pounds. The vegetables were ordered thrice boiled so as almost entirely to exclude carbohydrate from the diet, and the quantities of food were now more strictly regulated so as to make a ration of approximately 2500 calories.

On June 19, the ferric chloride reaction was negative; but there had been traces of glycosuria from time to time.

On July 13, he returned with a similar report, but had recently caught cold, and this had brought a return of glycosuria, concerning which he was very nervous. He was therefore readmitted to the hospital for the week July 13 to 19 for purposes of instruction. Physical examination was as before, except for enlargement of the liver to 5 cm. below costal margin. He was placed on a diet of approximately 2100 calories, with 90 gm. protein and 30 gm. carbohydrate (see graphic chart). He was discharged with instructions to weigh all food, adhere rigidly to this diet, and take a fast-day once every week.

On Aug. 8, he weighed only 58.8 kg., and complained of weakness, weariness, and hunger, but had shown no sugar since leaving hospital. Bran muffins were added to relieve both his feeling of emptiness and his constipation.

On Feb. 28, 1916, the report was similar. He was walking 6 miles daily for exercise. On this basis his diet was increased to 108 gm. protein, 30 gm. carbohydrate, and 2400 calories. Thereafter he continued at work with favorable reports until June 5, when the carbohydrate was increased to 40 gm. and the calories to 2500. Traces of glycosuria gradually came on, so that on July 17 the carbohydrate was again reduced to 30 gm.

The urine subsequently remained free from both sugar and ferric chloride reactions, and the patient gradually increased his exercise to 8 miles of walking daily.

On May 23, 1917, the weight was 56 kg., the blood sugar 0.116, and the carbon dioxide capacity of the plasma 59.9 per cent.

On June 13, 1917, the weight was still 56 kg. and diet was 2000 calories, with 50 gm. carbohydrate and 70 gm. protein. The blood sugar was 0.155 per cent, and the carbon dioxide capacity of the plasma 64 per cent. The urine remained negative for sugar and ferric chloride reactions.

Remarks.—This was one of the early cases, and the treatment contained errors accordingly. The diabetes was of moderate severity, and the attempt was made to treat it with as little inconvenience to the patient as possible, insisting upon a normal urine and a moderately reduced body weight, and hoping for a recovery of assimilation under these conditions. The result shows that such loose methods are not advisable even in a case of this type, and that tolerance is lost rather than gained under such a plan. The patient had felt unable to work at the time of his first admission to hospital. He has been kept in working condition during most of the time for 3 years. His tolerance has fallen slightly, so that now about 80 gm. carbohydrate is tolerated with a diet of 2200 calories. The blood sugar was never reduced to normal, as might easily have been done, and the slight downward progress seems to be nothing inherent in the nature of the condition, but rather due to the inadequacy of the treatment and the continuous slight overtaking of the assimilation. On the whole, a prolonged and conscientious attempt was made to treat this case from the standpoint of immediate comfort and efficiency, and the record is now believed to show that this treatment is unjustifiable even for a case apparently as well suited for it as this one.

Recent examinations have shown that the liver, which was normal in outline at the first examination, and afterward was obviously enlarged in examinations by different observers several months apart, is now distinctly subnormal in size. The superficial veins of the abdomen are becoming prominent. The diagnosis of cirrhosis seems evident, progressing through the hypertrophic to the atrophic stage. This has not suppressed the diabetes and dietary care should not be remitted, but the most rigorous measures appear unnecessary. The frequency of pancreatitis in connection with cirrhosis of the liver is worthy of investigation.

CASE NO. 6.

Female, married, age 48 yrs. Italian; housewife. Admitted July 23, 1914.

Family History.—Indefinite. Patient is ignorant of any special disease in family. (Husband, short and obese, is said to have developed mild diabetes since this patient's discharge.)

Past History.—Very healthy life. Patient keeps house for her husband and four children. Six children died young, perhaps because of tenement conditions. One of those living is mentally defective. Menses regular up to 1 year ago, absent since. She drinks four glasses of beer, one cup of coffee, and one cup of tea a day. Other habits are those of an industrious poor Italian woman.

Present Illness.—Patient was admitted on the pneumonia service on July 23, 1914.

Physical Examination.—A short, slightly obese woman with sturdy peasant appearance, and normal on physical examination except for consolidation and other signs of pneumonia of right lower lobe. The urine showed heavy sugar and ferric chloride reactions, though there had been no former complaints indicating diabetes.

Treatment was conducted first by the pneumonia service of the hospital. The temperature fell by lysis on the 5th, 6th, and 7th days, and on July 31 the signs in the right chest had cleared up and the patient was turned over to the diabetic service.

During the period of pneumonia the diet consisted of oranges and egg-nogs with whisky and cream, the caloric intake being about 1400 to 1600, as shown in the graphic chart. Glycosuria and ketonuria remained heavy during this time as indicated, but there were no symptoms threatening coma.

Diabetic treatment was begun on Aug. 1 with fasting, with addition of whisky because of the convalescent condition. She thus received about 600 calories of alcohol daily until Aug. 7 to 8. She was a very unwilling patient during this time, having been content to stay in the hospital during the pneumonia, but now that she felt well, she was determined to go home to her babies. She had never heard of diabetes and was accordingly unwilling to be treated. Her husband was of equally ignorant type, but fortunately he and certain relatives had seen a few deaths from diabetes and comprehended the necessity of dietetic treatment. Accordingly she consented to remain until completion of treatment. On Aug. 8, green vegetables were added to the whisky and gradually increased until on Aug. 14 they represented 80 gm. carbohydrate. The next day one egg was given, Aug. 17 two eggs, Aug. 18 three eggs, Aug. 19 four eggs, and the next day 100 gm. fish were added. A ration was thus gradually built up amounting to some 1400 to 1700 calories, with 100 gm. carbohydrate and almost the same quantity of protein. This seemed to be an adequate but not excessive diet for her body weight of 54 kg., and it was tolerated without glycosuria or ketonuria. She received several days' instruction in the diet kitchen in the preparation of her food. She was not required to weigh it, but was ordered to take the same kinds and quantities at home as she had been receiving in the hospital.

Acidosis.—A small point is noteworthy regarding the effect of alcohol. On fasting with whisky the ferric chloride reaction became absent on Aug. 3, and the glycosuria the next day. With continuance of 600 calories of alcohol daily, the ferric chloride reaction reappeared on Aug. 6. 600 calories of alcohol therefore did not suffice to keep it absent. It cleared up on Aug. 13 in consequence of the addition of green vegetables to the whisky, about 50 gm. carbohydrate in this form sufficing for this result.

Subsequent History.—After dismissal on July 31, nothing more was heard from the patient until Nov. 25, 1914, when she called at the hospital by request, bringing a specimen of normal urine and reporting that she had followed her diet faithfully and that daily urine tests had been uniformly negative. Circumstances prevented testing the carbohydrate tolerance at that time.

Nothing more was heard from her until she was finally located by the visiting nurse and called at the hospital by request on July 5, 1917. The urine showed heavy sugar and negative ferric chloride reactions. The patient claimed

to feel entirely well but looked pale and run down. She admitted that she had abandoned diet shortly after her previous report and since then had eaten starches, sugars, and the regular family diet without restriction. She was advised to reenter the hospital and resume treatment, but refused on the ground that her children required her presence at home.

Remarks.—The case is chiefly noteworthy from having been first discovered during an acute infection. Presumably diabetes had been present without noticeable symptoms before this time. It was evidently aggravated as usual by the infection. The case is essentially mild and readily controllable by treatment, but the patient's ignorance and neglect are responsible for continuance of active symptoms, which may be expected to bring serious trouble within a few years.

CASE NO. 7.

Female, married, age 36 yrs. American; clothing saleswoman. Admitted July 23, 1914.

Family History.—Father died at 52 of heart trouble. Mother alive and healthy. All grandparents lived to old age. Five brothers and two sisters of patient alive and well. No diabetes or other family disease known.

Past History.—Healthy life, but obesity from childhood. Only sickness scarlet fever. At the age of 15 patient weighed 135 pounds; before onset of present trouble, her weight was 168 pounds. At 18 she began work as a clothing saleswoman; married at 33 but continued work. No children; one miscarriage. Unhappy married life ending in separation. Habits said to be regular, alcohol denied. Patient was a light eater all her life and also indulged very little in candy or sweet dishes. Since onset of diabetes, for thirst and to stimulate strength, she has taken coffee to excess, at least 20 cups a day, 1 pound of coffee every 2 days. Nervous since onset of diabetes but not before.

Present Illness.—Symptoms began last Dec. with pruritus vulvæ. A physician made an examination and prescribed a local application without testing urine. She and her friends noticed rapid loss of weight, and she applied at the Board of Health for examination for tuberculosis, which was found absent. She then went to a medical school clinic, where the physician in charge diagnosed diabetes and merely gave her a list of things to eat and to avoid. During 4 months' attendance at the clinic no benefit was received, and pruritus vulvæ and loss of weight continued. Since Mar. there has been constant pain in calves of legs, described as like toothache. Within the past few weeks she has had six styes on the left eye, which healed uneventfully. Much of her hair has fallen out. There is polydipsia and polyuria but no polyphagia.

Physical Examination.—Nutrition still medium, though superficial tissues show flabbiness and wasting. Nervous facies and behavior. Posterior cervical glands slightly enlarged. Vagina and surrounding parts show superficial inflammation. Uterus retroflexed retroverted. Examination otherwise negative. Wassermann reaction negative.

Treatment.—For the first 3 days, the patient was allowed an observation diet running as high as 115 gm. protein, 80 gm. carbohydrate, and 2000 calories. On this her highest sugar excretion was 63 gm. The ferric chloride reaction, which was slight on admission, became heavy on this diet, indicating that the former diet had included more carbohydrate. 2 days of absolute fasting were then imposed. The glycosuria ceased but the ferric chloride reaction remained heavy. The next day 100 gm. lettuce and 100 gm. cucumber were allowed. Green vegetables were increased daily without other food until 33 gm. carbohydrate were given in this form on July 30. The ferric chloride diminished to a slight reaction, but glycosuria appeared. A fast-day with 35 gm. alcohol was then given, and as glycosuria immediately ceased, 27 gm. carbohydrate in the form of green vegetables were given the next day for the sake of acidosis. Glycosuria appeared, but the carbohydrate was continued for 2 days. Then Aug. 3 was a fast-day with 70 gm. alcohol. On Aug. 4, 12 gm. carbohydrate were given as green vegetables, and on Aug. 5, 17 gm. The ferric chloride reaction had been diminishing and was now absent. Although glycosuria remained absent, Aug. 6 and 7 were fast-days with respectively 65 and 87 gm. alcohol. A slight ferric chloride reaction returned. On Aug. 8, 90 gm. alcohol and 5.8 gm. carbohydrate (in green vegetables) were given. On Aug. 9, the alcohol was increased to 120 gm. and the carbohydrate to 16 gm.; Aug. 10, alcohol 105 gm., carbohydrate 17 gm.; Aug. 11, alcohol 90 gm., carbohydrate 22 gm. The alcohol was then diminished to 75 gm. and this program was continued to Aug. 16. The ferric chloride reaction had been well marked under the large doses of alcohol at the beginning of this period, but gradually diminished with the introduction of carbohydrate until it became negative. On Aug. 17 one egg was added, on Aug. 20 a second egg. A slow increase of diet was continued, until on Aug. 27 it included four eggs, 200 gm. meat, and green vegetables representing 41 gm. carbohydrate. Both glycosuria and ketonuria were now continuously absent, the exclusion of fat having been the principal means by which this end was attained. Fat was then gradually introduced, finally making a diet of about 100 gm. protein, 60 gm. carbohydrate, and 2100 calories. Slight glycosuria resulted and the diet was therefore diminished to 80 gm. protein and 1700 calories.

The patient began to keep irregular hours on visits outside the hospital and was absent one whole night, returning with glycosuria. On Sept. 28 she went out and failed to return. She reappeared on Dec. 7 showing 3.3 per cent glycosuria, which easily cleared up. She visited friends on Christmas and did not return for 2 days. Therefore on Dec. 27 she was dismissed for this conduct, and no further tracing of her case was attempted. The impression was received that the patient was a drug addict or an occasional alcoholic, and that her behavior was thus explained, but no real proof of this supposition was obtained.

Acidosis.—The only noteworthy feature is the fact that doses of alcohol from 75 to 120 gm. failed to clear up the ferric chloride reaction or prevent its reappearance. The efficient means of stopping the persistent acidosis was found in

continued undernutrition and carbohydrate up to the limit of tolerance, with abstinence from fat.

Remarks.—The initial treatment consisted in continuous undernutrition with as much carbohydrate as possible. After both glycosuria and ketonuria were thoroughly controlled, the diet was built up by the gradual addition of first protein and then fat. The weight at entrance was 52.8 kg. The lowest weight resulting from the undernutrition was 47.9 kg. on Aug. 19. Thereafter it gradually rose, and at the time of her first leaving on Sept. 28 the patient weighed 50 kg., which was a satisfactory state of nutrition for both comfort and strength. The case illustrates the treatment of diabetes of moderate intensity with the aid of only the simplest laboratory tests. The outcome was satisfactory except that the psychic instability of the patient precluded continuing treatment.

CASE NO. 8.

Male, married, age 29 yrs. American; printer. Admitted July 28, 1914.

Family History.—Father and mother are alive and well. Mother had a goiter removed at age of 40 for cosmetic reasons; there were no symptoms. Grandparents all healthy. Patient is the oldest of six children. No diabetes or other family diseases.

Past History.—Healthy life. Measles, mumps, and chicken-pox in childhood. Always took cold easily; never had sore throat. Slight pleurisy 4 years ago; in bed only 1 day. Regular life; no excesses. Never nervous. Married 1 year ago; wife well, never pregnant.

Present Illness.—In June, 1913, immediately upon return from honeymoon, patient noticed abnormal thirst and dryness in mouth. Physician immediately diagnosed diabetes but merely prescribed a diet list, and condition rapidly grew worse. Patient was then referred to a New York physician who ordered a diet of nothing but ham and lettuce. He lived strictly on this diet for 6 weeks, eating as much as 5 or 6 pounds of ham a day. Sugar diminished but did not disappear. Other treatments were tried with a steady downward progress. He then consulted a New York specialist, who placed him on strict diet with one "green day" each week, and three or four teaspoonfuls of sodium bicarbonate daily. The urine was never sugar-free, and the loss of weight and strength became worse. On July 25, 1914, patient entered a New York hospital, where a D : N ratio of 3 : 1 was demonstrated on carbohydrate-free diet. Coma threatened on this diet, but the addition of a slice of bread seemed to make him worse. He was then transferred to this hospital in critical condition.

Physical Examination.—An emaciated man appearing very weak. Face thin and nervous. Skin dry. Acetone odor. Drowsiness and increased respiration very evident. Knee jerks absent. Physical examination otherwise negative.

Treatment.—For the first 4 and a fraction days in hospital, the patient was placed on an observation diet as nearly carbohydrate-free as convenient, thrice cooking of vegetables having not yet been adopted. This diet, which represented

77 to 135 gm. protein, 6 to 12 gm. carbohydrate, and 2800 to 3300 calories, was all the patient could eat. He showed the usual inability to gain weight or strength on full feeding, and clinical evidences of acidosis increased. 20 gm. sodium bicarbonate and 20 gm. calcium carbonate were given daily. By Aug. 2 there was incipient coma with nausea, continuous dozing which was promptly resumed whenever patient was roused, hyperpnea, malaise, and weakness. Fasting was therefore begun from necessity. Whisky was given in 10 cc. doses hourly, amounting to about 100 gm. alcohol on the various fast-days. Calcium carbonate 20 gm. and sodium bicarbonate 30 gm. were given on Aug. 2. On Aug. 3 the bicarbonate was increased to 40 gm., on Aug. 4 it was diminished to 20 gm., and on Aug. 5 all alkali was stopped. Clinically, meanwhile, the condition seemed to grow worse during the first 24 hours of fasting; the sleep was noticeably deeper. Improvement on the following day was marked and all the threatening symptoms cleared up rather suddenly. Sugar-free diet resulted on Aug. 5, the 4th day of fasting, although the D : N ratio had been 3 : 1 on the feeding days. Because of the marked weakness, whisky was continued in doses just short of producing intoxication, and green vegetables were gradually added, beginning Aug. 7 with 100 gm. each of lettuce and cucumbers. On Aug. 10 the quantity of carbohydrate in this form amounted to 38.5 gm., and by reason of 240 cc. whisky, the total calories for this day were 1073. There was a day of whisky alone on Aug. 11. The program of alcohol and green vegetables was continued to clear up acidosis thoroughly, and 40 to 50 gm. carbohydrate were now assimilated daily without glycosuria. The ferric chloride reaction was abolished, but the patient was ravenously hungry and seriously weak. Accordingly, on Aug. 23 the carbohydrate was stopped, and the diet consisted of 4 eggs, 100 gm. butter, and 135 gm. alcohol. The eggs were then increased and the alcohol diminished daily, until on Aug. 27 the diet was 60 gm. protein, 37.5 gm. alcohol, and 1660 calories. Aug. 28 was a "green day" of nothing but alcohol and green vegetables with 55 gm. carbohydrate. This sort of program continued until Sept. 11. As usual, no benefit to weight or strength resulted from the attempt to feed to the limit. Accordingly, on Sept. 12 a lower diet was begun, carbohydrate-free, with 80 gm. protein and 1300 calories, the alcohol being at the time diminished to 20 gm. daily. For the weight of about 35 kg. this meant less than 30 calories per kg. daily, and this was diminished still further by the fast-days every 1 or 2 weeks. Exercise would presumably have been beneficial, but the tradition was followed of keeping a patient with severe diabetes as quiet as possible. Therefore he was weak and cold and spent most of his time in a chair close to the radiator, clad in heavy clothing and double underwear. Nevertheless, the condition at certain times began to appear rather promising, since the sugar and ferric chloride reactions were frequently both negative. A difference from the average case soon began to be noted, in that sugar kept unaccountably reappearing and the tolerance seemed to be perceptibly falling under conditions when it should have risen or at least remained stationary. With the progress of time it became more evident that something unusual was

breaking the patient down. Dr. Joslin chanced to see the patient on a visit and suggested the presence of tuberculosis, but physical signs and sputum examinations remained negative. Dec. 6 to Jan. 1, pancreas and duodenal feeding were attempted without benefit, as described elsewhere (Chapter IV). Thereafter the attempt at radical treatment of the diabetes was abandoned, and the patient was allowed at times to eat his fill of a selected diet. Although this diet amounted sometimes to 60 or 70 calories per kg., there was the usual absence of benefit to weight or strength, and the attempt to overfeed was doubtless a mistake. Certain days of lower diet and occasional fast-days were necessarily inserted because the increasing acidosis sometimes threatened coma. On Jan. 9 he was transferred to the metabolism ward of the Russell Sage Institute of Pathology at Bellevue Hospital for calorimetric studies by Dr. Eugene DuBois.¹ He returned to this hospital on Jan. 15. The diet of 2000 calories or over during most of Jan. failed to prevent further loss of both strength and weight. Both the weakness and the rapidly falling weight were probably associated with the seriously increasing acidosis. The steep elevations in weight shown in the graphic chart at times in this same period represented marked edema due to sodium bicarbonate in doses up to 80 gm. daily. Nevertheless on Feb. 1 the point had been reached where a choice was necessary between fasting and immediate death in coma. A 6 day fast with whisky was accordingly imposed, which stopped the glycosuria and cleared up the threatening symptoms, though the ferric chloride reaction was not made negative. A lower diet was then employed, mostly about 30 calories per kg., on which glycosuria remained almost continuously absent and greater comfort was enjoyed by reason of the absence of acidosis symptoms, though the patient was very weak. On Mar. 16 the patient had the symptoms of catching cold with fever and pain in the chest. Some dulness and crepitant râles were now detected. On account of the aggravation of the diabetes, fasting with alcohol was employed on Mar. 16 and 17, but the glycosuria increased. The D : N quotient on Mar. 16 was 2.3, on Mar. 18 it was 4.6. As death was imminent, the attempt at dietary restriction was abandoned and a liberal protein-fat diet with alcohol was permitted. By Mar. 22 the weakness had become extreme. Though there was chemical evidence of intense acidosis, the patient never went into typical coma. Death occurred at noon on Mar. 22, 1915; the patient recognized his wife shortly before this, though too weak to speak.

Acidosis.—The intense acidosis during the first days in hospital was mentioned above. On Aug. 1 the excretion of ammonia was 3.5 gm. and that of acetone bodies (expressed as β -oxybutyric acid) was 38.6 gm. A rapid fall was evident even in the first 24 hours of fasting. On Aug. 8, with 16 gm. carbohydrate in the diet, the excretion was still 1.1 gm. ammonia and 3.1 gm. β -oxybutyric acid. It is noteworthy that the period of 20 days up to Aug. 23, with a diet composed solely of alcohol and green vegetables in the quantities shown, failed to clear up the acidosis entirely, as indicated by the excretion of 0.76 gm. ammonia nitrogen and 0.48 gm. β -oxybutyric acid on Aug. 22. If allowance be made for the effect of the

40 to 50 gm. of carbohydrate, which was assimilated without glycosuria, it would seem that no evident antiketogenic effect was exerted by approximately 600 calories of alcohol in the diet daily. A specific character of the acidosis perhaps is recognizable in such cases, by comparison with others in which acidosis is absent on similar regimen. Neither carbohydrate nor alcohol, but undernutrition was the essential factor in controlling the acidosis at all periods of the treatment.

With a rather high carbohydrate-free diet beginning Aug. 23 there was a marked rise in ammonia excretion, showing the harmful effects of the attempt to build up strength or weight above the tolerance. With the low diet which began Sept. 11 there was a gradual improvement, so that even without carbohydrate in the diet the ferric chloride reaction became entirely negative on Oct. 7, and no more than traces reappeared during the time of radical treatment. Early in Dec., when the attempt was begun to nourish liberally on account of the assumed infection, there is another marked rise in the acidosis, going higher as the attempt was prolonged, until on Jan. 20 the ammonia excretion reached 5.1 gm. In consequence of 2 fast-days it fell sharply, then rose to 4.62 gm. on Jan. 28 in consequence of further excessive feeding. Then on fasting and lower diet it fell and remained at a much lower level until near the end, analyses in the last few days of life being lacking because of loss of some urine.

Beginning Jan. 25, the carbon dioxide capacity of the plasma was also determined. It is seen that although the body weight at that time was rising in consequence of edema from heavy bicarbonate dosage, the blood alkalinity fell sharply to a dangerously low level. With the fasting and alcohol beginning Feb. 1 it rose easily within normal limits, then ranged slightly below and slightly above the lower normal level for most of the remaining time, but dropped sharply almost to the coma level just before the fatal end.

A statement of the alkali dosage is necessary for proper interpretation of the ammonia and CO_2 curves. After the stopping of alkali on Aug. 5 as above mentioned, no more was given until Aug. 28. From Aug. 28 to Dec. 18 inclusive, the patient received daily 2 gm. each of sodium bicarbonate, calcium carbonate, and magnesium oxide, and 1 gm. potassium bicarbonate. These were given in the attempt to assure against a deficit or improper balance of any or all of these bases, as well as to neutralize acids. Similar mixtures have been used in a few other cases. The points in mind have been the reported wasting of bones and excretion of bone salts in diabetes, and also the vague idea sometimes suggested that a disturbance of the balance of salts or metals is at the bottom of diabetes. No effect of such mixtures upon the tolerance or general condition, and no advantage over the use of sodium bicarbonate alone, have been perceptible in any of the cases.

On Dec. 19, 6 gm. sodium bicarbonate were given, and 2 gm. on Dec. 20. The ammonia excretion following the huge diet of Dec. 30 was less than it otherwise would have been, because of the giving of 6 gm. sodium bicarbonate on Dec. 30, and 15 gm. sodium bicarbonate and 30 gm. calcium carbonate on Dec. 31.

Present Illness.—1 year ago patient consulted a physician for a severe cough which had lasted about 2 weeks, and also for a slight injury to his right knee due to a fall. He was told that he had "lung trouble" and was sent to the country. Here he began taking a larger diet than that to which he was accustomed, and especially a great deal of cereals and starchy foods. In about 2 weeks he began to notice polyuria and polydipsia. A physician then diagnosed diabetes. A list of carbohydrate-free foods, also "Metchnikoff's tablets" were prescribed. For the past 9 months he has been under treatment at one of the best New York clinics on practically carbohydrate-free diet. The severer symptoms date back 4 or 5 months, during which time he has lost 25 pounds in weight, has grown much weaker, and his cough has become worse. Constipation and abdominal cramps have been marked, with nausea and sometimes vomiting. There is a chronic cough, mostly at night, with expectoration of white mucus without blood. There was blood in the sputum on one occasion. He now drinks 20 to 30 glasses of water daily and passes as much as 8 quarts of urine. Polyphagia present.

Physical Examination.—Young man with nervous look, moderate emaciation, and general appearance of weakness. Eyes unduly bright, face flushed, skin in good condition. Some pyorrhea, and a few decayed teeth. Throat red, tonsils not visibly enlarged, cervical glands not palpable. A few subcrepitant râles in both apices posteriorly, and expiratory murmur slightly prolonged; lung sounds otherwise normal. Organs otherwise negative. Knee jerks absent. Blood pressure 80 systolic, 60 diastolic.

Treatment.—The patient was placed upon an observation diet of protein, fat, and green vegetables for 4 days, as shown in the graphic chart. Glycosuria was as high as 98 gm. on Oct. 11, but the excretion of acetone bodies was not above 1.4 gm. of β -oxybutyric acid. Fasting with whisky was begun on Oct. 12, and the urine became sugar-free on Oct. 15. Nevertheless, as the patient was well able to endure fasting, green vegetables were not begun until Oct. 18, when 6 gm. carbohydrate were given in this form, increased to 15 gm. on the next day, 30 gm. on the next, and 54 gm. on the next. Sugar was present in traces on the last 2 days (Oct. 20 and 21), therefore 1 more fast-day with alcohol was given on Oct. 22. On Oct. 23 the diet consisted of one egg, 30 gm. alcohol, and 600 gm. thrice cooked vegetables. The next day was similar, with two eggs and substitution of 20 gm. butter for the alcohol. Three eggs were given on Oct. 25, and four on Oct. 26, and then fat was gradually introduced in the form of butter and bacon. A little steak was added on Oct. 30. The highest diets of this period, Oct. 29 to Nov. 1, were only 40 to 60 gm. protein and some 1200 to 1400 calories. But the traces of sugar and ferric chloride reactions made a fast-day with alcohol advisable on Nov. 2. A higher diet was then attempted, up to 2700 calories on Nov. 12, with 17 gm. carbohydrate and 99 gm. protein. The rise in glycosuria was controlled by 1 fast-day with whisky on Nov. 16 and 2 complete fast-days on Nov. 30 and Dec. 1. Protein-fat diets were then employed during most of

Dec. and Jan., the short high calory periods being atoned for by other days of fasting or very low diet. The carbohydrate feeding shown in the graphic chart for the latter part of Jan. represents caramel, which was tolerated with very little glycosuria. It was evident from experience that the patient's carbohydrate tolerance was practically nil, and symptoms returned with any attempt at protein-fat overfeeding. Therefore, in Feb. he was placed on a diet of about 50 gm. protein and 1500 calories, which, if the body weight be set at 50 kg., would be 1 gm. protein and 30 calories per kg. A fast-day once a week served to reduce this by $\frac{1}{2}$, making it equivalent to $\frac{1}{4}$ gm. protein and 26 calories per kg. Exercise had not been adopted for such cases at that time, and this patient was kept mostly at rest. He pronounced this diet adequate for his appetite, and was dismissed on Feb. 17, free from glycosuria and acidosis and in condition for taking up some light occupation.

Subsequent History.—After several weeks experience with the diet prescribed at discharge, the patient had professed his full ability and willingness to live on it, and was expected to go to some nearby place in the country and report frequently concerning his progress. No reports were received. It was learned that he had told another patient in the ward that he was not satisfied to be relieved by diet. He showed an advertisement of a proprietary remedy for diabetes and announced his purpose to seek a complete cure. Instead of keeping his promise to the hospital, he went immediately upon departure to a southern state. He died in Mississippi on Apr. 17, exactly 2 months after discharge. This information was received from a life insurance official, who was unable to give any particulars concerning the death.

Acidosis.—The slightness of ketonuria at admission is presumably to the credit of the treatment given the patient at the clinic in the previous months. It was easily cleared up by the routine measures. The acetone body excretion remained low notwithstanding the high diets in Nov., but the ammonia rose to approximately 1 gm. on two occasions. It fell after the fast-day with whisky on Nov. 16, but the fall was particularly sharp in the 2 days of plain fasting, Nov. 30 to Dec. 1. Acidosis was easily controlled during the hospital stay. There was no doubt of the inherent severity of the case, however, and the probable cause for death 2 months after leaving hospital symptom-free would undoubtedly be coma.

Blood Sugar. Renal Function.—The few analyses from Oct. 11 to Nov. 2 indicated that the blood sugar was rather easily brought to normal. Traces of glycosuria appeared with a lower blood sugar level than usual for diabetic patients, and the findings suggested that the kidney was rather easily permeable. This is the more interesting in view of the fact that small quantities of albumin and casts were present in the urine at some times. This patient was also one of those who, from renal deficiency or unknown cause, are subject to marked edema under treatment. The sharp rise in weight on fasting and low diet, up to 56.2 kg. on Nov. 1, was an example of marked edema. Other peaks in the

weight curve likewise are explainable as edema, sometimes not visible, but in the marked instances plainly evident in face and extremities, with pitting about the ankles. The rapid clearing up of edema with sharp fall in weight as shown at various points on the chart was regularly accomplished by salt-free diet.

Remarks.—This patient was neurotic and secretive. Most of his difficulties in the hospital were neurasthenic, and the attempts to please him were responsible for most of the irregularities and excesses of the diet. He was admitted with a particular view to the suspicion of tuberculosis. The cough gradually cleared up during the diabetic treatment. In Jan. he had a 10 day attack of bronchitis. Examinations for tubercle bacilli on 6 days of this attack as well as on other occasions during his hospital stay were uniformly negative. He was kept in the fresh air most of the time and at dismissal was continuously free from cough or any perceptible signs in the chest. The diagnosis of the pulmonary condition is therefore uncertain.

The entire lack of ability to take carbohydrate without glycosuria on a diet of less than 30 calories per kg. is one index of the severity of the case. Theoretically, some degree of tolerance should have been built up by more radical under-nutrition, but the patient was not psychically suitable for thorough measures.

The treatment cannot be considered ideal in view of the dietary irregularities and excesses. It represents undernutrition to the extent of reducing the body weight from 53.6 kg. on admission to 47.6 kg. on discharge; *i.e.*, a loss of 6 kg. As a result the patient felt stronger and more comfortable, and was free not only from the urinary signs of diabetes but also from his former subjective symptoms. The marked neurasthenia remained. The outcome is satisfactory to the extent that the patient was kept in a tolerable condition for 5½ months in hospital and was symptom-free at the close, while the actual severity of his condition was demonstrated by death after 2 months of unregulated diet following discharge.

CASE NO. 10.

Male, unmarried, age 17 yrs. Irish American; plumber. Admitted Nov. 7, 1914.

Family History.—Grandparents lived to old age. Parents living and well. One brother died in infancy; one brother and three sisters living and well. No diabetes or other disease known in family.

Past History.—Healthy, vigorous life. Measles and whooping-cough in childhood. No other infections; no venereal disease, alcohol, or tobacco. Has worked hard as plumber's helper since stopping school at 14, but he was strong and the work was no strain on him. Always a heavy eater; particularly candy, ice cream, pastry, and everything sweet taken in large quantities. Normal weight 133 pounds.

Present Illness.—Last Jan. or Feb. the patient began to drink two gallons of water per day and pass urine correspondingly. He felt well at this time and was

1000 calories was made on Dec. 29. Jan. 5 was a complete fast-day, Jan. 26 another. Generally reduced diet was used instead of fast-days because of the patient's weakness. He gained strength very markedly during the course of treatment and began to look and act almost like a well boy. Exercise was employed with apparently great benefit, especially as he was naturally strong and muscular. He walked many miles daily, went skating on the ice, and undertook other activities.

Toward the close of Jan. he and his parents considered that a cure had been achieved and that he was ready to go to work. As long as he felt ill he was an ideal patient. At this time, feeling well, he began to rebel at diet and all other hospital rules. The glycosuria and ketonuria during and just preceding the month of Feb. are attributable not to the prescribed diet, but to violations on the part of the patient. It became necessary to discharge him on Feb. 8, and he was informed that in view of his conduct this hospital could have no further connection with his case. It was learned that he followed no regular diet thereafter, and died Mar. 9 with the usual acidosis symptoms.

Acidosis.—The only alkali given was 10 gm. sodium bicarbonate on Nov. 11. In the absence of alkali treatment the excretion of acetone bodies was relatively low, reaching only 13.2 gm. of β -oxybutyric acid on Nov. 10. For the same reason the ammonia excretion was high in comparison, being 3.4 gm. on Nov. 10, 4.75 on Nov. 11, and 4.46 on Nov. 12. It is evident that fasting with alcohol did not immediately bring about a low ammonia, but beginning Nov. 12 the steepest fall occurred, down to 1.5 gm. on Nov. 15, and 0.42 gm. on Nov. 20. The clinical symptoms cleared up much more strikingly than the ammonia.

On the too abundant carbohydrate-free diet of Dec., the ammonia never fell to a normal level. It seemed to rise quite markedly after stopping alcohol on Dec. 16, so that on Dec. 22 and 26 it was slightly above the level of Nov. 14 (2.18 gm.). Dec. 27, with a diet solely of whisky representing 85 gm. alcohol, brought a striking drop in the ammonia, and on the lower diet following this date the ammonia never returned to the height of this peak, but also did not fall to normal. It could presumably have been brought down to normal by the use of alkali, but the advisability of alkali for this purpose under the circumstances is open to question. In this same period the ferric chloride reaction was entirely negative. Alkali would presumably have made it positive and increased the excretion of total acetone bodies. The desirability of this change is also an unknown matter. The real trouble was an unsuitable diet.

Blood Sugar.—The accuracy of the single determination showing an unexpectedly low blood sugar on Nov. 13 is doubtful. While irregularities are possible, it seems more probable that the blood sugar remained close to 0.25 per cent until about the close of the fast and then it fell to below 0.15 per cent. The occasional analyses up to Dec. 15 showed a tendency to remain within normal limits. Further analyses were not possible at the time. More attention should have been paid to this point. In correspondence with the improvement otherwise, it would

seem that the case was still at a stage when normal blood sugar values were rather easily attainable, and such should have been insisted upon.

Remarks.—The earlier part of the treatment was well carried out, and the patient, threatened with coma, was rapidly freed from ketonuria, glycosuria, and hyperglycemia. This was still at an early period of experience with this method; it had not yet been learned that apparent restoration of tolerance is not to be trusted too far, and that weakened function does not so rapidly recover to this extent, but that it must be continuously spared by prolonged undernutrition. Therefore, a carbohydrate-free diet was built up too fast and too high. Even in the absence of laboratory danger signs, it is now known that such a procedure inevitably brings disaster later. The lower diet of early Jan. was more rational. But in general, instead of trying to make the patient feel too well and build him up too rapidly, a more stringent limitation of both diet and weight should have been insisted upon. The patient was received weighing 41.6 kg. After a sharp initial drop to 39 kg. in the early days of fasting, the weight remained stationary, then rose sharply as a result of water retention. Even with the weight of 45.6 kg. on Nov. 28 he did not appear edematous. His tissues had evidently been dried before and retained water subsequently, so that he looked and felt better. The water thus stored on undernutrition was then driven out by increase of the carbohydrate-free diet, probably especially by the increase of fat, so that by Dec. 15 weight had fallen to the same level as at entrance. Nevertheless, the period from Nov. 28 to Dec. 15 must be regarded as one of actual gain of body substance. There was some perceptible edema when the weight rose above 47 or 48 kg., as on Dec. 22 and Jan. 4. The patient was discharged weighing 45 kg., and at least part of the gain over the entrance weight may be regarded as actual increase of body tissue. This gain should be considered as harmful not only indirectly, owing to the fact that the patient became too confident from feeling too well, but also directly, inasmuch as tolerance ought to have been built up instead of weight. Trouble would have resulted later from this condition even if the patient had remained faithful, and it would have been necessary to make a radical restriction of his diet. Also the therapeutic possibilities are never so good after several months of imperfect treatment as at the outset. The cause of the final disaster was, however, the deep ignorance and lack of education of the patient and his entire family, who had no conception of the nature of the disease and were deaf to all advice as soon as the patient felt fairly well. Under such circumstances a successful outcome was precluded. The favorable side of the case is that such a degree of well-being and freedom from symptoms was attained during the 3 months in hospital, while the severity of the case was demonstrated by the death in coma 1 month after breaking diet.

CASE NO. 11.

Female, married, age 55 yrs. Austrian; housewife. Admitted Nov. 9, 1914.

Family History.—Father died at 55, cause unknown. Mother died at 70. Three brothers and three sisters of patient were healthy; one of them died at 65. Family are obese. No diabetes or other family disease known.

Past History.—Patient has been strong and well, though obese. As a young woman she weighed over 200 pounds, more recently she has considered 183 pounds her regular weight. No infections, except measles at 16. No sore throats. She was married at 21; four miscarriages; nine children born alive, four of whom died in infancy. All of those alive are more or less obese.

Present Illness.—10 years ago she began to notice a bitter taste after eating, also constipation. 7 years ago a doctor found 7 per cent sugar in the urine, and by dieting reduced it to 2 per cent. She had followed prescribed diets during these 7 years, but sugar was never below 2 or 3 per cent. She thinks she has lost weight chiefly in the last few weeks. She continued to do housework until last week, when she went into collapse, pale, exhausted, and vomiting blood. Her physician reported 7 per cent sugar in the urine. He prescribed a diet of nothing but green vegetables for 3 days. Vomiting then made eating impossible. Patient entered hospital in this condition with extreme weakness, anorexia and nausea, pain in chest and abdomen, hemoptysis, headache, and dyspnea. The blood brought up at first is described as being brighter and more abundant than now.

Physical Examination.—An obese woman with appearance of prostration, face pale, also extremely cyanosed, cyanosis extending into neck. Moderate constant dyspnea, a weak frequent cough bringing up sputum either bloody throughout or streaked with dark blood. Slight jaundice. Lungs: resonance, passing into dulness at bases, especially posteriorly; breath sounds become bronchial in character over dull areas and are everywhere rough. Coarse, loud râles everywhere. Heart is enlarged to 16 cm. to left of midsternal line and other signs are those of mitral regurgitation. Liver is easily palpable, lower border extending from 2 cm. below umbilicus obliquely into right flank barely above iliac crest. Pain and tenderness complained of over liver, also pain down left arm. Leg veins badly varicosed. Examination otherwise negative.

Treatment.—The patient necessarily remained in bed and was treated by the cardiac service of the hospital with digipuratum for her evident heart failure. The temperature ranged from 37 to 37.6°, the pulse from 92 to 112. The urine was strongly acid, with specific gravity 1020 to 1025 and considerable albumin. The general clinical record is given in Table VIII.

The patient was both weak and drowsy, and the symptoms were evidently due to a combination of acidosis and heart failure. She took no food on Nov. 9 and 10, nevertheless glycosuria was heavy and weakness seemed to be critical. The condition had arisen on a diet limited to green vegetables, and the consequences

Present Illness.—About 3 years ago abnormal weakness, thirst, and polyuria appeared. A physician found glycosuria of $7\frac{1}{2}$ per cent. He ordered abstinence from sugar and pastry. The glycosuria thus diminished to 2 per cent and the patient felt fairly well, but after 8 months on the same diet the sugar rose to $5\frac{1}{2}$ per cent and weakness returned. He has been unable to work for the past 2 years. For the past week he has been confined to bed because of weakness and pains in chest and back. There has been cough, especially at night for 2 months past. No fever and no hemoptysis now, but there was spitting of blood on three occasions last winter. 18 months ago small ulcers appeared on both feet and have slowly extended instead of healing; they are painful only when he walks. He is now nervous and constipated, and teeth have decayed rapidly. He has continued to lose weight.

Physical Examination.—Patient still appears comfortably nourished, with good color in face. Tonsils slightly enlarged; part of left one is missing. Viscera normal to examination. Blood pressure 150 systolic, 95 diastolic. A few patches of lichen planus on arms. Legs show small varicose veins threatening to ulcerate at some points. The skin is pigmented and scaly, somewhat eczematous. Several small superficial ulcers are present on ankles and feet. No gangrene. Strong pulse in dorsalis pedis arteries.

Treatment.—Supper was given on the day of admission and then fasting immediately begun. Though glycosuria cleared up in 2 days, the patient being over weight was given 4 days of absolute fasting followed by 2 alcohol days, then 4 days of green vegetables, then 3 fast-days, and then a diet of moderate undernutrition. The superficial infections cleared up promptly. It is a question whether the trace of glycosuria on Nov. 16 on taking 220 cc. whisky was attributable to the alcohol. As frequently found at the outset in cases of this type, the food tolerance was rather low. Early in Dec. a diet with only 10 gm. or less of carbohydrate caused occasional traces of glycosuria, and in the period Dec. 17 to 25 the attempt to give 15 to 40 gm. carbohydrate had to be abandoned because of persistent glycosuria. At the same time the total diet, if the mean body weight be taken as 80 kg., represented approximately 1 gm. protein and only 25 calories per kg. On strictly carbohydrate-free diet the patient proved able by Jan. 7 to 8 to take 116 gm. protein and 2600 calories without glycosuria. As he had now been reduced by about 11 kg., it was considered advisable in view of his age to allow a diet of this sort and let him have the benefit of improved living conditions in the country and such exercise as he might be able to take. He was therefore discharged on Jan. 9 with this purpose in view.

Subsequent History.—The patient reported at intervals that he was free from glycosuria, and occasional examinations at the hospital showed absence of sugar, very slight ferric chloride reaction, and a tendency to gain weight on the prescribed diet. Though he looked well he complained of continual weakness which made him unable to work. He was very faithful to all instructions, and when unable because of poverty to obtain the prescribed food he fasted altogether. He was readmitted to the hospital May 5 for further treatment.

Second Admission.—The weight at this admission was 82.6 kg.; *i.e.*, about 4 kg. less than at his former admission and about 7 kg. more than at his former discharge. His food tolerance appeared perceptibly higher, as he was now able to take a diet of some 120 gm. protein, 50 gm. carbohydrate, and 3000 calories without glycosuria. On account of the weekly fast-days these figures must be reduced by $\frac{1}{7}$ to give the actual average intake. Undernutrition was shown by the fall in weight during stay in hospital. The weight gained outside of hospital was evidently due to unintentional overstepping of the prescribed quantities. Two determinations of the blood sugar gave values below 0.15 per cent. A fairly liberal diet was permitted with a view to overcoming the marked weakness, and exercise within the patient's limited capacity was also encouraged for this purpose. Shortly before his second dismissal he was made accustomed to a diet of about 100 gm. protein, 50 gm. carbohydrate, and 2500 calories, which represented a reduction below his known tolerance to allow for unintentional errors. He was dismissed on June 29 greatly improved in all respects, and was advised again to take a rest in the country for general hygienic reasons.

Subsequent History.—He reported in person on Sept. 7 with normal urine, feeling able to do moderate work. On Nov. 29 he was seen again; sugar and ferric chloride reactions were regularly negative and he was making his living at his usual work. He had gained about 2 kg. since discharge. The same condition has continued with steady improvement up to the present. He now feels well constantly and carries on his work without difficulty. His diet satisfies him and urine remains normal.

Remarks.—This case is a good illustration of a numerous type—diabetes relatively mild but finally bringing the patient to a state of disability. The clearing up of such a condition generally proves to be neither quick nor easy. The most important therapeutic measure is the reduction of weight, which, however, may not have to be carried to the point of emaciation. The patient is benefited slowly. Unless he has full confidence in the physician, he is likely to abandon treatment because of the tedious privations of diet and the apparent lack of benefit. At first he sometimes even looks and feels worse than before.

For the sake of strength, liberties were taken here in the direction of high feeding which would have meant disaster to a younger patient. More protein and less fat would doubtless have been better. With a weak patient at such an age, it was considered that the slight persistent ferric chloride reactions could be temporarily ignored. The outcome justified the procedure, since the continued freedom from glycosuria finally brought with it freedom also from ketonuria; but probably results could have been obtained still more rapidly by taking account of the acidosis and giving fairly liberal protein for the sake of strength, very little fat, in order that the patient might burn off his own fat, and a little carbohydrate if possible. The salvation of this patient lay in his absolute fidelity. He occasionally underwent serious privations on account of poverty without once being tempted to take forbidden food. His age is clearly a factor in the favorable out-

come. He shows a tendency to gain tolerance with time. He is able to keep on a normal level of nutrition, and is not impaired in comfort or usefulness at present by his diabetes.

CASE NO. 13.

Female, age 11 yrs. American; schoolgirl. Admitted Nov. 14, 1914.

Family History.—Paternal grandfather died of cancer. Antecedents otherwise healthy. Parents healthy. Five brothers and sisters of patient healthy. No obesity or other abnormalities.

Past History.—Patient always well, apparently the strongest of the six children. Whooping-cough and measles before 5, mumps at 6, all mild without sequelæ. Adenoids removed at 6. No sore throats. Regular life, not nervous. Candy and sweets taken in very limited quantity. Appetite, bowels, sleep, normal. Highest weight 59 pounds in 1913.

Present Illness.—Sugar was found in urine April 21, 1914, the reason for medical examination being only slight languor for a very few days preceding. Weight at this time 57 pounds. She was placed immediately on the usual carbohydrate-free diet, with gluten bread and occasionally a little ordinary bread, a quart of milk every day, and a little oatmeal gruel. For the past 6 weeks the quantity of oatmeal has been increased. Butter and cream were used as liberally as possible and egg-nogs were given between meals. On this maximum caloric diet she steadily lost weight. Weight 1 week ago 52½ pounds. She was given Fowler's solution of arsenic sometimes. Sodium bicarbonate was given to the extent of ¼ teaspoonful three times a day for a few days several weeks ago, but was stopped because it seemed to upset the stomach. For 2 weeks past the increased respiration of the child had attracted the attention of her attendants, but she still seemed cheerful and alert. Hair falling out rapidly for past few weeks. Bowels constipated.

Physical Examination.—A fairly normal looking, though thin little girl, lying quietly in bed with noticeable but not extreme polypnea. Cheeks are flushed more than normal. Teeth in good condition. Both tonsils moderately enlarged. No lymph gland enlargement. Blood pressure 105 systolic, 75 diastolic. General dryness of skin, most marked on legs. Examination otherwise negative.

Treatment.—The patient received a moderately restricted diet of 1000 calories for 1 full day in hospital (Nov. 15) when, with 46 gm. protein and 57 gm. carbohydrate in the diet, she excreted 46.8 gm. sugar. Fasting was then begun with about 20 cc. of whisky daily. Glycosuria ceased after 3 days of fasting. On Nov. 19 green vegetables were added to the extent of 3 gm. carbohydrate, and 4 gm. on Dec. 20 and 21. The glycosuria of Dec. 20 seemed to be clearly due to this quantity of carbohydrate, since violations of diet were positively excluded. It cleared up spontaneously the next day, as this sort of glycosuria often does. On Nov. 22, 40 gm. sugar-free caramel were given² in doses of

² 40 gm. caramel given on Dec. 29 not shown in graphic chart.

5 to 15 gm. throughout the day. No glycosuria resulted, though the tolerance was so low. As the patient needed a diet to conserve strength, the food on Nov. 23 consisted of 3 eggs and 14 gm. alcohol. Nov. 24, 50 gm. steak were added. Nov. 25, the meat was increased to 100 gm. On the following days fat was added in the form of bacon and olive oil, so that on Nov. 29 to 30 the diet was approximately 46 gm. protein and 1100 calories, or 2 gm. protein and 50 calories per kg. for a weight of 22 kg. This allowance, abundant even for a child, caused glycosuria. It was checked by a sharp reduction of diet. The glycosuria shown at intervals during the next 3 months was always slight, generally no more than faint traces in certain periods of the day, often indistinguishable if the tests were performed upon the mixed 24 hour urine, and sometimes connected with urinary calculi or with the use of vegetables.

The condition was complicated by the former trouble. In Dec., the patient complained of pain in back and bladder region, and painful urination. Later bloody urine was passed and some small clots. On Dec. 21, examination was made by a urologist, and the next day x-ray plates were taken. Nothing positive was found, but on subsequent days a few tiny calculi were passed. Several milder attacks of this character occurred subsequently, and seemed in each instance to aggravate slightly the tendency to glycosuria.

The diet was carbohydrate-free in the strictest sense, inasmuch as this patient could not tolerate thrice cooked vegetables, but showed glycosuria when attempts were made to use them. For example, on Jan. 23, after 2 weeks of complete sugar-freedom, 250 gm. thrice cooked celery were added to the diet and glycosuria appeared. The vegetables were stopped and the diet reduced, and the glycosuria ended. Then, on Jan. 25, 100 gm. each of thrice cooked celery, asparagus, and Brussels sprouts were added, and on Jan. 26, 100 gm. each of the asparagus and Brussels sprouts without celery. The slight glycosuria was checked by a fast-day with 11 gm. alcohol on Jan. 28. On Jan. 29 the attempt to use 300 gm. thrice cooked vegetables was resumed, and it was again necessary to stop glycosuria by a fast-day on Feb. 1. Traces of glycosuria then reappeared when diet was resumed without the vegetables, indicating that some injury had been done, but a glance at the graphic chart will show that the patient soon was able to take a higher diet without glycosuria when all vegetables were omitted (e.g. 45 gm. protein and 670 calories on Jan. 23, with vegetables, with glycosuria; 45 gm. protein and 850 calories on Feb. 26, without vegetables, without glycosuria). The ability to tolerate higher diets during the first half of Apr. (up to 63 gm. protein and over 1900 calories on Apr. 17) must be attributed to a gradual gain in tolerance. Improvement was finally indicated by the ability to remain sugar-free on decidedly higher diets.

As the home conditions were good and the parents absolutely trustworthy, it was considered feasible to let the patient take a vacation at this critical period in her treatment, for relief from the abnormal hospital environment. She was therefore dismissed on June 5 with the idea that she might be able to spend perhaps 2 or 3 weeks at home.

Acidosis.—This was first measured by analyses of the acetone bodies and ammonia. At the outset, the characteristics of acidosis without alkali treatment were seen in the moderate ketonuria and high ammonia. Beginning Nov. 15, 20 gm. each of sodium bicarbonate and calcium carbonate were given daily. The sodium bicarbonate was stopped on Nov. 25, but the calcium carbonate continued until Dec. 4. The beginning of protein-fat diet on Nov. 23 caused a rise of the ammonia from 0.45 gm. up to 0.98 gm. notwithstanding the use of alkali. The stopping of sodium bicarbonate on Nov. 25 brought an immediate jump of the ammonia up to 1.8 gm. Seemingly the continuance of 20 gm. calcium carbonate daily did not serve to prevent this high ammonia. Also as usual the bicarbonate apparently served to keep up the ferric chloride reaction, for this quickly became pale after bicarbonate was discontinued. It is seen that the ammonia gradually fell to a level which may probably be considered normal on protein-fat diet, also the ferric chloride reaction became negative, not in consequence of the use of carbohydrate which was formerly considered necessary to combat diabetic acidosis, but solely by reason of the gradual undernutrition. Determinations of the blood alkalinity were begun on Jan. 29 and showed a subnormal level of 47 vol. per cent. On Feb. 6, the level was still lower, *viz.* 41 per cent, and on Feb. 13 a still lower value of 39.5 per cent was found. The condition took care of itself without the use of any alkali, and the combining power of the plasma remained at or above 50 vol. per cent until the close of Apr. Up to this point the ammonia excretion and the ferric chloride reaction proved the more sensitive indicators. It will be noted that the ammonia curve touched its lowest point at practically the identical time with the lowest point of the weight curve, namely the middle of Feb., and the ferric chloride reaction was negative at the same time. With the increase of protein-fat diet came a gradual and practically parallel rise of the ammonia and weight curves; also ferric chloride reactions appeared and increased correspondingly. In the fasting periods, Apr. 29 to May 1 and May 16 to 18, the plasma bicarbonate gave indications of acidosis not revealed by the other tests. The ferric chloride reaction was not perceptibly altered, and the ammonia excretion distinctly fell in both fasts. The lowering of the plasma bicarbonate may serve as a delicate indicator under such circumstances, since it sometimes falls to a point giving warning of dangerous acidosis in fasting, and at this point clinical symptoms correspond. The degree of the fall was not dangerous here, and clinical symptoms were absent. In the period May 15 to 19 inclusive, 5 gm. sodium bicarbonate were given daily with 30 cc. whisky, to test whether this combination of alkali and alcohol had any effect upon the fasting acidosis. The result showed only a slight difference as compared with the period Apr. 29 to May 1. The ferric chloride reaction was unchanged, the ammonia was a bare trifle lower and the plasma bicarbonate a trifle higher, but the difference was within the range of accidental variation. Carbohydrate from 10 to 30 gm. in the forepart of May failed to clear up the ferric chloride reaction, which also persisted through fasting, but became negative on the fast-day of May 23 and remained so until the diet was in-

creased on June 2. Here it is evident that simple increase of fat produced this reaction.

Blood Sugar.—This was determined only occasionally in the period Apr. 16 to May 21, samples being taken in the morning before breakfast. The first two determinations were approximately 0.15 per cent. This was considered too high, and the period of almost 4 days of fasting (Apr. 28 to May 1 inclusive) was imposed for the purpose of bringing it down. It was thus made and kept normal (as far as fasting values were concerned) until the increase of carbohydrate to 30 gm. on May 14 brought glycosuria with hyperglycemia of 0.18 per cent the following morning. A similar fasting period then succeeded in bringing it down almost to normal. The alkali given as above described during this phase did not serve to bring the blood sugar lower. Hyperglycemia again resulted from the subsequent diet containing 10 gm. carbohydrate, and this was one of the reasons for omitting this carbohydrate.

Weight and Nutrition.—In the period Nov. 16 to 22 inclusive, with practically no nitrogen intake, there was a loss of 20.55 gm. nitrogen in the urine. In the first 3 months in hospital, undernutrition is indicated by the fall in weight from 21.2 kg. on Nov. 16 to 16.8 kg. on Feb. 16, being a loss of 4.4 kg., or about one-fifth of the weight at entrance. The diet of this period, after the brief excess in Nov., was in the neighborhood of 45 gm. protein and 700 calories, or a little over 1 gm. protein and 35 calories per kg. of weight, but the rather frequent days of fasting or low diet reduced the average materially below this figure. Gain in weight began with the increase of diet in the latter part of Feb. In consequence, both sugar and ferric chloride reactions were present early in Mar. Thereafter the ferric chloride tests and the unduly high ammonia were the chief indications of improper diet.

In the early half of Apr. the ration was generally 63 gm. protein and 1700 to 1900 calories (about 3.3 gm. protein and 90 to 100 calories per kg.) with fast-days somewhat reducing this average. On Apr. 19 a better balanced diet was instituted, consisting of 49 gm. protein, 5 gm. carbohydrate, and 1322 calories, increased by May 14 to 57 gm. protein, 30 gm. carbohydrate, and 1593 calories. Distinct glycosuria resulted at this time. After a period of fasting, a decidedly lower diet was given beginning May 19. Though the ability had been shown to tolerate 10 gm. carbohydrate during this time, it was considered safer to boil out carbohydrate in the diet at home. Accordingly the diet prescribed at discharge consisted of 68.5 gm. protein, 250 gm. thrice cooked vegetables, and 1500 to 1600 calories (about 3.5 gm. protein and 80 calories per kg., reduced by weekly fast-days to about 3 gm. protein and 70 calories average).

At discharge the weight was 19 kg.; *i.e.*, 2.2 kg. less than at admission. The half year of treatment thus represented undernutrition to this extent. There was no gain, and if anything a slight loss of strength, also no growth in stature. The child was thoroughly cheerful, and able to be about and keep herself amused all day.

Subsequent History.—The progress at home was better than expected. Reports and samples of urine showed continued absence of both sugar and ferric chloride reactions. On July 1 the addition of 5 gm. carbohydrate was tolerated. On Aug. 1 an increase to 10 gm. carbohydrate brought a trace of glycosuria. The allowance of 5 gm. continued to be tolerated, and the child gained also in weight and appearance. Oct. 3, occasional traces of sugar were reported, and on advice the patient returned to the hospital on Oct. 15 for further treatment, having succeeded in remaining in good condition at home for 4 months instead of the few weeks anticipated.

Second Admission.—The patient returned weighing 20.8 kg.; *i.e.*, with a gain of 1.9 kg. over her weight at discharge and a loss of 0.5 kg. from her weight on first admission. Her appearance and actions indicated a decided gain in vigor. On the same carbohydrate-free diet prescribed at discharge she showed moderate glycosuria, marked hyperglycemia (plasma sugar 0.25 per cent), a well marked ferric chloride reaction, and a slightly subnormal plasma alkalinity. Accordingly fasting was begun on Oct. 17, and sugar-freedom resulted within the first 24 hours. After an additional 24 hours of fasting, a carbohydrate tolerance test with green vegetables was begun for the usual diagnostic and therapeutic reasons. Beginning as usual with 10 gm. carbohydrate on Oct. 19, an increase of 10 gm. carbohydrate was made daily, with the result that 60 gm. carbohydrate was established as the tolerance. The traces of glycosuria on Oct. 25 and 26 exemplified the false limit sometimes encountered in such tests, when there is a trivial excretion on a certain intake, which disappears after this intake is continued or increased. This affords no comparison with the tolerance on the previous admission, because no test was then made with carbohydrate in the absence of other foods. In consequence of this undernutrition with carbohydrate to the point of tolerance, the blood sugar as determined mornings before breakfast fell to normal, the ferric chloride reaction became negative, and the plasma bicarbonate rose to normal. After a fast-day on Oct. 31 to clear up the glycosuria resulting from the carbohydrate test, a diet was begun which was better planned than on the previous admission; namely, 50 gm. protein, 10 gm. carbohydrate, and 1000 calories. Because of glycosuria it was necessary on Nov. 8 to reduce the carbohydrate, and after Nov. 15 it was regularly 5 gm. For a body weight of 20 kg., this diet represented 2.5 gm. protein and 50 calories per kg. The weekly fast-days reduced this to an average of approximately 2.14 gm. protein and 43 calories per kg. The general well-being was definitely improved by this lower diet and the introduction of carbohydrate, as compared with what was observed on the previous admission. The carbon dioxide capacity of the plasma, which had been as low as 45 per cent, rose to 55 per cent without the use of alkali. The blood sugar, which had risen with the appearance of glycosuria at the close of the carbohydrate test, continued unduly high, but remained below 0.2 per cent and gradually fell below 0.15 per cent. The patient was dismissed on Dec. 14 weighing 19.3 kg.; *i.e.*, 1.5 kg. below her weight at this admission, and 0.4 kg. above her weight at the former discharge.

Exercise.—During the former time in hospital the child was kept at rest, partly because of weakness. This time she was given regular exercise to the limit of comfortable endurance. No detailed studies were made, but it was evident that no striking increase in tolerance was produced in such a severe case of diabetes. Existing glycosuria was not cleared up by exercise, also it was not possible to raise the carbohydrate ration higher with exercise than without. On the other hand, the exercise certainly did no harm; it may have had a share in the gradual reduction of the hyperglycemia; and it unmistakably improved the strength, well-being, and enjoyment of the child. The exercise was mostly in the form of ball-tossing, walking, roller-skating, and other play.

Subsequent History.—The patient remained sugar-free at home, and took up some school work in Feb., 1916. Increase of carbohydrate to 10 gm. was tolerated without glycosuria. In May she caught cold, showed traces of sugar almost constantly, and lost $1\frac{1}{2}$ pounds in 2 weeks by reason of the undernutrition necessary to keep down glycosuria. Her former tolerance returned with recovery from the cold. Glycosuria remained absent practically continuously until July, when persistent traces of sugar made it advisable for the patient to return to the hospital.

Third Admission.—July 7, 1916. The weight at this admission was 20 kg.; *i.e.*, 0.7 kg. more than at discharge $6\frac{1}{2}$ months previously. The height was 132 cm. Under regular diet, July 7 to 10 inclusive, there were still marked sugar and ferric chloride reactions. The plasma sugar on July 11 was again 0.25 per cent, and a rigid period of undernutrition, including fasting and a carbohydrate test, was therefore instituted. The tolerance for carbohydrate was identical with that in the previous October. The treatment reduced the blood sugar to 0.13 per cent, but it rose to 0.22 per cent on resumption of the previous diet. The weight was thereby reduced to 17.2 kg., which was lower by 4 kg. than at the first admission. The patient was still cheerful and active, and returned home in this condition.

Subsequent History.—In Aug., on account of slight glycosuria, carbohydrate was omitted from the diet. The disturbance seemed to be associated with indigestion. Otherwise the sugar and ferric chloride reactions remained negative. The patient attended school half of each day, and took automobile rides and other recreation. In Oct. bloody urine reappeared and two small calculi were passed. This trouble seemed to affect her diabetes very badly, and for this reason she reentered the hospital Oct. 24, 1916.

Fourth Admission.—Weight 19.3 kg. Appearance thinner, paler, and weaker than previously. The change for the worse is said to date from the attack of calculi. The urine by this time was free from blood, and physical and x-ray examinations were negative. The patient was made sugar-free by 2 days of fasting, then given green vegetables representing 5 gm. carbohydrate the first day, increasing by 5 gm., daily up to 50 gm., which was the limit of tolerance; *i.e.*, a loss of 10 gm. as compared with previous tests. She was then placed on a diet of 30 gm. pro-

tein, 20 gm. carbohydrate, and 600 calories, and was encouraged to exercise within the limits of her strength. A routine fast-day was given once a week. Because the strength remained low, this diet was changed on Nov. 23 by diminishing the carbohydrate to 10 gm. and increasing the protein to 40 gm. For the same reason on Dec. 4 carbohydrate was omitted from the diet and the protein increased to 45 gm. The patient at this time took walks of 8 blocks without weariness, and was outdoors much of each day. Bland's pills were given because of anemia. The patient remained in hospital until Feb. 1, 1917, when she was dismissed on a carbohydrate-free diet of 40 gm. protein and 700 calories, weighing 17 kg.; *i.e.*, 1.2 kg. less than at this admission, and 4.3 kg. less than at her original admission in Nov., 1914.

Acidosis.—The ferric chloride reaction remained constantly negative. Traces of acetone were constantly present, as must be expected on such a diet. There was a daily excretion of 0.18 to 0.64 gm. ammonia nitrogen, the output being lower in the earlier period of lower calories with carbohydrate in the diet. Symptoms of acidosis were entirely absent, and the carbon dioxide capacity of the plasma was 65.3 per cent at dismissal.

Blood Sugar.—Hyperglycemia was continuous, in general close to the threshold of glycosuria as shown in the charts of former periods. The blood sugar at dismissal was 0.2 per cent.

Subsequent History.—The condition continued the same at home as in hospital, the patient remaining very thin but bright and active. In Mar. a "green day" was advised in the middle of each week to break the monotony of the diet, diminish the total calories, and introduce carbohydrate. Traces of sugar appeared only occasionally and at first cleared up with the routine fast-days. The usual slow downward progress occurred under these circumstances, but owing to the derangement of the hospital organization by the military emergency, the patient was not required to return for treatment until Oct. 10, 1917. By this time she had been seriously weakened by the frequent fasting necessary to control glycosuria, though she was still up and about.

Fifth Admission.—Oct. 10, 1917. Weight 16.6 kg. The patient had stood the trip from Massachusetts very well. One day of fasting cleared up the slight existing glycosuria. On the second fast-day the plasma sugar was 0.098 per cent, CO₂ capacity 55 per cent. On the evening of the second day the fast was broken with 5 gm. carbohydrate in the form of a salad. The urine was continuously negative for both ferric chloride and nitroprusside reactions, and the nitroprusside test of the plasma was likewise negative. Carbohydrate was increased by 5 gm. daily without glycosuria. Oct. 16, breakfast was taken as usual, but collapse occurred about 10 a. m. and death about noon, preceded by slight tetanoid convulsions. The urine at this time was still normal. The blood showed hemoglobin 22 per cent, plasma sugar 0.02 per cent, CO₂ capacity 69.7 per cent. The employment of the carbohydrate test was a mistake, for though the child was up and about until the day before death, the low blood sugar on the second fast-day was a

plain indication of exhaustion, and protein should have been fed instead of carbohydrate. Nothing, however, could long have prevented the fatal termination under the circumstances at this time.

Remarks.—The patient presented juvenile diabetes of great severity. Within about half a year she had come close to coma and had lost carbohydrate tolerance almost completely. It is evident that the assimilation had already fallen too low to support growth, owing to lack of treatment in the earlier stage. Under treatment she was then kept alive and in tolerable comfort and activity for nearly 3 years. Two aspects of the progress may be noted.

On the one hand, no special tendency to recovery of assimilative function has been manifest. During the first period of over 6 months in hospital, it is true that the food tolerance decidedly improved, but this result was merely the accompaniment of some 2 kg. loss of weight and does not necessarily indicate any change in the fundamental assimilative power. At the second admission the weight was up almost to the original figure, but other conditions were different. Active diabetes was present again at this admission. The carbohydrate tolerance was tested with exclusion of other foods. Thereafter carbohydrate could be included in the diet, but this was on a lower ration than during the first admission. Real improvement in assimilation would have meant that the child could grow in weight and stature; on the contrary, the third and fourth admissions represented further loss of weight. The carbohydrate tolerance in July, 1916, was the same as in Oct., 1915, but as the latter test was at a lower body weight, the result may be interpreted as actual downward progress.

On the other hand, the record furnishes evidence against the "spontaneous" character of such downward progress. Hyperglycemia was almost continuous, and glycosuria and ketonuria recurred rather frequently throughout the entire 3 years. A partially depancreatized dog under similar conditions would have gone into hopeless diabetes much sooner. Any inherent downward tendency should have been perceptible in this type of case in this length of time. The slow change observed is abundantly explainable by the prolonged slight overstrain of the weakened function.

CASE NO. 14.

Male, married, age 51 yrs. American; optician. Admitted Nov. 16, 1914.

Family History.—Father died of typhoid at 28, mother of heart trouble and dropsy at 55. Two sisters living and well. Patient has been married 23 years; one child dead, one living and well. Tuberculosis, cancer, syphilis, diabetes, and other family diseases denied.

Past History.—Healthy life. Scarlet fever in childhood. Occasional sore throats. Gonorrhoea twice. Syphilis denied by name and symptoms. In Apr., 1914, he was confined to bed with so called dry pleurisy and had cough and slightly blood-tinged expectoration for 3 or 4 weeks. Constipation, slight indigestion, moderate or poor appetite. Alcohol used rather freely but not to drunkenness. Moderate tobacco.

Present Illness.—7 years ago patient states that he strained himself lifting a trunk. He had pain in the back for several months, therefore had his urine examined and sugar was found. He claims never to have had any of the typical diabetic symptoms. He now complains of indefinite neuritic pains in back and legs. His best weight was 140 pounds 6 years ago; now 112. A few days after admission the patient's wife volunteered the information that he had undertaken a number of different treatments for his diabetes at different times, but had never adhered to any prescribed diet for even a brief time.

Physical Examination.—A fairly developed, poorly nourished man. Teeth mostly absent, little decay in those remaining, slight pyorrhea. Throat congested but tonsils not visibly enlarged. Cervical, axillary, epitrochlear, and inguinal glands slightly enlarged. Reflexes very active. Blood pressure 100 systolic, 70 diastolic.

Treatment.—After 2 days of observation on a low protein-fat diet, fasting was begun on Nov. 18. On Nov. 20 to 22 he received 27 to 35 gm. alcohol. This 5 day fast greatly diminished but did not quite abolish glycosuria. The ferric chloride reaction, which was negative on the day of admission, became strongly positive on the carbohydrate-free diet and on fasting. The weight fell sharply from 50.6 to 47.6 kg. On Nov. 23, 300 gm. thrice cooked vegetables were given to appease the patient, who was discontented. This program continued up to and including Dec. 1. As such vegetables are reckoned as having too little food value to count, the treatment represents 2 weeks of practically continuous fasting except for the alcohol mentioned. The continuance of glycosuria aroused suspicion. Accordingly the patient was removed from the ward to a private room, and glycosuria abruptly ceased (Nov. 26). He was then returned to the ward, and was sufficiently impressed by his sugar-freedom that he followed diet with some degree of fidelity thereafter, though some of the traces of glycosuria are doubtless to be attributed to slight violations. A low diet was begun, and it was found that the tolerance was actually very low, the smallest quantity of carbohydrate bringing on glycosuria, while even on protein-fat diet traces of sugar were frequent, apart from any stealing of food. The patient was discontented and unreliable, and the irregular shifts of diet resulted largely from attempts to please him. The general outcome of the treatment was to reduce his weight from the original 50.6 kg. to 44.8 kg., with the result that glycosuria was absent on a carbohydrate-free diet of 53 gm. protein and over 2200 calories, but a well marked ferric chloride reaction persisted. Thorough treatment was not carried out because the patient had never been seriously ill and would not have endured rigorous measures. Accordingly he was allowed to go on Mar. 2, with his condition improved but by no means satisfactory, on a prescribed diet of about 50 gm. protein and 1500 to 1750 calories.

Subsequent History.—On Apr. 1, patient returned to the hospital reporting that he had followed diet, had remained permanently sugar-free, had gained 6 pounds, and was enjoying greatly improved health. His appearance conformed to the

statement, but a sample of urine showed a trace of sugar. Information from other quarters indicated that he had not adhered strictly to his diet. On Apr. 9, he again reported and his urine was found sugar-free. On May 20, he reported showing a slight glycosuria, and information was given by his family that he had departed somewhat from his diet. Since then nothing has been heard of him.

Remarks.—The case illustrates diabetes of long standing, apparently doing the individual little harm but bringing progressive injury in the course of years, and undoubtedly destined not only to impair comfort and usefulness, but also to shorten life. As frequently found in such cases, a normal state of the urine is very difficult to establish and maintain, and rigorous restriction of food and reduction of weight for a number of months are necessary for a satisfactory result. Such patients are often not convinced that these measures are necessary, especially since they feel decidedly worse during the period of rigorous restriction. Fidelity brings ultimate reward in comfort and longevity. On the other hand, the penalty of carelessness is often slow in appearing, and accordingly the lesson is often learned too late.

CASE NO. 15.

Male, married, age 42 yrs. Scotch; bookkeeper. Admitted Nov. 16, 1914.

Family History.—Entirely negative as far as can be learned from wife.

Past History.—Healthy life.

Present Illness.—Patient is known to have had diabetes for about 2 years past, with practically no symptoms except some loss of weight and strength. He has continued at his work until the present week. He was not supposed to be seriously unwell until last evening, when a doctor was sent for hurriedly and found him in coma to such a degree that he could not be roused enough to recognize persons. The physician cleared out considerable feces by the use of cathartics and enemas and gave a few small doses of sodium bicarbonate by mouth. This morning the patient was still in coma, but was apparently a little more easily roused.

Physical Examination.—Fairly good muscular development along with moderate emaciation. Routine physical examination negative. Knee jerks absent. The usual picture of coma, except that hyperpnea is not striking. Respiration is full, but quiet. When forcibly roused the patient regains consciousness sufficiently to utter words in drunken meaningless fashion, but not to recognize his wife or doctor. With some difficulty he can be induced to swallow medicine and to pass urine.

Treatment.—This was the first case of actual coma received, and the orthodox treatment was attempted, with an intravenous infusion of 1 liter of 4 per cent sodium bicarbonate solution prepared without heat and sterilized by filtration through porcelain. The injection was apparently well borne; pulse, respiration, and consciousness showed no appreciable change during the period of injection, which lasted about an hour. 15 cc. whisky were given hourly. The patient

was received at 5:30 p.m. The infusion was finished at 7 p.m., and death occurred suddenly and without warning at 7:50 p.m.

The following laboratory data may be noted. Heavy glycosuria and ketonuria both before and after bicarbonate infusion, not determined quantitatively because of loss of considerable urine. Blood sugar 0.316 per cent. Sodium chloride in serum 6.11 gm. per liter. Sodium chloride in urine 0.2 gm. per liter before infusion. The urine passed after bicarbonate infusion was pale and abundant as before, but contained no chlorides.

Remarks.—Though few patients ever come out of actual coma, this man was one who appeared to have a fighting chance. At that time it was hoped that the alkali in the customary dosage would reinforce whatever benefit he might derive from fasting. Without the intravenous alkali he might have had a chance. Later experience makes it seem probable that when a patient in this condition receives an injection of alkali in this manner and quantity, no immediate harm and sometimes an apparent benefit is perceptible, but sudden death is likely to occur within a few hours.

CASE NO. 16.

Female, married, age 47 yrs. American; housewife. Admitted Nov. 17, 1914.

Family History.—Father died of cancer at 61. Mother had diabetes; died of sepsis from varicose veins in legs at 74. Brother aged 61 has mild diabetes. Patient's husband died 20 years ago, aged 34, of some condition resulting from alcoholic excess. Three children; the two older living and well; the youngest was mentally deficient and died last July at the age of 20, after having been treated from childhood for syphilis.

Past History.—Healthy childhood. Measles and mumps when very young. Chlorosis before marriage. Married at 20; two children within a year of each other; no miscarriages. Third child, born 4 years after second, showed syphilis, and patient after its birth had sore on tongue and hair fell out. There was also a genital chancre. Symptoms cleared up after 1 month of treatment with blue ointment. No further symptoms or treatment. Regular habits. No excess in alcohol, tea, coffee, or sweets. Never nervous until recent years. Ordinary weight 180 pounds.

Present Illness.—5 years ago patient began to feel weak and lost 20 pounds in weight. Physician found glycosuria of $4\frac{1}{2}$ per cent. She has dieted more or less since then, but has been sugar-free only occasionally, never more than a few months. Lowest weight 143 pounds last August. Menstruation stopped 6 months ago. Especially for the past 3 weeks she has felt weak and miserable and been troubled with thirst, headache, pains in knees, cold feet, pruritus vulvæ, failing vision, and loosening and falling out of teeth.

Physical Examination.—Height 158 cm. A rather obese woman, looking strong but nervous. Several teeth missing; others loose. Throat normal. No

palpable lymph node enlargement. Murmur of mitral regurgitation. Area of cardiac dullness slightly enlarged. Arteries hardened. Blood pressure 225 systolic, 110 diastolic. Albumin and casts in urine. Knee and Achilles jerks slight. A few small copper colored scars on legs. Uterus slightly retroverted. Right Fallopian tube slightly tender. Blood shows strong Wassermann reaction. In addition to diabetes, there was a diagnosis of chronic mitral insufficiency, chronic interstitial nephritis, latent syphilis, arteriosclerosis, and cystitis. Twice during hospital sojourn the patient complained of dizziness and fainted, and was treated for short periods with digipuratum. Syphilis was not treated at this time, and the effect of dietetic treatment of the diabetes was tested alone.

Treatment.—As shown in graphic chart, the patient fasted Nov. 18 to 20 inclusive, receiving respectively 45 and 75 cc. whisky on the last 2 days. On Nov. 21 she received cauliflower, celery, and asparagus to the amount of 17.5 gm. carbohydrate. As the primary object was to reduce weight, 3 more days of practical fasting (Nov. 22 to 24) followed, the only food being 800 gm. thrice cooked vegetables daily. On Nov. 25, one egg was added. This diet was rapidly increased to about 1100 calories on Dec. 6 and 2300 calories on Dec. 19. All attempts to introduce even small quantities of carbohydrate led to glycosuria, and, as shown in graphic chart, numerous periods of low diet or fasting were employed to diminish the weight further. She was finally (Jan. 27 to 29) placed on a carbohydrate-free diet of 66 gm. protein and 1400 calories. This, for her weight of 54.5 kg. at that time, was about 1.2 gm. protein and 26 calories per kg. The patient insisted that this diet with addition of 500 gm. thrice boiled vegetables satisfied her appetite perfectly, and as she was very eager to be home and had received the necessary instruction, she was allowed to leave in this condition. All subjective symptoms had disappeared and she felt fully strong and well.

Subsequent History.—The progress continued to be favorable at home, and in Feb. the diet was increased by 400 calories of bacon. Sugar remained constantly absent and the ferric chloride diminished to a trace. It became entirely negative about June 1. The plasma sugar on June 1 was 0.114 per cent. The weight was 54.5 kg. By Oct. 5, the patient had gradually increased the quantity of food, the weight had risen to 59.8 kg., and the plasma sugar to 0.196 per cent, with negative sugar and ferric chloride reactions in urine. Blood pressure 250 systolic, 160 diastolic. She was advised to avoid gaining weight. Excellent subjective health and normal urine continued, and 1 year after discharge she reentered the hospital by request for examination and advice.

Second Admission.—Jan. 31, 1916. The weight at this time was 63 kg.; namely, 8.6 kg. above that on dismissal and 2 kg. below that at former admission. The urine showed negative sugar but a trace of ferric chloride reaction. Feb. 2 a fast-day was given, and then a carbohydrate tolerance test, beginning with 10 gm. carbohydrate and increasing by 10 gm. daily until by Feb. 23 to 25 the limit of tolerance was reached with 220 gm. carbohydrate. After a fast-day on Feb. 27 to clear up the slight glycosuria, a diet was instituted of 90 gm. protein, 20 gm.

carbohydrate, and 2000 calories (1.5 gm. protein and 34 calories per kg., reduced by weekly fast-days to about 1.3 gm. protein and 30 calories average). On this diet the patient was dismissed, weighing 59.5 kg.

Acidosis.—The patient was admitted originally with chronic glycosuria and negative ferric chloride reaction. The result of fasting, notwithstanding 75 cc. whisky on Nov. 20 and 17.5 gm. carbohydrate on Nov. 21, was the development of a ferric chloride reaction. This persisted during most of the first stay in hospital. It could doubtless have been cleared up by repeated periods of carbohydrate (without other food) to the limit of tolerance. But the tolerance at that time was low, and for a patient with such inherently mild diabetes at a fairly advanced age, it was considered sufficient to pursue a treatment of progressive undernutrition, knowing that the trivial acidosis would disappear as soon as the tolerance was built up. This expectation was fulfilled in the period after leaving hospital. With rise of weight, traces of ketonuria had returned at the time of second admission; these were readily cleared up by the carbohydrate tolerance test, and by increasing carbohydrate in the diet. Since then ketonuria has remained permanently absent. As shown in the second graphic chart, the plasma bicarbonate was slightly below the lower normal limit; but the tendency was upward, and no alkali was employed.

Blood Sugar.—This was easily kept at normal level by regulation of body weight. On this point the patient might be brought into line with the type formerly called "fat sensitive." It will be observed in the second graphic chart that hyperglycemia was present on Feb. 2 after a diet of 2350 calories made up chiefly of fat with very little carbohydrate. This elevated blood sugar is seen to have fallen to normal subsequently when the carbohydrate was decidedly increased and the total calories diminished. Though nephritis and arteriosclerosis were present with hypertension, there was no tendency to a stubbornly high blood sugar.

Subsequent History.—The patient has reported at intervals to date, feeling entirely healthy and leading a fully normal life with faithful attention to diet. Weight June 19, 1917, 63.6 kg. This increase of weight has been borne without any glycosuria. The high blood pressure remains, also the albumin and casts in urine. Lately she has complied with advice given several times before and has taken a few salvarsan injections, without alteration of clinical findings. The cardiorenal symptoms are perceptibly increasing, and death from this cause is to be expected.

Remarks.—Two possible etiologic factors are here present, one heredity, the other syphilis. Notwithstanding these, and even in absence of syphilitic treatment, the entire tendency under suitable dietetic treatment through nearly 3 years of observation has been upward and not downward. This success has been attained by regulation of the total caloric ration and body weight. It is practically certain that a progressive downward tendency could have been observed if the weight had been built up with high calory, carbohydrate-poor diet. Such a tendency is distinctly indicated by the findings at several times when weight was

gained. Another interesting feature is that in Apr., 3 months after the first dismissal, the patient had an acute otitis media and underwent paracentesis under ether, but showed no sugar throughout this illness. From present indications the prognosis in such a case is satisfactory from the standpoint of diabetes, and life and comfort are apparently limited only by the other diseased conditions present.

CASE NO. 17.

Female, married, age 69 yrs. Russian Jew; housewife. Admitted Nov. 17, 1914.

Family History.—Indefinite on account of ignorance. Most of family seemingly lived to considerable age, and patient knows of no family diseases. Patient has been married 43 years. Seven children; four died in infancy, cause unknown; one is in a public institution with diagnosis of dementia præcox; the other two are middle-aged and well.

Past History.—Measles in childhood. Came to New York from Russia 26 years ago. Hygienic surroundings bad. No diseases of consequence, except empyema with pneumonia 20 years ago. This was drained, and two subsequent operations were necessary before the sinus was closed a year later. She has had no symptoms pointing to tuberculosis. She has long complained of indigestion, gas, and constipation. 6 years ago she underwent an operation for uterine prolapse; there was a laparotomy and removal of some sort of tumor, concerning which she knows nothing except that it was not cancer.

Present Illness.—Time of onset unknown, but during the past 7 years her weight has steadily diminished from 180 down to 108 pounds. Polyphagia never marked, and polydipsia noticed only in the past few days. 6 weeks ago pain began in the right foot with some discoloration around the great toe and heel. Local measures did not benefit it. A physician suspected gangrene immediately upon seeing it and found heavy glycosuria present. This was the first diagnosis of diabetes. She is now unable to walk because of pain in this foot, which is also painful when she remains in bed.

Physical Examination.—Patient fairly nourished, lying in bed with quiet respiration, but with decided sweet odor of breath. Dirt and pediculi noticeable. Numerous teeth missing or carious. No gland enlargements except in groins. A few bronchitic râles. Heart slightly enlarged. Blood pressure 215 systolic, 150 diastolic. Depressed scars on left thigh, pigmented scars on right shin. Swelling, reddish blue discoloration and tenderness of great toe and over and under first and second tarsometatarsal joints of right foot. The heel of this foot is painful, the skin is lifted up and evidently has fluid under it.

Treatment.—Patient received supper on the day of admission, consisting of 25 gm. Akoll biscuit, 10 gm. butter, and a cup of coffee. The next day she fasted with 35 cc. whisky, and became sugar-free in 24 hours. The ensuing days were also fast-days, with whisky up to 90 cc. On Nov. 23, one egg and 300 gm. thrice

boiled vegetables (cauliflower and asparagus) were added. The diet was then rapidly increased, particularly in its fat component, as shown in Table IX.

It is seen that the great increase of fat intake on Nov. 29 was accompanied by sharp increase of both glycosuria and ferric chloride reactions. The simultaneous increase of protein in the diet did not serve to prevent this increase of acidosis. Also it is difficult to attribute the glycosuria of 11 gm. to the increase of only 5 gm. protein on Nov. 29, as compared with the preceding day. Furthermore, though this glycosuria was only 11 gm., because the high diet was composed chiefly of fat, the injurious after-effect is likewise characteristic of fat. For the entire first week in Dec. the diet was only once as high as 500 calories; Dec. 5, 6, and 7 were fast-days with alcohol, yet the aglycosuric condition was difficult to restore. Beginning Dec. 8 the attempt was made to build up a diet, beginning with eggs, butter, and thrice cooked vegetables. Whisky was never entirely discontinued, and in Jan. the intake represented about 65 gm. alcohol daily. The protein was generally 40 to 60 gm.; *i. e.*, a little above or below 1 gm. per kg.

TABLE IX.

Date.	Diet.				Weight.	Urine.		
	Protein.	Fat.	Alcohol.	Calories.		Volume.	Sugar.	FeCl ₃ reaction.
1914	gm.	gm.	gm.		kg.	cc.	gm.	
Nov. 27	47	135	43	1746	50.6	1540	+	+++
" 28	57	179	15	2005	51.6	2005	+	++
" 29	62	509	15	5096	50.5	1115	11.15	+++
" 30	37	259	10	2629	51.3	1190	+	+++
Dec. 1	37	259	15	2664	51.0	860	+	++

of weight. The calories were kept at approximately 1000 to 1200, or about 20 to 24 calories per kg. for 50 kg. body weight. The traces of glycosuria indicated in the graphic chart were very slight, and were mostly connected with the use of thrice cooked vegetables. The tolerance for carbohydrate was so low that 300 to 500 gm. of vegetables of Joslin's 5 per cent class, boiled through three waters in the usual way, brought on these traces of glycosuria. In Jan. these vegetables were omitted. The patient being an old woman with small appetite, it was possible to place her on a ration made up of coffee, soup, whisky, eggs, meat, fish, butter, and olive oil. She remained practically sugar-free on this regimen, since the traces of glycosuria noted thereafter were mostly very faint reactions in the urine of single periods during the day, undiscoverable if mixed with the 24 hour urine. The undernutrition is indicated by the continuous fall in weight during 2½ months, from 53.5 kg. on admission to 45 kg. on discharge. She was discharged on Feb. 1, very happy with her condition. The incipient gangrene had healed early, and she had been restored to comfort and activity. She felt able to con-

tinue her diet amid the difficulties of her home conditions. Slight albuminuria and casts present on admission still continued at discharge, and the systolic blood pressure was 205 mm.

Subsequent History.—The patient was unable to continue her diet successfully at home. As she evidently required continuous care, she was advised to enter a semipublic institution, where she has since lived and is kept on a moderately restricted diet, with 1 to 3 per cent sugar constantly in the urine and continual pain in the right foot, which does not completely disable her and has not been accompanied by any return of actual gangrene.

Acidosis.—As respects acidosis, it will be noted that she entered with a negative ferric chloride reaction, evidently because of the carbohydrate in her former diet. The ferric chloride reaction appeared on the 4th day of fasting, about as might be expected in a normal person, and it is again noticeable that 300 calories of alcohol did not prevent the appearance of this reaction. The reaction was never a heavy one, and in a feeble woman of this age it was not considered advisable under the circumstances to impose the rigorous measures which would have been necessary to make the urine quickly normal. Theoretically, this continued slight acidosis and the diet keeping her barely on the verge of glycosuria all the time were wrong, and under ideal conditions actually better results could have been achieved by more rigid measures, cutting her diet and weight still lower and bringing about a normal state of the urine and at least some slight carbohydrate tolerance. Practically, there was a strong likelihood that she would not be able to follow the necessary diet outside the hospital, and it seemed therefore unwise to attempt an ideal result. Under the plan pursued, her condition at discharge was a good one for her years, and by persisting in the same program she would almost certainly have gained gradually some carbohydrate tolerance and lost her trace of acidosis; but her mental and social state interfered with this result.

Remarks.—This patient was admitted as presenting early diabetic gangrene with senility and arteriosclerosis, the idea being to test the effect of therapy in such a case. Simple protection and occasional hot air baths were the only local measures employed, but healing proceeded uninterruptedly and apparently as rapidly as possible at this age. It was striking that pain in the foot could at first be produced at will by food. Excessive diet which brought return of glycosuria was found to bring complaint of pain the same day, although the patient was kept ignorant of the laboratory tests. On discharge the foot appeared entirely normal, except for coldness to touch and some loss of tissue in the formerly discolored areas. Pain, tenderness, and disability had disappeared. The loss of weight under treatment, amounting to about one-seventh of her entrance weight, did not serve to weaken her. On the contrary, she went out with improved strength.

The case well illustrates a familiar therapeutic situation. In numerous cases of diabetes in advanced senility, in one sense the diabetes is mild, the glycosuria

is not excessive, the acidosis does not threaten coma, and the patient seems to go along for years with little injury. Some form or degree of harm ordinarily results sooner or later, frequently, as in this case, gangrene. On treatment, the apparently mild diabetes proves by no means easy to control. The tolerance from the standpoint of complete sugar-freedom is surprisingly low, and months of privation and reduction of weight and sometimes also of strength are necessary to atone for the harm caused by years of lack of care. Only three courses are open. One is rigorous and conscientious treatment, just as in a younger patient. This is difficult and tedious for both physician and patient; but when circumstances permit it to be carefully carried out, the ultimate results are more favorable than in younger persons, and the improvement of health and apparently of longevity prove that the previous glycosuria was not harmless but was largely responsible for symptoms attributed to senility or other causes. The other extreme is complete disregard of diet. This course may be expected to bring death from gangrene or other accident, sometimes even coma, in a large proportion of patients. Here again due weight may not be given to diabetes as the predisposing cause back of the infection or other terminal condition. The middle course is one frequently adopted; namely, a moderate regulation of diet with the aim of preserving strength and comfort and not paying too much attention to laboratory findings. In the case of this patient, the alleged comfort of such a course consists actually in continuous pain in the right foot and the danger of gangrene at any time. It is also scarcely reasonable to suppose that the foot is the only part of the body injured by the diabetes.

CASE NO. 18.

Male, unmarried, age 16 yrs. American; errand boy. Admitted Nov. 18, 1914.

Family History.—Grandparents' history not certain. Father died at 42 of cirrhosis of liver. Mother and two sisters of patient alive and well.

Past History.—Healthy life. Chicken-pox at 6. Tonsillitis in 1912. No other illnesses. Habits regular. No alcohol, very little tobacco. No excessive sweets or carbohydrate. Never nervous. Ordinary weight 133 pounds.

Present Illness.—Only 3 weeks ago, during the last week of Oct., first symptoms were noticed in the form of thirst, polyuria, polyphagia, weariness, and sleepiness. During present month he has been unable to read by artificial light because of blurring. Nov. 1, he stopped work and consulted a physician, who found 5 per cent glycosuria. Patient claims to have followed restricted diet since then, including gluten bread. He has never become sugar-free.

Physical Examination.—Normal in appearance though rather thin and nervous. Teeth in good condition. Tonsils slightly enlarged. A few small palpable glands in neck. Knee and Achilles jerks exaggerated. Blood pressure 135 systolic, 60 diastolic. Examination otherwise negative.

Treatment.—The diet on Nov. 19 consisted of 105 gm. protein, 17 gm. carbohydrate, and nearly 2000 calories. The glycosuria diminished to traces, and sugar-freedom could doubtless have been readily attained without fasting. Nevertheless, for the sake of more rapid and radical improvement, 4 days of fasting were imposed (Nov. 20 to 23). To make the fast easier, thrice cooked vegetables in quantities increasing up to 1500 gm. daily were permitted. The trace of ferric chloride reaction which developed cleared up spontaneously.

On Nov. 24 two eggs and 20 gm. butter were added, increased on the next day to four eggs and 40 gm. butter. Meat and bacon were subsequently added. The negative ferric chloride reactions, Dec. 1 to 4, on diets of 2200 to 2300 calories without carbohydrate and composed chiefly of fat, stand in strong contrast with what other patients often show when sugar-free on the same sort of diet. Thereafter the patient proved able to tolerate as much as 2900 calories with 60 to 80 gm. carbohydrate and 107 to 130 gm. protein. He was dismissed on approximately this diet but with calories diminished to about 2500. General instructions were given, but the food was not required to be weighed. The liberal diet (over 2 gm. protein and 50 calories per kg.) was permitted with the idea of satisfying the patient and allowing him to work hard, and in the hope that it might be tolerated in view of the early and mild stage of the diabetes. The average was reduced slightly by the fast-day ordered every 2 weeks. Also instead of weighing food, the patient was instructed to keep careful account of his own weight and never let it go above 120 pounds (*i.e.* 13 pounds below his full normal weight). Any gain over this was to be checked by fasting and reduced diet.

Subsequent History.—Reports indicated that the patient adhered to his diet until cherries became ripe in summer, when he started glycosuria by eating cherries. As he then broke diet in other respects, he was instructed to return to the hospital on July 15.

Second Admission.—In addition to glycosuria, decided ketonuria was present this time, notwithstanding 125 gm. carbohydrate in the diet on July 16. 3 days of fasting with nothing but coffee and soup were imposed (July 18 to 20), followed by a carbohydrate tolerance test, starting with 20 gm. carbohydrate in the form of green vegetables. The quantity was increased by 20 gm. carbohydrate daily, until on Aug. 4, 350 gm. carbohydrate were taken without glycosuria. Without attempting to push the carbohydrate higher, a fast-day was given on Aug. 5, with only coffee and soup. A diet was then instituted of 100 gm. protein, 100 gm. carbohydrate, and 2600 calories. Later the carbohydrate was raised as high as 200 gm. Traces of glycosuria occurred on this diet. It is noteworthy that even without glycosuria and with this high carbohydrate intake, some distinct ferric chloride reactions were present. On Aug. 21, the carbohydrate was diminished to 5 gm., the protein remaining about 100 gm., and the total diet about 2500 calories. On Aug. 28, 100 gm. carbohydrate were resumed, and the protein and total diet diminished to 84 gm. and 2400 calories respectively. The patient was

discharged on this diet. His weight was 56 kg. at this admission, (*i.e.* a return to his full normal weight which had been forbidden) and 51.8 kg. at discharge (still about 1 kg. higher than at his first admission).

Subsequent History.—Nothing further was heard from the patient until a letter from his sister, reported his death on Nov. 11, 1915. Inquiries revealed that the mother had no control over the boy, who refused to follow diet or allow his urine to be tested. The physician who referred the boy to this hospital was out of town. After the usual polyuria, polydipsia, and loss of weight and strength, the patient late in Oct. began complaining of indigestion, and a few days before death showed a high degree of nervousness and excitement. A local physician treated these symptoms of acidosis with tablets for the indigestion, sedatives for the nervousness, and tonics for the weakness. Heavy breathing was noted at the end, but actual coma was only a few hours in duration.

Remarks.—The condition was at a very early and favorable stage when treatment was begun. The well marked ferric chloride reactions without glycosuria on the high carbohydrate diets of Aug. 16 to 20 possibly indicate the intrinsic severity of the case. Undoubtedly the violations of diet and the gain in weight between the two admissions constituted a serious setback. Nevertheless, the carbohydrate test up to Aug. 4 showed that the tolerance was still high, and the blood sugar later in Aug. was found to be easily brought to normal. The later course was the typical uninterrupted downward progress of severe untreated diabetes, owing entirely to the fault of the patient and of the local practitioner who then treated him. No dietetic treatment could accomplish anything in a patient so irresponsible as this.

Concerning the diets prescribed in the hospital the following may be remarked. The change to practically carbohydrate-free diet on Aug. 21 is the typical old-fashioned method. It is observed that in spite of the high caloric intake (nearly 50 calories per kg.) the blood sugar promptly fell to normal and the results might be called favorable. The fact is that the ferric chloride reaction persisted, and continuance of such a high intake would inevitably have brought disaster later, no matter how favorable the laboratory findings for the time being. The diets allowed this patient were unduly high, for the following reasons. First, it had not yet been established whether the patient at such an early stage might recover sufficient tolerance to carry the full load of diet and weight. Second, this patient was given exercise involving considerable labor (see Chapter V), and it was anticipated that he would perform considerable muscular work at home. Third, it was evident from his general character that he would not endure any real privations, and he was therefore placed on a diet which left no excuse for violations, being fully satisfactory in protein, carbohydrate, and total quantity, and calling only for abstinence from sugar and reasonable limitation of starch. As stated, later experience has made it evident that such treatment is bad, and always results in the downward progress which was formerly regarded as spontaneous and inevitable. The attempt to try this method in this case failed on account of the patient's disobedience.

CASE NO. 19.

Female, married, age 39 yrs. Russian Jew; housewife. Admitted Nov. 18, 1914.

Family History.—Parents lived to old age. Patient had four brothers and nine sisters; all are living or died of typhus or accidental causes in Russia. No diabetes, cancer, tuberculosis, syphilis, or nervous diseases known in family.

Past History.—Born in Russia; came to United States 26 years ago. Hygienic surroundings poor. Measles and whooping-cough in childhood. Typhus at 12. 16 years ago a so called abscess in throat, said to have been cured by lancing. 7 years ago patient had a convulsion after a confinement; had to be in hospital 3 weeks and was sick for 3 months. Some shortness of breath on exertion for 2 years past. She was married 18 years ago. Husband living and well. Four children living and well; one born dead, full term; one miscarriage. Habits regular, no excesses. Frugal diet, poor in sweets but also in vegetables.

Present Illness.—Began with pruritus vulvæ $1\frac{1}{2}$ years ago. A doctor prescribed a salve which was ineffective. 1 year ago polydipsia commenced. She drank 60 glasses of water a day. Polyphagia began 6 months ago. She has lost 38 pounds during the past year, falling from her normal weight of 146 pounds to 108 pounds. Sleeplessness, weakness, pains in back also complained of. She consulted two different physicians who, notwithstanding these typical symptoms, told her she was "run-down" and prescribed tonics without examining urine. 4 weeks ago she came to New York for further medical advice. Diagnosis of diabetes was made and she was in a hospital for 2 weeks on a diet limited absolutely to meat, eggs, fish, cream, cheese, and string beans. Her condition failed to improve, and on her physician's advice she made application at this Institute. Her chief complaints are extreme weakness and persistent headaches.

Physical Examination.—A well developed woman without evident discomfort or dyspnea, appearing only slightly undernourished, but with flabbiness of skin indicating considerable loss of weight. Nephritic countenance, with slight edema about eyes and general pallor. Ocular examination negative. Teeth show neglect; many missing; those remaining show caries and pyorrhea. Throat appears normal. Heart normal. Slight empyema. Reflexes normal. Examination otherwise negative. Blood pressure 90 systolic, 70 diastolic. Wassermann negative.

Treatment.—(No graphic chart.) On her first day in hospital (Nov. 18) the patient received a carbohydrate-free diet of 12 gm. protein and 411 calories, and excreted 8.3 gm. sugar. Notwithstanding the great weakness complained of and the presence of nausea and colic, fasting was begun the next day and continued for 5 days. Alcohol was permitted because of weakness, but not more than 80 cc. whisky per day could be taken because of nausea. The ferric chloride reaction was negative on admission, positive on the first fast-day and diminished so that it was fully negative like the sugar reaction on the 3rd day of fasting. 180 gm.

thrice cooked vegetables were given on the 4th and 5th days. A very low diet was then begun, consisting of two eggs and 500 gm. thrice boiled vegetables. The weight, which was 47.2 kg. on admission, diminished to 44.6 kg. on Nov. 24. The patient complained of great hunger. The diet was rapidly increased until on Dec. 5 it consisted of 60 gm. protein, 2 gm. carbohydrate, and 3600 calories. This was tolerated without glycosuria or ketonuria, but the carbohydrate tolerance was very low. On Dec. 7 the addition of 200 gm. green vegetables containing 9.8 gm. carbohydrate resulted in slight glycosuria. The weight by this time was up to 48.8 kg. and the patient was much improved subjectively. The glycosuria was checked by a fast-day with 45 cc. whisky, then carbohydrate-free diet resumed, at first very low (25 gm. protein and 250 calories), but again rapidly increasing until on Dec. 19 it contained 138 gm. protein and 3330 calories. The attempt to include 7 to 12 gm. carbohydrate in the form of green vegetables again resulted in slight glycosuria. Without a fast-day, the carbohydrate was stopped and the total diet diminished to 600 calories, followed by an increase as before. On Dec. 28 the weight was 47.4 kg., and a diet of 100 gm. protein and 22 gm. carbohydrate were tolerated without glycosuria. The same was true of the diet of 91 gm. protein and 27 carbohydrate on Dec. 29. The assimilation of carbohydrate here is explainable by the lower weight and the lower total diet; namely, 2200 calories on each of these days. Likewise 103 gm. protein, 24 gm. carbohydrate, and 2400 calories were tolerated on Dec. 30. The patient was discharged on Jan. 3, 1915, on a carbohydrate-free diet of 110 gm. protein and 2500 calories, with 600 to 800 gm. thrice cooked vegetables daily. She felt well and fit for work and was continuously free from both glycosuria and ketonuria. Her weight at discharge was 47.6 kg., or practically identical with the weight at admission.

Subsequent History.—The patient followed her diet faithfully, and on Apr. 20 the addition of 10 gm. carbohydrate was permitted. Her weight tended to increase, and was 50.4 kg. on Aug. 2, 1915, and 55.8 kg. on Jan. 11, 1916. She was then instructed to take a fast-day once every 2 weeks. One feature of her history is that 7 weeks after discharge (Feb., 1915) and again in Nov., 1915, she had severe colds or gripe with fever, which confined her to bed 1 or 2 weeks, while no more than traces of glycosuria appeared. Her progress continued steadily favorable, and in Jan., 1916 she was referred to another clinic for further guidance and observation. She was seen again in Apr., 1918, still following diet and doing her housework without complaint.

Remarks.—The case gives the usual illustration that the way for a weak and undernourished diabetic to gain strength and well-being is by therapeutic under-nutrition. Abrupt initial fasting is sometimes dangerous in patients showing the condition here described at the outset, but was well borne in this instance. With sugar-freedom and loss of weight, the patient felt distinctly better; and in view of her age and the relative mildness of the case it was considered safe to augment her diet rather rapidly. As is frequent in such cases, with an adequate ration of

protein and calories, the carbohydrate tolerance was practically nil. With the weakened condition and the apparent absence of tolerance, this might have been classed in standard text-books as a severe case. The relative mildness was shown by the steady improvement when the urine was merely kept sugar-free. It is also of interest that occasionally patients of this sort, handicapped by ignorance and poverty combined, prove able to follow diet with fidelity, test their urine conscientiously, and achieve satisfactory results.

CASE NO. 20.

Female, married, age 38 yrs. American; housewife. Admitted Nov. 19, 1914.

Family History.—One brother died of tuberculosis at 29 years of age. Family otherwise healthy.

Past History.—Scarlet fever, measles, chicken-pox, whooping-cough, and diphtheria all before 7th year. Also at age of 2 patient had a fall injuring left knee so that she was unable to walk until 13, and the leg is still stiff. Has had headaches all her life. Lately they are limited to the menstrual period, and are localized in migraine fashion on the left side of the face. Numerous sore throats during the past year. Habits regular. No excesses, no special fondness for sweets or starches. Married 13 years ago. One child born 12 years ago died of heart trouble a few hours after birth. A second living and well. Venereal diseases and symptoms denied.

Present Illness.—Glycosuria was discovered 1 year ago when patient went to a hospital for another cause. Since then there have been no symptoms except the gradual loss of 50 or 60 pounds of weight. She has noticed a darkening of the skin about her eyes during this time. This began in the form of small dots which have increased and fused until they form a very noticeable broad brown ring around her eyes. She has been on a moderately restricted diet with continuous glycosuria, and has been taking sodium bicarbonate and citrate for the past few weeks. Nervousness has developed and she tires easily. She was referred to the Institute by her physician on suspicion of bronzed diabetes.

Physical Examination.—Height 150 cm. A nervous, frightened looking woman, well nourished, with sweetish odor of breath. Slightly elevated bronzed circle $1\frac{1}{2}$ to 2 cm. wide about both eyes is most striking characteristic of face. Teeth neglected, three missing, one carious; no pyorrhea. Throat normal. Heart shows signs of well compensated mitral regurgitation. Blood pressure 140-110. No enlargement of lymph nodes except in axilla. Knee jerks present on right, absent on left (injured side). Examination otherwise negative. No pigmentation except that about eyes.

Treatment.—Patient was first kept on an observation diet without fasting. No special peculiarities were noticed, and she was able to tolerate 75 to 80 gm. protein, 30 to 40 gm. carbohydrate, and 1500 to 1800 calories with no glycosuria

or only traces. Ketonuria was stubbornly persistent but never dangerous in degree. Slight albuminuria present on admission cleared up completely and did not return. The observation diet as a whole represented undernutrition, inasmuch as the weight fell from 53 kg. at entrance to 48.5 kg. on Dec. 18. The condition about the eyes proved to be xanthelasma, and nothing was found to indicate a true bronzed diabetes. Accordingly a more radical treatment was instituted in the latter part of Dec., especially with a view to reducing weight. From Dec. 20 to Jan. 6 the diet contained nothing but whisky and green vegetables. Traces of glycosuria appeared when the carbohydrate intake was approximately 60 gm. By this means the urine was at last made free from both sugar and ferric chloride reactions (Jan. 5 and 6). Carbohydrate was then excluded by thrice boiling the vegetables, and two eggs were added. The diet was then built up, so that on Jan. 13 to 14 it consisted of about 80 to 90 gm. protein, 30 gm. carbohydrate, 60 gm. alcohol, and 2200 to 2300 calories. The weight had thus been reduced to 46.6 kg.; *i.e.*, a loss of 6.4 kg. since admission. Though the ferric chloride reaction had reappeared, it was deemed safe to let the patient go home on this theoretically excessive diet, in order that she might carry on her housework comfortably and continue to improve in strength and nervous control, the expectation being that in such a case and under such conditions the gradual gain in tolerance resulting from continued sugar-freedom would take care of the persisting abnormalities, notably the ketonuria.

Subsequent History.—The patient adhered faithfully to her diet at home, carried on her housework, nursed her daughter through pneumonia, gradually lost her nervousness, and remained continuously free from glycosuria but with a slight ferric chloride reaction constantly present, even with addition of 10 gm. carbohydrate to the diet on Apr. 20. On June 2 she was readmitted to the hospital because of complaint that she was not feeling so well and that her nervousness was returning.

Second Admission.—The weight at this admission was 43.8 kg.; *i.e.*, 2.8 kg. less than at discharge. The general condition was much better than at the former admission. The pigmentation about the eyes appeared neither to have increased nor diminished. The urine was entirely free from sugar, as the patient reported it had been continuously, but the ferric chloride reaction had become heavy, and the 24 hour urine contained 1.96 gm. ammonia nitrogen. The symptoms complained of were presumably associated with this acidosis. It was therefore deemed desirable to proceed radically to abolish acidosis. This could not be done by simple addition of carbohydrate to the diet, for on June 3 the giving of 30 gm. carbohydrate with 84 gm. protein and 1700 calories caused well marked glycosuria. On the other hand, the acidosis diminished by simple reduction of diet, so that on June 5, on a carbohydrate-free diet of 66 gm. protein and 1300 calories, there was excretion of only 0.56 gm. ammonia nitrogen. Therefore on June 6 and 7, fast-days were given, with an allowance of 300 cc. coffee, 300 cc. clear soup, and 50 cc. whisky. On June 8, alcohol was discontinued and never

again used for this patient. Green vegetables representing 10 gm. carbohydrate were added on this day, and the usual carbohydrate tolerance test was instituted, with increase of 10 gm. carbohydrate in green vegetables daily. A trace of glycosuria appeared on June 14 with 90 gm. carbohydrate, but this did not represent the true limit of tolerance, because glycosuria ceased, and the true limit was reached only with about 150 gm. carbohydrate on June 23. Further increase up to 170 gm. on the following days caused only slight but continuous glycosuria. Under this program the ferric chloride reaction became negative and the ammonia excretion held a low level. After a fast-day on June 28, a regular diet was gradually built up with one fast-day every week. Even with 37 to 45 gm. carbohydrate in the diet the ferric chloride reaction reappeared, but diminished, and on July 13 became negative with 67 to 75 gm. carbohydrate in a diet otherwise composed of 75 to 100 gm. protein and 1600 to 2100 calories. The weight on July 24 was 41.8 kg.; *i.e.*, a loss of 2 kg. during this period in hospital, or a loss of 11.2 kg. since her first admission. She was discharged to continue this diet at home.

Subsequent History.—The patient continued to follow treatment faithfully, and improvement continued with constantly normal urine. She passed through an attack of grippe in Nov., 1915, without return of glycosuria. She has led a fully normal life except for attention to diet, does her work easily, has lost all nervousness, and feels well in every respect. In addition to her reports, she came for personal examination on July 18, 1916. Her weight was then 45.2 kg.; *i.e.*, a gain of 3.4 kg. since discharge. Her general appearance was excellent, with pigmentation unchanged. The urine was normal, the CO₂ capacity of the plasma 50.3 per cent, the plasma sugar 0.189 per cent. This hyperglycemia received no special treatment, for since there had been such obvious improvement before, it was considered probable that it would continue, with ultimate reduction of blood sugar, without more radical measures in a case of this type.

Remarks.—Aside from points already noted, the case again illustrates the benefit resulting from general therapeutic undernutrition in a patient who had already suffered considerable loss of weight and strength from diabetes. Both the treatment and the improvement were gradual in character. Results could have been achieved more quickly by following up the alcohol-carbohydrate period of Dec., 1914, with undernutrition sufficient to keep the ferric chloride reaction negative, at the same time building up carbohydrate tolerance more rapidly. As usual in such cases, however, the simple continuance of freedom from glycosuria brought steady improvement, so that at the second admission there was a considerable carbohydrate tolerance and acidosis was easily abolished without interruption of the steady gain in well-being. The patient now weighs enough for fully satisfactory looks, comfort, and strength. There is a complete contrast in these respects with her former condition at a higher weight. An attempt to return to the former weight would doubtless bring a return of the previous troubles. There has probably been little or no absolute improvement

in the power of assimilation, neither is there any evidence of any progressive decline. The patient is merely living within her assimilative power. As far as can be judged from the experience of nearly 3 years, she can continue to do so without difficulty, and the general trend seems to be upward rather than downward.

CASE NO. 21.

Female, married, age 46 yrs. Scotch, housewife. Admitted Nov. 20, 1914.

Family History.—Father died in accident. Mother died of heart trouble at 42. Patient was the only child. Diabetes, tuberculosis, cancer, syphilis, or nervous disorders in any relatives denied. Patient married twice. Has had only one child, who is alive and well; no miscarriages.

Past History.—Measles, mumps, and whooping-cough in childhood. Came from Scotland to United States at age of 17. Scarlet fever 15 years ago. Operation for ventral hernia 1 year ago. Subject to occasional headaches ever since she can remember. Also has shortness of breath on exertion. Occasional sore throats. No use of alcohol. Drinks six or eight small cups of tea daily. Up to 15 years ago weight was 146 pounds; since then it increased, so that at the time of her operation a year ago it was 266 pounds. During this year she has lost 36 pounds.

Present Illness.—About 6 months ago patient began to notice polyuria, polydipsia, polyphagia, and increasing nervousness, with rapid loss of weight. These have been the only symptoms. No treatment by diet.

Physical Examination.—Height 155 cm. A large framed, plethoric, obese woman with dry skin, a nervous expression, and bilateral arcus senilis. Teeth neglected, some missing; those remaining show caries and pyorrhea. Tonsils a trifle hypertrophied. Slightly large thyroid palpable. No lymph node enlargement. Heart slightly enlarged. Slight emphysema. Knee jerks active. Leg veins markedly varicosed. Blood pressure 175 systolic, 120 diastolic. Trace of albumin in urine, but no casts.

Treatment.—The most obvious requirement was to reduce weight. The most noteworthy initial observation was that in 4 days of absolute fasting this very obese woman failed to develop any ferric chloride reaction and showed absolutely no symptoms of acidosis. On the following 4 days she received only moderate quantities of whisky (not above 50 gm. alcohol). It is evident that they did not prevent the appearance of a slight ferric chloride reaction. This reaction was negative on Nov. 28, when only 10 gm. alcohol were given, as if the larger quantities of alcohol had tended to produce rather than prevent it. On Nov. 29, a carbohydrate-free diet of 93 gm. protein and 2260 calories caused a trace of glycosuria. The subsequent diets represent very marked undernutrition. It is obvious from the graphic record that the patient not only had practically no carbohydrate tolerance but also tended to show traces of glycosuria even on very low carbohydrate-free diets. She was of the type spoken of in older text-books

as relatively independent of diet ("paradoxical tolerance"). That is, her glycosuria had never been excessive, and if tested she would doubtless have proved her ability to assimilate most of the carbohydrate of any diet. Yet complete sugar-freedom was difficult to achieve even with the most radical restrictions. Blood sugar analyses were not made. It is probable that a continuous marked hyperglycemia was responsible for the frequent traces of glycosuria, and that this varied little with diet. The principal result of treatment was to bring the body weight down from 108 kg. to 90 kg. No special attempt was made to conserve the body protein. Nitrogen balances would undoubtedly have turned out strongly negative. Nevertheless, there was a gain in well-being, and at discharge there were no symptoms except those referable to arteriosclerosis, the former migraine attacks, and other conditions apparently independent of the diabetes. The diet prescribed at dismissal was approximately 75 gm. protein, 60 gm. carbohydrate, and 1300 calories, representing, for a weight of 90 kg., only about 0.8 gm. protein and 15 calories per kg. The trace of glycosuria on Jan. 24 may be regarded as of the accidental type sometimes resulting from a sudden increase of carbohydrate. It appeared that the patient could carry this diet without glycosuria and with a bare trace of ferric chloride reaction. She stated that her appetite was reasonably well satisfied, and she felt better when eating and weighing less. The trace of albumin present in the urine at admission remained unchanged, but casts could very seldom be found. The treatment was not considered complete at dismissal, but undernutrition was to be continued at home.

Subsequent History.—The patient continued free from glycosuria at home, with a persisting trace of ferric chloride reaction. She was not required to weigh her food, and her estimates were probably enlarged with increase of appetite, for her weight at first held practically even, being 90.6 kg. in Aug., 1915. By Oct. there was an increase of 2.6 kg. The sugar in the whole blood was then 0.128 per cent, in the plasma 0.161 per cent. Sugar remained absent from the urine; the ferric chloride reaction continued present. She was instructed to fast 1 day every 2 weeks:

On Nov. 29, the weight was found to be 101.4 kg., plasma sugar 0.143 per cent, CO₂ capacity of plasma 43.2 per cent. The blood pressure was 240 systolic, 140 diastolic, and there had been symptoms referable to hypertension. She was instructed to fast 1½ days every week.

On Jan. 11, 1916, the blood pressure was 220 systolic, 120 diastolic. The weight was 101.5 kg. with clothing, 99 kg. stripped. She was instructed to remain in bed for a week on a diet of nothing but low percentage green vegetables. The urine was entirely negative for both sugar and ferric chloride reactions.

On July 13, 1916, the blood sugar was 0.128 per cent, plasma sugar 0.156 per cent, CO₂ capacity 56.9 per cent. Sugar and ferric chloride reactions in urine remained negative. Though recent dietary instructions theoretically established an intake of only 1000 calories, the patient's estimates were evidently too high and the weight continued to rise, being now 103.2 kg. stripped. The patient

has remained so well that she has not been closely supervised. She still continues to lead a normal life, and suffers only from headaches and occasional attacks referable to hypertension.

Remarks.—Complication of this case with obesity and arterial hypertension called for no special alteration in the treatment of the diabetes. The entire condition rendered a reduction of weight desirable. By this simple measure the carbohydrate tolerance, which appeared so very low, was easily raised, and the case stood revealed in its true light as one of intrinsically mild diabetes. It must again be mentioned that the initial stage of treatment of such a case sometimes presents difficulties and dangers such that fasting may have to be employed cautiously and after special preparation; but in this instance the fasting offered no difficulty and the obesity was no obstacle to the gradual disappearance of the ferric chloride reaction. The case thus opposes the idea that the available fat supply is the sole determining factor in fasting acidosis. Under a mild therapeutic régime hyperglycemia has been persistent. It need not be attributed in any degree to the hypertension; on the contrary, the hyperglycemia sometimes described in cases of hypertension is more probably an indication of pancreatitis and mild diabetes. This being one of the earlier cases of the series, conservatism seemed to favor leniency in the treatment. Fuller experience indicates that the right plan would be to reduce the weight sufficiently to keep the blood sugar normal. Nevertheless, in view of the mildness of the case, if the patient follows a fairly reasonable diet without letting her weight rise too high, she can probably go through life without further trouble from her diabetes.

CASE NO. 22.

Male, married, age 52 yrs. American Jew; cigar manufacturer. Admitted Nov. 20, 1914.

Family History.—Father died of pneumonia at 74. Mother, now 74, has kidney trouble. One brother living and well. Two sisters died in childhood, a third of appendicitis at 15, a fourth is living but has carcinoma of breast. No tuberculosis, syphilis, or nervous disorders in family. Patient has been married 31 years; wife living and well. Five children; one died of diphtheria in infancy, four living and well.

Past History.—Practically never sick from childhood up. Neisser infection twice. Syphilis denied. At age of 21 patient was rejected for life insurance because of alleged Bright's disease. He consulted eminent specialists, and the slight albuminuria was classified among the earliest examples of orthostatic albuminuria. For many years he has never been without albumin and casts in urine, but has had no symptoms other than these and has never had to miss a single day from business. For part of his life patient drank considerable wine in connection with business dealings, and smoked 15 to 20 cigars a day. He started as a poor boy and became a millionaire, and has lived at highest nervous tension.

In the past 10 or 12 years he has had 25 or 30 hysteric attacks in which he was practically irresponsible. He is accustomed to rich living. Bowels constipated.

Present Illness.—2 years before admission symptoms began with extreme hunger and thirst, loss of weight, bad breath, and cramps in the legs. On account of failing vision he consulted an oculist, who immediately asked for a specimen of urine and diagnosed diabetes. The diet since then has been slightly restricted qualitatively, but quantitatively two or three times as much as required by a normal appetite. The loss of weight has continued nevertheless.

Physical Examination.—A slightly built, somewhat emaciated man with pale complexion and nervous, feeble appearance. Several teeth missing; those present show slight caries and pyorrhea. Throat somewhat congested; left tonsil not visible, right protrudes slightly. Slight generalized lymph node enlargement. Heart very slightly enlarged to left. Arteries palpably sclerosed. Blood pressure 135 systolic, 110 diastolic. Liver edge 2 cm. below costal margin. Reflexes normal. Examination otherwise negative. Urine shows slight albumin and numerous hyaline casts.

Treatment.—The patient's extreme nervousness, as also headaches and terrors at night, required the use of codeine during the early days in the hospital. He was kept on an observation diet for the first 3 days, poor in carbohydrate, and particularly with total calories limited to about 1600 on Nov. 21 and 900 on Nov. 22. The glycosuria was thus greatly diminished. Nevertheless fasting was instituted as soon as the general condition seemed to permit. Owing to weakness, the patient was in bed during the fast. On Nov. 23 and 28 the fasting was absolute. On the intervening days whisky was given, but never above 70 cc. Glycosuria ceased with the first day of fasting. With continuance of the fast, the ferric chloride reaction diminished to traces. On Nov. 29 a carbohydrate-free diet of 45 gm. protein and 2080 calories was tolerated without glycosuria, but brought back a heavy ferric chloride reaction. On the next day the diet was diminished to 23 gm. protein and 600 calories. The weakness and nervousness still being salient features and the patient being very hungry, a liberal diet was permitted on the subsequent days, rising by Dec. 19 to 97 gm. protein, 33 gm. carbohydrate, and 3000 calories. Traces of glycosuria were frequent on this high diet, and well marked ferric chloride reactions continued. By this time the general condition had improved and the patient had grown more accustomed to hospital life and dietary restrictions. Accordingly, on Dec. 21 a more rigid treatment of the diabetes was undertaken. On that day the only food was 50 gm. alcohol. Green vegetables were gradually added to the alcohol, representing 7.5 gm. carbohydrate on Dec. 22 and increasing to 107 gm. on Dec. 28. The ferric chloride reaction was still stubborn notwithstanding this carbohydrate intake without glycosuria—an illustration that food is not the only controlling factor. In view of the patient's weakness and irritability a more liberal diet was again resumed. He was dismissed on Jan. 15, 1915, on a diet of approximately 100 gm. protein, 15 gm. carbohydrate, and 2400 calories. The body

weight was 50 kg. at admission, 47.2 kg. at discharge, the period of treatment thus representing undernutrition to the extent of a loss of 2.8 kg. weight. There had been a notable gain in strength, so that the patient was now outdoors daily and was becoming restless owing to a desire to return to work. The nervousness was greatly lessened and he felt that life was again worth living. Albuminuria and casts persisted, but several functional tests during the stay in hospital had shown a normal index of urea excretion. The patient, being still weak, was instructed not to work more than half of each day and to pay attention to rest and general hygienic measures.

Subsequent History.—The urine continued negative to sugar and ferric chloride tests, with the usual albumin and casts present. By Feb. 10 the weight had risen to 53.2 kg. The blood pressure was 153 systolic. The patient at this time was working 6 or 7 hours a day, was taking horseback rides and other exercise, and reported himself free from nervousness, sleeping soundly at night, and enjoying life. In appearance he was very greatly improved. By Apr. 12 there had been a further increase of 2 kg. in weight. The blood pressure was 180 systolic, 135 diastolic. He was warned that the gain in weight was contrary to instructions, and the diet was ordered changed to 115 gm. protein, 20 gm. carbohydrate, and 1600 calories; *i.e.*, the protein and carbohydrate were slightly increased and the fat decidedly diminished. This allowance of about 30 calories per kg. was expected to maintain his nutrition without further increase of weight. On July 7 the patient reported that he had been feeling as well as in his earlier years before the onset of diabetes. Occasional headaches recurred but were relieved by catharsis. There had been a further slight increase of weight up to 54.4 kg. The blood pressure was 195 systolic, 160 diastolic. The patient had departed slightly from diet, particularly by adding bread occasionally, and the urine showed a trace of glycosuria and a moderate ferric chloride reaction. This trace always disappeared with a single fast-day, and he was warned to adhere to diet and keep sugar absent.

Second Admission.—The patient made no further report until he reentered the hospital Jan. 24, 1916, slightly more than a year after discharge. He had carried on his large business continuously and efficiently during this time and also had enjoyed much recreation. He returned with glycosuria again present, in consequence of too many visits to restaurants in the course of his amusements. The weight was 50.2 kg.; *i.e.*, 0.2 kg. more than at previous admission. He had been running down lately by reason of his indiscretions in diet, but nevertheless was far stronger and in better condition in all respects than at his previous admission. Physical examination practically as before. Blood pressure 200 systolic, 135 diastolic. All the conditions being more favorable, measures were now instituted for a radical clearing up of both glycosuria and ketonuria. 4 days of absolute fasting were imposed (Jan. 28 to 31). This was followed by a carbohydrate period in the form of the usual tolerance test, *i.e.* on Feb. 1 green vegetables were given containing 10 gm. carbohydrate, and this was increased by 10 gm. daily. The

traces of glycosuria on Feb. 4 and 5 were accidental in character and disappeared with further increase of carbohydrate intake. A tolerance of 150 gm. carbohydrate was thus demonstrated on Feb. 15. By this time the ferric chloride was entirely negative, the blood pressure had gradually diminished to 160 systolic, 120 diastolic, and the patient was feeling well enough to have recovered from the fears which had brought him back to the hospital. Accordingly at this point he suddenly announced that urgent business matters required his attention and that he must leave immediately. He was therefore discharged on the following day with instructions not to return.

Third Admission.—Nothing more was heard from him until on Oct. 17, 1916, his wife telephoned that he had had an attack of apoplexy and was in a critical condition. He was found in an excessively excited state, with partial right sided hemiplegia. The body weight was again 50.2 kg.; the blood pressure 190 systolic, 125 diastolic, the blood sugar 0.305 per cent, the CO₂ capacity of the plasma 81 per cent. The urine showed moderate sugar and negative ferric chloride reactions. He was placed on a diet of 65 gm. protein, 10 gm. carbohydrate, and 1000 calories. On this diet glycosuria diminished to only occasional traces, but the blood sugar never fell below 0.2 per cent. Only slight glycosuria resulted from an increase of diet to 65 gm. protein, 35 gm. carbohydrate, and 1600 calories. Meanwhile, with rest, the paralysis was gradually clearing up. In Dec. and Jan. it seemed feasible again to undertake thorough treatment of the diabetes. A week of fasting (Jan. 7 to 13) was well borne. At the end of it the ferric chloride reaction was negative, the ammonia nitrogen excretion only 0.12 gm., the plasma bicarbonate 68 per cent, but the blood sugar was still 0.222 per cent. A carbohydrate test with the usual increase of 10 gm. daily showed a tolerance of only 30 gm. carbohydrate in the form of green vegetables. Treatment was conducted according to the usual principles, the protein being kept low (50 gm. or less daily) partly on account of the renal condition. Rigorous undernutrition brought the usual results, so that in Feb. a tolerance of 120 gm. carbohydrate was demonstrated, and the stubborn hyperglycemia was at last reduced, not to normal, but well below the renal threshold. By Mar. the patient was able to tolerate 65 gm. protein, 10 gm. carbohydrate, and 1400 calories. His weight had been reduced to 41 kg.; *i.e.*, a loss of 9.2 kg. The paralysis had gradually diminished so that he was able to be about again and to make some use of his right arm. He was improved sufficiently that he was no longer trustworthy in regard to diet. He was discharged with the feeling that life could not be greatly prolonged.

Remarks.—The case represents the treatment of diabetes in the presence of nephritis. It is evident that such a combination presents no obstacle to the carrying out of the usual method. A diet low in both protein and calories is beneficial from the standpoint of both the diabetes and the nephritis, and there is no antagonism in any of the measures required. In this instance the patient was saved from threatening weakness and nervous collapse connected with his

diabetes, and it was possible, as shown especially in the second admission, to make the urine normal and bring the blood sugar also to a normal level. Disaster came from the side of the nephritis. The patient is failing but was alive at last report.

CASE NO. 23.

Male, married, age 44 yrs. American; insurance agent. Admitted Nov. 27, 1914.

Family History.—Father and mother living and well. One sister died in infancy, and a brother of pneumonia. No diabetes or other special disease in family. Patient married 20 years. Two children, one living and well at 17 years; the other died in a difficult labor. An interesting addition to this history at time of admission is that patient's mother has since developed diabetes at the age of 74.

Past History.—Measles, mumps, and chicken-pox in childhood. Healthy life. Neisser infection at 19; syphilis denied. 14 years ago had "bloody dysentery" for a week. Habits regular; moderate drinking and smoking. Appetite normal.

Present Illness.—9 years ago, after much worry in business, glycosuria was discovered when patient applied for life insurance. His family physician prescribed diet and pronounced the condition only a transient glycosuria. Subsequently life insurance was granted. He has had constant medical supervision and the tendency to glycosuria has steadily increased, so that during the past 2 years he has never been sugar-free, and the amount has varied from 3 to 7 per cent. His weight has diminished from 195 to 165 pounds. He can still do considerable work, but feels a decided impairment of strength and endurance. No polyphagia. Urine not more than 3 liters. He avoids sugar and most starches, but his diet includes oatmeal, two slices of fraudulent gluten bread, fruits, vegetables, and occasionally a potato. He was referred to the Institute by a competent general practitioner because both glycosuria and ketonuria were heavy on the diet stated. The physician was in the old-time dilemma of hesitating to increase glycosuria by adding carbohydrate, and fearing to increase acidosis by withdrawing carbohydrate.

Physical Examination.—Height 172.5 cm. A well developed, adequately nourished, healthy appearing man. Teeth in good condition. Tonsils slightly enlarged. Liver edge 3 cm. below costal margin. Examination otherwise negative.

Treatment.—The patient was kept for a week on an observation diet of 95 to 120 gm. protein, 10 to 20 gm. carbohydrate, and 1800 to 2400 calories. The highest ammonia nitrogen excretion was 2.31 gm. There were no symptoms of danger or even discomfort. Fasting was begun on Dec. 5, first absolute, then (Dec. 6 and 7) with alcohol up to 52.5 gm. This was followed by a low carbohydrate-free diet, but glycosuria promptly returned (Dec. 10 to 11) on about 50 gm. protein and 1600 calories. Ferric chloride reactions persisted, and the ammonia

excretion was practically as high as at the beginning. The case had been taken as a mild one. These signs indicated that notwithstanding the absence of striking symptoms, the real condition was by no means trivial and nothing but radical undernutrition could bring a satisfactory result. The patient was absolutely obedient and gave his full confidence, and a rigid program was therefore instituted. With a view to combating acidosis, food was given chiefly in the form of alcohol, the highest intake being about 260 cc. whisky on certain days in Feb. The general plan of treatment is best seen from the graphic chart. Protein-fat diets were given on a few days, for example, Jan. 15 to 17, but for the most part the diet consisted only of whisky with addition of carbohydrate from time to time up to the limit of tolerance. This limit was very low. The giving of 40 to 70 gm. carbohydrate in the form of green vegetables with no other food but whisky was sufficient to cause glycosuria on repeated occasions in Dec., Jan., and Feb. The maximum alcohol doses above mentioned, with the addition of these quantities of carbohydrate, failed to abolish the persistent, fairly heavy ferric chloride reactions. Also it was not possible to allow an adequate diet and await a later recovery of tolerance for clearing up acidosis, because the total food tolerance remained persistently low. For example, on Jan. 17 a carbohydrate-free diet of 89 gm. protein and 1790 calories gave rise to glycosuria lasting 2 days. Under such conditions it is generally necessary to master both the glycosuria and the acidosis before much real improvement of assimilation can be expected. At the end of Mar. and first of Apr. the patient's weight touched its lowest point, 51.4 kg.; *i.e.*, a loss of 19.2 kg. during 4 months of severe continuous undernutrition. The patient had come to the hospital looking strong and robust. By this time he appeared thin and weak. His strength was definitely diminished, and his general decline seemed so evident that only full confidence on his part and on the part of those conducting the treatment permitted the completion of the necessary program. But about this time the ferric chloride reactions grew steadily paler, until they were negative in certain urine specimens of each day and not more than traces in the other periods. Also a recovery of assimilation was evident, such that on Apr. 5 to 7 a diet of approximately 100 gm. protein, 20 gm. carbohydrate, 100 gm. alcohol, and 2200 calories was tolerated without glycosuria. Exercise had not been employed in the earlier treatment, because of uncertainty as to its effects in the presence of marked undernutrition and a persistent tendency to acidosis. It was now begun and rapidly increased up to the limit of strength. The high calories in the later diets were permitted in proportion to the amount of physical labor performed. On Apr. 8 it appeared feasible to discontinue alcohol, and except for the fast-day on Apr. 11 it was never resumed. On Apr. 9 and 10 the diet was made approximately 100 gm. protein, 30 gm. carbohydrate, and 1500 calories. This was increased rapidly to 2700 to 3000 calories with the same protein and carbohydrate. A regular fast-day each week diminished the average intake to about 86 gm. protein and 2300 calories daily, or about 43 calories per kg. for the weight of approximately 54 kg. at that time.

The patient, though thinner, now both felt and looked far better than at admission. He was up to full strength in every way and able to carry on his regular business and in addition take much exercise and recreation daily. He was discharged in this condition on May 8 to spend the summer in the country. He was instructed to report in 6 weeks and not to gain more than 2 pounds in this time.

Subsequent History.—In the country he spent his days in walking, riding, swimming, tennis, and other exercise, building up strength while keeping weight within prescribed limits. In Aug. ferric chloride reactions ceased to appear. The urine never showed sugar except traces on rare occasions when he made unintentional mistakes in diet. He returned to resume his regular business in the city in Sept.

On account of persistent hyperglycemia, exercise was increased, the patient preferring this to a reduction in diet. Daily exercise was taken in the form of horseback riding, athletic exercises under an instructor, swimming, and boxing. He also walks to business, an average of about 8 miles daily, frequently walks 20 or 30 miles on Sundays, and also plays tennis and squash three or four times a week. His business duties occupy about 5 hours a day, and in the remaining hours he has made a trained athlete of himself. Because hyperglycemia still persisted, on Dec. 17 the diet was made 130 gm. protein, 50 gm. carbohydrate, and 2500 calories, this change representing particularly an increase in carbohydrate and a diminution in total calories. At the same time he was allowed to increase his office work by 1 hour. On New Years day, 1916, the patient added a large baked potato to his diet without glycosuria, but was warned against a repetition. Traces of glycosuria appeared in subsequent months on rare occasions, and accordingly on July 10, 1916, the diet was diminished to 130 gm. protein, 40 gm. carbohydrate, and 2200 calories. In the entire time since then there was a trace of sugar in the urine only on 2 days. The weight at last report was 68.4 kg., in comparison with the 70.6 kg. at the time of first beginning treatment in hospital. The general strength and subjective condition are the best the patient ever enjoyed.

Acidosis.—Though mostly slight, this was notably stubborn, and the mastery of it was one of the most difficult features of the treatment. The prolonged program of undernutrition, with alcohol short of intoxication and carbohydrate to the point of glycosuria, resulted in a slow decline of the ammonia to a normal level about the middle of Feb. There was a prompt rise with the addition of small quantities of protein and fat to the diet late in Feb. and early in Mar., followed by another slow decline. Also, in addition to the tenaciously persistent ferric chloride reaction, the CO_2 capacity of the plasma indicated the same chronic tendency to acidosis. From the graphic curve it can be seen that the values were generally near the lower normal limit and frequently fell considerably below this. Sodium bicarbonate was used twice; namely, 50 gm. on 1 day to check the particularly marked fall of the plasma alkalinity at the close of Feb., and 30 gm.

daily on Mar. 8 and 9. These doses gave immediate relief from slight symptoms of malaise of which the patient complained at this time. But obviously his fundamental trouble was not lack of alkali, and the treatment had to be directed to the causes underlying the state of acidosis.

At the time of discharge from hospital the ammonia nitrogen excretion was still 0.8 to 1.2 gm.; and some color was shown with ferric chloride in certain urine specimens every day, while specimens in other portions of the day were negative. As mentioned, the ferric chloride reactions became fully negative in Aug. and have remained so since. Acidosis has also remained absent by other tests. On July 25, 1916, the CO₂ capacity of the plasma was 60.6 per cent, and it has since remained high.

Exercise and Blood Sugar.—It seems probable from other experience that no harm would have been done and progress might have been hastened by using exercise in this case from the outset. The improved assimilation of carbohydrate and other food might have aided in a quicker clearing up of acidosis. Exercise was carried to a higher point in this patient than in any other of the series. As stated, he has made a trained athlete of himself and has enjoyed the highest vigor and subjective health. In a general way it seemed evident that exercise improved his assimilation. Precise experiments concerning the effect of exercise upon his blood sugar were not performed.

It will be noted in the graphic chart that the blood sugar in the latter part of Mar. was below 0.15 per cent and fell to normal. With the higher carbohydrate and higher total diet in Apr. it rose as high as 0.17 per cent, but came down, apparently as a result of exercise, to a nearly normal level at discharge. After leaving hospital the patient's weight gradually rose and the blood sugar likewise increased. On Oct. 6, with weight up to 60.9 kg., the sugar in whole blood was 0.185 per cent, in plasma 0.208 per cent. It was at this point that a maximum of exercise was begun, the patient preferring this to a reduction of diet. Nevertheless on Oct. 18 the sugar in the whole blood was 0.192 per cent, in the plasma 0.208 per cent, while the patient was feeling in splendid condition. On Oct. 25 the blood sugar was again 0.192 per cent and the plasma sugar 0.208 per cent; on Oct. 28 the plasma sugar was 0.222 per cent; on Nov. 15 the blood sugar was 0.161 per cent, plasma sugar 0.222 per cent. Traces of glycosuria had formerly been cleared up on repeated occasions by exercise, but it seemed evident that the diet was too high, so that exercise could not lower the hyperglycemia or entirely prevent recurrences of these traces of sugar. Accordingly the diet was modified on Dec. 27 as above noted. On July 10, 1916, the blood sugar was 0.156 per cent, the plasma sugar 0.217 per cent. The weight as above mentioned was higher than before; namely, 68.4 kg. On July 25 the blood sugar was 0.143 per cent, the plasma sugar 0.169 per cent. On Aug. 2, 1916, the blood sugar was 0.167 per cent, the plasma sugar 0.178 per cent. A reduction of body weight is the one means which may be expected to control the hyperglycemia. The chief value of exercise from the standpoint of permanent results probably consists in burning

up surplus calories and keeping down excess weight. Exercise has doubtless been somewhat overdone in this case.

Nitrogen Loss.—In the prolonged period of almost protein-free diet, it is evident that much protein must have been lost from the body. The nitrogen analyses of the urine are very incomplete. If the known points of the nitrogen output are joined to make a curve as shown in the graphic chart, a reckoning from such a curve will give a rough idea of the depletion of body nitrogen. The general undernutrition is evident from the following table:

	77 days.	Per day (average).
Total nitrogen output.....	511.32 gm.	6.61 gm.
Protein intake.....	1236.20 “	16.10 “
Nitrogen “.....	197.80 “	2.50 “
“ deficit (output — intake).....	313.52 “	4.14 “
Alcohol calories in diet.....	28979	376
Food “ “ “.....	24284	316
Total “ “ “.....	53263	692

Alcohol.—Prolonged high dosage of alcohol in this patient was for the purpose of keeping up strength by supplying calories and if possible aiding to diminish acidosis. According to clinical indications it was of value for the first purpose. There is no evidence that it had any value for the second purpose. If the thing were to be done over, less alcohol or none would be used. Better and quicker results could doubtless be obtained by a low protein diet, without fat, with vegetable periods interspersed. Body nitrogen and strength would be better conserved by the protein. Alcohol is probably injurious rather than beneficial as regards acidosis.

Remarks.—The outstanding feature of this case is that a patient in seemingly good physical condition was subjected to over 3 months of continuous undernutrition and brought into a thinner and seemingly worse condition as a therapeutic measure on the basis of laboratory findings alone. The case was not mild as imagined when the patient was admitted. It is believed, on the contrary, that trouble was shortly impending. The condition confronted was an assimilation of carbohydrate or protein so low that glycosuria resulted from a very low intake, and a mild but very stubborn acidosis. An attempt to give any considerable quantities of protein and carbohydrate would have resulted in continuous glycosuria. The use of any considerable quantities of fat would have increased or prolonged the acidosis. Accordingly the only escape lay in undernutrition until this dilemma could be broken. The undernutrition was therefore pushed to the necessary point without hesitation because of any clinical appearances. The result was successful as stated, and it is believed that a successful result could not have been attained on any program overtaxing the patient's tolerance

on the side of either carbohydrate or fat. The ultimate outcome has been good from both the clinical and the laboratory standpoints. The persistent hyperglycemia is the one unfavorable feature. Unless it diminishes in the natural course of improvement under present treatment, a reduction of body weight will have to be ordered; otherwise there may be downward progress and somebody may call it spontaneous. With simple precautions now, the situation promises a favorable outcome of an unexpectedly difficult case.

CASE NO. 24.

Male, married, age 44 yrs. American; manufacturer. Admitted Nov. 28, 1914.

Family History.—Father and mother still alive. The former has glycosuria, discovered 4 years ago, but no other symptoms.³ A paternal aunt died of cancer. A brother and a sister of the patient are well. Patient has been married 30 years. Wife had two miscarriages, then one child, who is alive, aged 19.

Past History.—Healthy life, spent in small town in Indiana. Measles and mumps in childhood. Neisser infection at 19. Syphilis denied. Rheumatism 10 years ago; joints involved successively and very painful; night sweats; illness lasted about 6 weeks but was not severe enough to confine to bed. Occasional sore throats before and since this time. 8 years ago patient had indigestion, with pain after eating, pale feces, and yellowness of skin. This continued about a year and he lost 25 pounds weight, but finally recovered under forced feeding. No fever or sharp pain at any time. There is a discharge from the left ear dating from boyhood. Hearing is much impaired in this ear. No excesses in alcohol or food. For many years he smoked 6 to 10 cigars daily. Last Mar. he diminished his smoking to a minimum; has noticed no benefit. Normal weight is 165 pounds.

Present Illness.—7 years ago, on account of loss of weight, extra food was taken and considerable candy eaten. There was no special appetite, and no thirst or other symptoms, and the food and candy were taken merely with the idea of putting on weight. His eyesight then began to fail, and he consulted an oculist who examined the urine and diagnosed diabetes. A diet was later prescribed, and on this he regained some weight. Within a year, however, there was further loss of weight, and polyphagia, polydipsia, and polyuria were present. He then spent 10 days in a diabetic sanitarium, and became sugar-free for the first time in 10 months on carbohydrate-free diet with whisky and sodium bicarbonate. For the past 5 years he has made annual trips to this sanitarium, remaining for 10 days to 10 weeks at a time. During the past 3 or 4 years he has not become sugar-free on these trips. During the past year he was worn out by nerve strain attendant upon a defalcation and a lawsuit. On the last day of the trial he had to be carried to court on a cot to testify, and has been bed-fast

³The father refused all dietary restrictions, and died of diabetes in Jan., 1919.

for the 2 months since that time. He was brought to this Institute from Indiana with his physician in attendance, and had to be wheeled or carried.

Physical Examination.—Height 173 cm. A well developed, extremely emaciated man, showing evidence of profound weakness but no acute distress. Teeth in good condition. Throat congested. Slight enlargement of lymph nodes in left axilla and groins. Knee jerks sluggish. Routine examination otherwise negative. The most striking feature aside from the emaciation is a lemon yellow color of the skin, most pronounced on the face, but noticeable also over most of the body; the conjunctivæ are bluish white and not jaundiced, and the urine is free from bile. The color suggests pernicious anemia. Blood examination showed hemoglobin 80 per cent, red cells 4,000,000, leucocytes 6,000, with normal differential count. Lipemia of heaviest degree present; plasma like cream. Wassermann negative. Urine free from albumin and casts. Blood pressure only 70 systolic, diastolic doubtful at about 55.

Treatment.—Because of the extreme weakness and the absence of threatening acidosis, the patient was given for 2 days a diet like that to which he had been accustomed; *i.e.*, on Nov. 28 and 29 about 100 gm. protein, 20 to 30 gm. carbohydrate, and 2000 to 2100 calories. On Nov. 29 he excreted 45 gm. sugar and 2.5 gm. ammonia nitrogen; on Nov. 30 (the first fast-day), 20.5 gm. sugar and 2.78 gm. ammonia nitrogen. Fasting was begun on Nov. 30, with some misgivings on account of weakness. Because of tendency to nausea only 30 gm. alcohol were given the first day, increased to 70 gm. by Dec. 5. Glycosuria was absent by Dec. 5, and the ammonia nitrogen had diminished to 0.88 gm. (total N output 3.83 gm.). The ferric chloride reaction was much diminished but still well marked, and the blood plasma was still intensely lipemic. The patient's strength showed no decline whatever on account of the fasting, and possibly a slight improvement. He was able to sit up in bed to read, and could walk to the bathroom with assistance. The fasting was therefore prolonged through Dec. 6, making 6 days. On Dec. 7, one egg, 10 gm. butter, and 500 gm. thrice cooked vegetables were added to the whisky. This was increased daily, so that on Dec. 10 the intake was 52 gm. protein and 1450 calories. On this diet a glycosuria of 9.9 gm. appeared. A fast-day with 100 cc. whisky on Dec. 12 failed to clear up the glycosuria. Only one egg and 20 gm. butter were added to the whisky on Dec. 13, yet glycosuria persisted. On Dec. 14, another fast-day with 140 cc. whisky cleared up the sugar and the ferric chloride reactions. On Dec. 15, a diet of only 17 gm. protein and 600 calories (450 of which were alcohol) caused glycosuria of 2.61 gm., this sugar being doubtless partly attributable to the 1000 gm. thrice cooked vegetables allowed for the sake of bulk. This glycosuria persisted under similar conditions on Dec. 16, so that a fast-day with 140 cc. whisky became necessary on Dec. 17. Beginning Dec. 18, all vegetables were omitted in the attempt to build up strength. A diet was given on Dec. 18 and 19 of 52 gm. protein in the form of eggs, 420 calories of alcohol, and olive oil to bring the total calories up to 2600. The ammonia excretion rose, and persistent traces of glycosuria appeared. The diet was sharply reduced, so that on Dec. 21 it con-

sisted of only two eggs and 130 cc. whisky. The eggs were increased until on Dec. 26 seven were given. Though such diets were frequently below 1000 calories and composed largely of alcohol, traces of glycosuria remained persistent. It became established during this time that the patient could not tolerate even the carbohydrate of 200 gm. thrice boiled vegetables such as celery or Brussels sprouts, and the protein of six or seven eggs also sufficed to cause glycosuria. Under such circumstances the prospects for nourishing a patient already seriously weak seemed hopeless. But the notable feature was that the patient's strength and spirits continually improved during the time when he should theoretically have been starving. He became able to sit up in a chair, but was confined to bed almost continuously under orders.

On Jan. 5, 50 cc. whisky, 200 gm. thrice boiled celery, and 100 gm. thrice boiled asparagus were taken without glycosuria. On Jan. 6, meat and bacon were added, and the diet was 20 gm. protein, 600 gm. thrice boiled vegetables, and 480 calories. This was tolerated, but on the next day (Jan. 7) 36 gm. protein and 900 calories with only 400 gm. thrice boiled vegetables (celery, spinach, and Brussels sprouts) caused glycosuria. Diets of this sort or lower were continued, with almost continuous slight glycosuria. The carbohydrate intake shown by the graphic chart Jan. 21 to 28 was in the form of caramel, which was tolerated in quantities of 15 to 30 gm. daily without glycosuria. Under these low diets the body weight gradually fell, while the strength slightly increased and the ferric chloride reactions became pale or negative. With the progressive improvement it became possible early in Feb. to raise the diet to approximately 68 gm. protein and 1400 calories, 250 of these being alcohol calories. In the latter part of Feb. the intake could be markedly increased, and in Mar. and Apr. the diet ran as high as 80 to 90 gm. protein and 2500 calories (of which 250 were alcohol) and 200 to 300 gm. thrice cooked vegetables. With this there was a fast-day weekly. During Feb. the patient was allowed out of bed, and in Mar. he was encouraged to make trips from the hospital for exercise. On Mar. 12, he was able for the first time to walk a mile. Thereafter he took steadily increasing exercise, and high diets were allowed not only to build up strength but also to support muscular activity. Glycosuria was limited to bare traces demonstrable only in certain fractional specimens of certain days and not in the mixed 24 hour urine. But at the beginning of Apr. a more definite glycosuria appeared, also the blood sugar on Apr. 3 was 0.27 per cent. Accordingly food was stopped, making the diet on this day less than 900 calories. On Apr. 4 only 130 cc. whisky were given, and on the following days only whisky and soup. After these 3 days of practical fasting, the blood sugar was down to 0.1 per cent.

Then on Apr. 7, 5 gm. carbohydrate were given in the form of green vegetables, and these without other food were increased on the following days, until 50 gm. carbohydrate were taken without glycosuria (Apr. 10). On Apr. 12, the high protein-fat diets with weekly fast-days were resumed, with resultant hyperglycemia, so that on Apr. 28 the blood sugar was 0.31 per cent. Accordingly 4

days of absolute fasting were imposed, followed by a carbohydrate tolerance test in regular form. The tolerance was found to be almost 100 gm. carbohydrate. Up to May 20 diets were given below 1500 calories, containing 10 to 15 gm. carbohydrate. Then, because of glycosuria and hyperglycemia, carbohydrate was omitted, but resumed again in June. By this time the patient could tolerate a daily ration up to 80 gm. protein, 20 gm. carbohydrate, and 2000 calories, with an absolute fast-day each Sunday. He was dismissed on such a diet, with the carbohydrate diminished to 15 gm. The urine was normal, and the clinical condition, aside from the emaciation, was good.

Acidosis.—The excretion of as much as 2.75 gm. ammonia nitrogen at first indicated a rather marked acidosis, but dangerous symptoms were never present. An intense ferric chloride reaction was present, and there was the usual odor of the breath, but no dyspnea. As shown in the graphic chart, the ammonia rapidly fell during the initial fast. On Dec. 8 the ammonia nitrogen was 0.74 gm. and the ferric chloride reaction was negative. Protein-fat diet, together with the use of whisky, sent the ammonia nitrogen up to 1.68 gm. on Dec. 11. It then fell promptly when the diet was reduced, and beginning Dec. 18 rose still higher as the diet was made higher than before, reaching the summit on Dec. 21. It again fell with reduction of diet, and even on the large carbohydrate-free diets of Mar. and Apr. never returned to the former height. The ferric chloride reaction became consistently negative in the period Jan. 15 to 28. Many of the traces indicated elsewhere were only tinges of color in individual fractions of the 24 hour specimens. For the sake of improvement in strength, the above mentioned high diets of Mar. and Apr. were continued in spite of the well marked ferric chloride reactions which they produced, with the idea that as long as the tolerance was rising and the urine kept sugar-free, the mild acidosis could be left for disposal in the future. The curve of the blood bicarbonate, beginning Jan. 24, also reveals the slight chronic acidosis. Alkali was seldom used. 15 gm. sodium bicarbonate were given on the day of admission; also, toward the close of the initial fast, 15 gm. on Dec. 2 and 3, and 5 gm. on Dec. 4, all as precautionary measures. On Feb. 19, 10 gm. bicarbonate left the urine slightly acid. On Feb. 20, 20 gm. turned the urine alkaline. Likewise the carbon dioxide capacity of the plasma rose within the lower normal limit on Feb. 20 for the first time. It was still approximately at this level on Feb. 22, following the fast-day of Feb. 21. But then, because of the high fat diet or merely loss of the administered alkali, it fell steeply to the lowest value yet observed; namely, 40 per cent on Feb. 24. It promptly rose again on Feb. 25 without the use of alkali, and the tendency now to remain closer to the normal level may be interpreted as one indication of the general improvement. The fasting and minimal diets Apr. 3 to 11 brought another sharp fall, but thereafter on Apr. 15 it rose still higher than before. Again the fasting of Apr. 29 to May 2 brought another sharp drop below normal, followed by a rising tendency; so that on a moderate total diet containing a small quantity of carbohydrate the blood alkalinity at the last determination on June

24 was fully normal and higher than at any point in the entire previous record. Correspondingly the ammonia output was within normal limits, and the ferric chloride reaction in the urine had become consistently negative.

Alcohol.—Whisky was given in moderate quantities for the sake of keeping up strength. It seemed clearly beneficial for this purpose. The patient felt less well with larger doses, and it was never pushed to any high quantity. There is no evidence of any effect in clearing up acidosis. After Apr. 7 alcohol was (as in all cases when possible) discontinued altogether. The clearing up of the acidosis progressed uninterruptedly, so that the impression is created that the alcohol was without influence in this regard.

Blood Sugar.—A solitary determination on Jan. 25 showed a strictly normal value of 0.1 per cent. No further analyses were made until Apr. 1, when the level was 0.145 per cent. The diets had been high, and at this time were raised to the maximum; namely, almost 3000 calories on Apr. 2. The result was glycosuria, with hyperglycemia of 0.27 per cent on Apr. 3. The subsequent 3 days of fasting and alcohol brought the blood sugar down to 0.1 per cent on Apr. 6. On Apr. 8, with carbohydrate feeding, it rose promptly to 0.182 per cent without glycosuria. On the ensuing carbohydrate-free diet of 2200 to 2500 calories it rose steadily higher, up to 0.312 per cent on Apr. 28. 4 days of fasting restored a normal value of 0.118 per cent in the plasma on May 3. It will be noticed that in these periods of feeding and fasting the rise and fall of the blood sugar and body weight were parallel. A small amount of carbohydrate in the diet from May 11 onward was in excess of the true tolerance, as indicated by the rising blood sugar, which reached 0.20 per cent on May 18; and though it still rose to 0.232 per cent on May 22, the omission of carbohydrate and a fast-day on May 23 brought a fall to 0.138 per cent on May 24. With restoration of carbohydrate in the diet the blood sugar again rose, reaching 0.2 per cent on June 15. In general, it is seen that the hyperglycemia is a more delicate index of the tolerance than the glycosuria. On the other hand, it is by no means a sole criterion of the condition or progress. The normal blood sugar of Jan. 25 was the result of 2 months of semistarvation. At later periods the blood sugar was higher, though the patient's diabetes was definitely improved, in the sense that he could tolerate more of all classes of food and more easily remain free from both glycosuria and ketonuria. In other words, an identical diet would doubtless have caused greater hyperglycemia in Jan. than in June. The hyperglycemia at the time of discharge was the one noticeably abnormal feature in the condition, but, as the subsequent experience showed, it could be borne by such a patient without preventing the general tendency to improvement under treatment.

Body Weight.—The patient, whose normal weight was 75 kg., entered weighing 44.2 kg., *i.e.*, 59 per cent of his normal weight, or a loss of 30.4 kg. During fasting his weight rose by water retention, the sodium bicarbonate of Dec. 2 and 3 probably being responsible for the summit of the weight curve on Dec. 3. The rise of weight was accompanied by well marked edema of the ankles. The patient

stated it had been present at former times to a still greater extent. With the continuous undernutrition there was a slight progressive fall in weight, the lowest point being 39.8 kg. on Feb. 5. Thereafter with the increased diets the weight steadily rose, so that the patient was discharged on June 28 at precisely his entrance weight of 44.2 kg.

Nutrition.—The salient feature is the degree of undernutrition imposed upon a patient already extremely emaciated and weak. The patient himself had not expected to live. Notwithstanding this state of weakness, he not only withstood a 6 day fast successfully, but also bore 2 months of radical undernutrition thereafter.

From Nov. 30 to Feb. 2 the following calculation can be made.

	65 days.	Per day (average).	Per day per kg.*
Protein in diet.....	1655.8 gm.	25.40 gm.	5.80 gm.
Total nitrogen in diet.....	264.9 "	4.07 "	0.09 "
Alcohol calories.....	23362	359.4	8.00
Food ".....	28249	434.6	10.00
Total ".....	51611	794.0	18.00

* On 44 kg. weight.

The case at first seemed hopeless, with the combination of emaciation and weakness on the one hand and inability to tolerate a living diet on the other. The extreme restrictions necessary for controlling the diabetes were rigidly carried out, and the unmistakable gain in strength along with loss of weight under these conditions was the most surprising feature. At dismissal, with the identical body weight as at entrance, the physical condition was transformed. The man had come as a helpless bedridden invalid supposedly at the point of death. At discharge he was still very thin, and strangers regarded him as having tuberculosis or cancer, but he was able to make the trip to his home unattended and carry his two heavy suitcases without assistance.

Subsequent History.—The patient resumed his business duties and also took considerable daily exercise as instructed, chiefly in the form of walking. He remained free from glycosuria and other symptoms, with continuous improvement in strength and health, until he committed a few minor indiscretions in diet, consisting only in the addition of a few eggs and vegetables beyond the prescribed quantity. Persistent glycosuria resulted, which did not stop on omitting all carbohydrate or on the routine fast-days. He reported his condition promptly and was advised to return to the hospital.

Second Admission.—The patient returned Oct. 17, 1915, weighing 45.2 kg.; *i.e.*, a gain of 1 kg. The glycosuria and ketonuria on his regular diet were both rather heavy. The ammonia nitrogen was up to 1.54 gm. The carbon dioxide capacity of the plasma was as low as 46 per cent, and the plasma sugar was 0.35 per cent. But the physical strength was still as good as at discharge, and the

task of treatment was far easier than before. Blood pressure 102 systolic, 82 diastolic.

After 1 week of observation on the diet which had been tolerated at the former discharge, fasting was imposed Oct. 24 to 31. The urine was sugar-free on Oct. 30. On Nov. 1, 10 gm. carbohydrate were given in the form of green vegetables, followed by the usual increase of 10 gm. daily, and definite glycosuria appeared with 40 gm. carbohydrate. This may be compared with the 100 gm. tolerance in the previous May and with the zero tolerance at the outset of treatment.

Beginning Nov. 8, a diet of 75 gm. protein, 5 gm. carbohydrate, and 1800 calories caused glycosuria. Therefore carbohydrate was omitted, and the protein diminished to 50 gm., and total calories to 1300. This diet represented approximately 1.1 gm. protein and 30 calories per kg., but the weekly fast-days brought the average down to approximately 0.9 gm. protein and 26 calories per kg.—a low diet especially in view of the rather vigorous exercise which the patient was encouraged to take. Nevertheless, the blood sugar remained unduly high and traces of glycosuria were frequent.

Beginning Nov. 25, an attempt was made to increase protein while keeping the total calories the same by subtracting an equivalent of fat. The protein was thus gradually raised to 110 gm. on Nov. 30, the calories remaining 1300. The blood sugar rose markedly, and glycosuria appeared with 100 gm. protein on Nov. 29.

Beginning Dec. 12, radical undernutrition was maintained until Jan. 7 in the most favorable manner possible, namely by restriction or almost complete exclusion of fat. The protein was at first kept unchanged at 50 gm. On Christmas day as a special indulgence, 85 gm. protein were granted to allow the patient to enjoy turkey. After Jan. 28 the regular protein allowance was 60 gm. Owing to exclusion of fat, the total calories were only 300 daily up to Dec. 17. For the week of Dec. 20 they were increased to 600 by addition of alcohol. By increase of protein and fat they were brought up to 1000 on Jan. 3 to 6. The most striking effect of the exclusion of fat was not upon the ammonia but upon the blood sugar, which was brought well within the normal limits. Also the tolerance was improved, so that beginning Jan. 8 the patient was able to tolerate a diet of 70 gm. protein, 15 gm. carbohydrate, and 1900 calories. The body weight was down to 43.2 kg., or 1 kg. less than at the former discharge, but the strength and general condition were better than at any former time. The patient was discharged on Jan. 18 to resume his business in his home town.

Acidosis.—As mentioned, the ammonia output and carbon dioxide capacity of the plasma indicated a slight acidosis on admission. The high point of the ammonia nitrogen at 2.5 gm. on Oct. 26 does not necessarily mean that the ammonia rose on fasting. The only previous determinations had been on Oct. 17 to 18, and it is possible that toward the close of the week of feeding the ammonia was higher than on Oct. 26. After this date the ammonia fell sharply, and reached a still lower point with the carbohydrate tolerance test on Nov. 3. With protein-

fat diet it again shot up to 2.5 gm. N on Nov. 11. On Nov. 15, following a fast-day, it was again found at the lower level of 0.7 gm., rising again with protein-fat diet. But as this diet was only 1300 calories, the ammonia remained decidedly lower than it had been with 1800 calories. Thereafter the curve slopes gradually down to the normal output of 0.35 gm. at discharge. The ferric chloride reactions were easily cleared up and remained negative. The carbon dioxide capacity rose with fasting to the lower normal limit on Oct. 30. With a slight fluctuation it came safely up within normal values with the carbohydrate tolerance test on Nov. 5. With the 1800 calory diet composed chiefly of fat, it fell steeply below the lower normal level on Nov. 10. Thereafter it fluctuated above and below the lower normal limit. The highest value, namely 71.6 per cent, was shown on the fast-day of Dec. 12. At discharge it was exactly at the lower normal limit of 55 per cent.

Blood Sugar.—At admission the plasma sugar was 0.35 per cent, and with continuance of observation diet reached 0.43 per cent on Oct. 21, and 0.44 per cent on Oct. 22. It fell sharply on fasting, so that on the second fast-day (Oct. 25) it was down to 0.17 per cent. The succeeding fluctuations are not explained. The behavior for several days is so bizarre that the accuracy of some analyses is called into question. But on Oct. 29, the day when glycosuria ceased, the plasma sugar had fallen to 0.23 per cent. With the carbohydrate tolerance test it rose to 0.325 per cent on Nov. 4. On Nov. 8, following the fast-day of Nov. 7, it was down to 0.2 per cent. The diet of 1800 calories caused a rise to 0.44 per cent on Nov. 11. Thereafter, with the diet of 1300 calories, it will be seen that the sugar tended to be up during the week and down on the morning after the weekly fast-day, but hyperglycemia was continuous. The rigorous undernutrition beginning Dec. 12 was what definitely brought the blood sugar down within normal limits. On the liberal diet with 15 gm. carbohydrate at discharge, hyperglycemia again resulted to the extent of 0.16 per cent plasma sugar. This was the one unfavorable feature at discharge.

Exercise.—Beginning Nov. 11, the patient was exercised daily to the point of exhaustion, being required to walk up and down 8 flights of stairs 6 times daily, walk 3 or 4 miles, and toss a 6 pound medicine ball for half an hour daily. With this amount of labor the diet of 1300 calories was definite undernutrition, yet neither the body weight nor the blood sugar diminished very perceptibly. The clinical condition was rather unfavorably affected, however, and the patient was tired and exhausted from the prolonged exertions. Therefore, beginning Dec. 12, he was kept in bed during the period of marked undernutrition, and gained in well-being by reason of the rest. With the higher diets which began in Jan. he was allowed to take moderate exercise, and was advised to continue this at home.

Subsequent History.—The patient remained at home from Jan. 18, 1916, to June 25, 1917, and during this time missed only 6 days from his regular business, in consequence of slight additions to the diet, or on two occasions because

of colds. The weight was up to 48.1 kg. One of the colds mentioned then caused a setback requiring slight reduction of diet, so that during the summer the weight was approximately 46 kg. On Jan. 13, 1917, at the patient's request, he was allowed to diminish his diet from 1900 to 1500 calories, which he said satisfied him, and on this basis he omitted the weekly fast-days. On May 31, 1917, a telegram was received from the patient stating that he had yielded to a holiday temptation to eat strawberry shortcake and pie, and was showing heavy glycosuria in consequence. He was instructed to fast himself sugar-free, and did so successfully. On June 13, he accidentally increased his diet by 300 calories, and showed a trace of sugar in consequence.

Third Admission.—On June 25, he appeared unexpectedly at the hospital, stating that he had decided to travel for a change, and had dropped in to report, and to stay for examination if desired, especially as he was now finding trouble in remaining sugar-free after his recent indiscretions. The weight was 45.5 kg. Although slight glycosuria and ketonuria were found present, the condition was now very simple from the therapeutic standpoint, and the opportunity was employed to carry out a test of the effect of fat feeding, as described in Chapter VI.

Remarks.—The heavy lipemia which was such a striking feature of this case at the outset would have been an interesting feature to study chemically if circumstances had permitted. Presumably it was responsible for the remarkable yellow color of the patient, but this color persisted with little diminution long after the blood plasma had become entirely clear. This color of the skin was very well marked at the second admission. By the third admission it had almost entirely disappeared and the complexion had begun to look normal.

Also, though the weight was only 1.3 kg. more than at the original admission, the face and bearing were different. The patient was still excessively thin, but with the change in facial expression, complexion, and energy of movement, strangers no longer looked upon him as a sick man, and he behaved in all respects like a normal person. The outcome is therefore a satisfactory one under the circumstances. The diabetes seems to be under control, and any manifestations appearing can in each instance be cleared up more easily and quickly than on former occasions—one indication of favorable progress. The diabetes was genuinely severe, as demonstrated by the prolonged intolerance of food and by the entire history. The heavy lipemia may probably be included among the symptoms of severity. Death must have resulted within a brief period in the absence of radical treatment. The ultimate prognosis in a case at this age is generally better than in younger persons, and the tendency to improvement seems more permanent and genuine.

This patient furnishes another example of the absence of any perceptible spontaneous aggravation in a very severe case of diabetes under observation for 2½ years; but the possibility of downward progress due to chronic pancreatitis may yet have to be considered. The patient describes himself as feeling better than for many years past. He carries on his work successfully and enjoys life. Fur-

thermore, he has had no more attacks of cold and grippe than at periods before his diabetes, and no greater difficulty in recovering from them. Notwithstanding the still low tolerance, the outlook at the present time appears favorable for some time to come.

CASE NO. 25.

Female, married, age 50 yrs. Austrian Jew; housewife. Admitted Nov. 28, 1914.

Family History.—Parents lived to old age. Four brothers and two sisters are well. No heritable disease in family. Patient has been married 28 years. Had six children and later three miscarriages. One child died of diphtheria, another in an accident; the other four are well, aged 13 to 26 years.

Past History.—Healthy life. Patient came to United States from Austria at age of 28 and has lived in fairly hygienic surroundings. Erysipelas, in 1912 and again in Jan., 1914, was practically the only infection. Venereal disease denied, although 3 years ago a general eruption is said to have appeared over the whole body and disappeared after a few days. 8 or 9 years ago, left-sided hemiplegia occurred suddenly and improved gradually within 6 months. A second stroke occurred in Jan., 1914. Edema of ankles has been noticed during past 2 years. Habits have been regular. No alcohol or other special indulgence.

Present Illness.—3 years ago a routine urine examination revealed sugar. Since then one test every month has always shown sugar but never acetone. For 2 years past there has been dyspnea and palpitation on slight exertion, so that she has been practically confined to her house. Dyspnea also has frequently made her unable to sleep lying down at night, so that she has had to stay in a chair. No polyphagia, polydipsia, or polyuria. She has been on a lax anti-diabetic diet of protein, fat, and green vegetables unrestricted in quantity, and two rolls and a slice of bread daily. Weight 3 years ago 211 pounds, now 186 pounds. 1 week ago the patient went to a hospital clinic, and was ordered to stop carbohydrate. Thereafter she began steadily to feel worse and has shown a progressively increasing stupor during the past few days, with nausea which has led to vomiting during the past 2 days.

Physical Examination.—A large framed, obese woman lying in bed in a stuporous condition and irrational when roused. The odor of the breath is partly sweetish, partly foul. Some dyspnea is present, but seems of a panting and nervous type rather than Kussmaul air-hunger. The face is slightly edematous and pits on pressure. Exophthalmos and apparent photophobia. Pupils react to light and accommodation. No jaundice. Pyorrhea and receding gums. Tonsils slightly enlarged. Signs of slight left-sided paresis. Thyroid lobes hard and definitely palpable; isthmus not felt. Lymph nodes not enlarged. Some bronchitis and emphysema. Cardiac dulness extends 4 cm. to right of midsternal line and 13 cm. to left in fifth interspace. Soft systolic blowing murmur at apex. Aortic second sound markedly accentuated. Walls of radial arteries not palpable. Abdomen obese and flaccid, negative to examination. Knee and Achilles

On Dec. 9, this was increased to two eggs and 20 gm. butter; and though no vegetables or other sources of carbohydrate were given, a trace of glycosuria appeared, and continued when one egg was given on Dec. 10 and two eggs on the subsequent days. The protein intake ranged from 15 to 46 gm. and the total calories averaged well below 1000, even including alcohol, until on Dec. 17 and 18 a diet of eggs and olive oil was given, without vegetables or whisky, representing 44 to 50 gm. protein and 1900 to 2000 calories. Such diets sufficed to maintain a continuous glycosuria. This cleared up when nothing but two eggs was given on Dec. 20. But on Dec. 21, the feeding of only 80 gm. asparagus, containing 2.2 gm. carbohydrate, caused a trace of glycosuria. To clear this up 3 fast-days with whisky were necessary, on Dec. 24 to 26. Then, on Dec. 27, the feeding of two eggs and 500 gm. thrice boiled vegetables brought back a decided trace of glycosuria. After omission of all vegetables, the frequent traces of glycosuria still continued on low diets limited to eggs, olive oil, soup, and coffee, none of these diets containing more than 52 gm. protein and 1300 to 1950 calories. The subsequent treatment represented a continuance of such undernutrition. The principle was adopted of giving protein to conserve body nitrogen and alcohol to assist weakness, while keeping fat and calories at a very low figure and compelling the patient to burn off her body fat.

She remained almost without appetite, and on Feb. 4 mentioned being hungry for the first time. The ferric chloride reaction was much diminished and the occasional traces of sugar were only very faint reactions in fractional specimens on certain days. The patient was desirous of continuing treatment at home, and as all immediate danger was over and the one necessity was merely a continuance of undernutrition, she was allowed to go out on a diet of 1250 calories, 350 of which were alcohol. She was instructed to take a fast-day whenever sugar appeared and once every 2 weeks if it did not appear. She was also warned against constipation and was encouraged to take exercise. At the time of discharge she was beginning to take short walks, which tired her considerably. Aside from the weakness, symptoms were absent and she felt well.

Second Admission.—Feb. 11, 1915. The patient was readmitted 5 days after discharge. She had followed her diet but had had no bowel movement during this time. The former symptoms recurred in milder form, and she was drowsy and vomiting occasionally when received. The glycosuria was 0.6 per cent, and the ferric chloride reaction was heavier than at discharge. A low ammonia value was found on Feb. 13 after 3 days of fasting. There was no albuminuria, but the face and ankles were again puffy and pitted on pressure. Blood pressure 170 systolic, 110 diastolic. 30 gm. sodium bicarbonate may have played a part in the edema. The treatment was carried out on the same lines as before, the most important feature being the purgation with 2 gm. compound jalap powder daily, which yielded the same enormous stools as before. The first 12 days in hospital, up to Feb. 23, represented almost continuous fasting. 200 calories of alcohol were given almost daily during this entire period in hospital. The acute

symptoms passed off easily. The food tolerance was obviously higher than before, and a more liberal diet was gradually built up, finally reaching 83 gm. protein and 2000 calories at the time of discharge on Mar. 25. Traces of glycosuria were frequent but easily controlled. Albuminuria was constantly present after the initial days. The blood pressure on Feb. 16 was 205 systolic, 130 diastolic; on Feb. 20, 185 systolic, 140 diastolic. The patient was feeling stronger and in better condition in all respects than at the former discharge. The diet prescribed to be followed at home was carbohydrate-free, containing 100 gm. protein (1.5 gm. per kg.) and 1500 to 1750 calories (23 to 26 calories per kg.). It was considered probable that she could remain free from glycosuria on this diet, and if so the slight persisting ketonuria would gradually take care of itself.

Subsequent History.—Reports showed that the patient remained sugar-free and continued to gain in strength and well-being at home. On May 21, her son telephoned that she had had some sort of stroke during the night and an ambulance surgeon had diagnosed pulmonary edema. Her death occurred the same day, and the certificate of the coroner's physician assigned chronic nephritis as the cause. There was no sugar in the urine at any time.

Acidosis.—The acidosis was never quantitatively high, and the coma was atypical in character. There was the familiar history of onset shortly after exclusion of carbohydrate from the diet, but constipation seemed to be a more important factor. More complete analyses of blood and urine would have been valuable had they been possible at this time. Along with the general food intolerance, the ammonia nitrogen was slow in reaching normal limits, but at the first discharge was down to about 0.56 gm. At the second admission the figure 0.28 gm. ammonia nitrogen was obtained after 3 days of fasting; there might well have been a much higher ammonia earlier in the attack. Such a possibility is strengthened by the rise to almost 2 gm. ammonia nitrogen with the diet of only 1100 calories on Feb. 26. The ferric chloride reaction became pale toward the close of each stay in hospital, and accordingly no further attention was paid to it, since with continuance of undernutrition and freedom from glycosuria it was certain to become negative.

Estimations of the carbon dioxide capacity of the plasma were made beginning Feb. 23, and confirmed the tendency to chronic acidosis. Inasmuch as sodium bicarbonate had been used rather liberally in the opening days of each hospital period and had presumably raised the blood alkalinity, there is some ground for supposing that such analyses if made during the stuporous attacks would have indicated a true acidosis coma. Subsequently, in the absence of bicarbonate, the carbon dioxide capacity of the plasma in Feb. and Mar. ranged between 45 and 53 per cent. There is no evidence that alkali dosage would have altered the subjective condition, which was good; and the fundamental acidosis process could be influenced only by continuance of the undernutrition program as adopted, whereas the giving of alkali would only have masked the laboratory indications.

Blood Sugar.—Only one determination was made. This was 0.118 per cent before breakfast on Mar. 22. There is no evidence of a renal glycosuria, but on the other hand a continuous hyperglycemia seems excluded, notwithstanding both diabetes and nephritis.

Undernutrition.—During the initial fast, Nov. 29 to Dec. 7, inclusive, the patient lost 94.3 gm. nitrogen in the urine. Dec. 8 to 11 the ingestion of 7.5 to 15 gm. protein daily left the nitrogen output at its minimal fasting level of about 8 gm. daily. The degree of undernutrition in the first period in hospital is shown by the following calculations:

	13 days.	Per day (average).
Total nitrogen output.....	127.19 gm.	9.78
Protein intake.....	46.70 "	2.60
Nitrogen " (protein ÷ 6.25).....	10.35 "	0.79
" deficit (output—intake).....	116.84 "	8.99
	70 days.	Per day (average).
Alcohol calories.....	18518	264.5
Food ".....	25701	495.7
Total ".....	54219	760.2

Owing to the clinical condition it was not feasible to weigh the patient until Dec. 6, when the weight was 76 kg. The obesity was diminished as rapidly as feasible by undernutrition, while the body nitrogen was protected as far as possible by allowing protein in quantities just short of producing any considerable glycosuria. Fat was the element which was mainly eliminated from the diet, and general undernutrition and the burning off of body fat was regarded as the most important therapeutic measure. At the first discharge the weight was 68.4 kg., and at the second admission and discharge respectively it was approximately 66 kg.; *i.e.*, 10 kg. below the first weight. Strength, well-being, and food tolerance had risen in proportion to the fall in weight.

Remarks.—The importance of emptying the bowels when there is impending coma, especially in certain cases, has been pointed out by former writers. In this instance it seemed the most important therapeutic measure. Though there were chemical indications of acidosis as above noted, the urine was easily made alkaline and the actual quantity of acid formed was evidently not great. A feature of therapeutic interest is the fact that a very obese patient already suffering from acidosis with nausea and vomiting came through safely with simple fasting. There is no evidence of any specific value of the alcohol used. The danger of increased acidosis from fasting in patients of this type is obviously to be borne in mind; but a coma which comes on with feeding can generally be treated by fasting. The reduction of the excessive body weight was beneficial

from every standpoint. Judging by the threatened coma and subsequent almost complete intolerance of food, the case might be called extremely severe, but with mere continuance of undernutrition sufficient to bring the excessive weight down to normal or slightly below the average normal, the condition would almost certainly have stood revealed in its true light as one of fairly mild diabetes. For this reason, with falling body weight and rising general health, the traces of glycosuria and ketonuria were ignored to an extent never ventured in younger patients. Also this patient's nephritis was far more dangerous to her than her diabetes. The existence of nephritis in no way interfered with the treatment of the diabetes. Though the blood pressure diminished as the ordinary consequence of hospital care, there is no indication that the nephritis was improved by the diabetic treatment. It so happened that death came early from some embolic or other accident, but the case nevertheless illustrates the benefit of proper treatment of diabetes even in the presence of complicating conditions.

CASE NO. 26.

Female, age 14 yrs. American; schoolgirl. Admitted Dec. 7, 1914.

Family History.—No diabetes in family. Mother's mother died of cancer, and mother's grandmother of "dropsy." Several more remote relatives died of tuberculosis. Patient's father is healthy, the mother nervous but fairly strong. There have been no other children and no miscarriages.

Past History.—Girl has been healthy though rather nervous. Measles at 3, chicken-pox at 4, mild whooping-cough at 5. She began school at 6th year, was bright and studious but not overworked. Ate large quantities of candy. Always constipated. Fairly normal menstruation began at 12. For about 2 years before the present illness there was frequent twitching of face, limbs, and trunk during sleep. No such movements when awake.

Present Illness.—In Feb., 1913, the patient had an attack of vomiting after eating heavily, and for a few days was nervous and without appetite. During the following 3 weeks polyphagia, polydipsia, and polyuria were noted, also weariness and sleepiness. Strength then failed progressively until she became too weak to dress herself. A physician consulted in Mar. diagnosed diabetes and prescribed carbohydrate-free diet. On this the patient remained sugar-free until June, but lost weight even though bread and potatoes were gradually added to diet. Glycosuria then reappeared, but remained absent from June to Dec. on carbohydrate-free diet. It then became persistent, and a trip was made to consult a specialist, who placed the patient in a hospital for 2 weeks and allowed only small quantities of carbohydrate-free food. Glycosuria ceased but ketonuria persisted, and all symptoms recurred promptly on returning home. The family physician then allowed an abundance of carbohydrate. The subsequent symptoms have been the usual loss of weight and strength, and falling out of much of the hair. Menstruation ceased with the first period after the onset of diabetes.

Physical Examination.—A tall, emaciated, nervous appearing girl, without acute distress. Teeth in good condition. Tonsils not enlarged. No lymph node enlargements. Skin dry. General physical examination negative. Right knee jerk present, left not obtained. Achilles jerks lively. Blood pressure 105 systolic, 70 diastolic.

Treatment.—The glycosuria for 16 hours following admission was 44.5 gm. On Dec. 8 to 10, under an observation diet of 30 to 65 gm. protein, 3 to 10 gm. carbohydrate, and 900 to 1300 calories, the urine contained 6.8 to 14.3 gm. sugar and showed heavy ferric chloride reactions. Fasting was begun Dec. 11, with 200 calories of alcohol daily. Glycosuria was absent in 24 hours. 140 gm. thrice cooked vegetables were allowed on Dec. 13, 5 gm. carbohydrate in the form of green vegetables on Dec. 14, and 9 gm. carbohydrate on Dec. 15. A trace of glycosuria appeared. Nevertheless the vegetables were increased, up to 44 gm. carbohydrate on Dec. 17, then diminished while two or three eggs were added. With this continuance of undernutrition the trace of sugar cleared up. On Dec. 26 a diet of 51 gm. protein, 9 gm. fat, and 1200 calories caused another trace of glycosuria, which cleared up with the fast-day of Dec. 27. Alcohol was discontinued on Jan. 9. It was still given on fast-days to the extent of 200 calories, up to Feb. 21. In early Jan., diets of approximately 40 gm. protein, 6 gm. carbohydrate, and 1000 calories twice caused slight glycosuria, which later cleared up, and at the end of the month a diet as high as 80 gm. protein, 16 gm. carbohydrate, and 1700 calories was borne without glycosuria. An attempt on Jan. 30 and 31 to raise the carbohydrate to 25 gm. resulted in glycosuria, checked by the routine fast-day of Feb. 1. In the succeeding week the diet was further increased until on Feb. 5 to 6 glycosuria resulted from 90 gm. protein, 30 to 40 gm. carbohydrate, and 2400 calories. Thereafter still higher diets were tolerated, but on Feb. 27 glycosuria was produced by 84 gm. protein, 50 gm. carbohydrate, and 3000 calories. Not only the laboratory findings but also the weakness and nervousness which were the essential complaints were improved. Also, on admission there had been a marked albuminuria with casts, but albumin gradually diminished to a trace and casts were absent. The patient was discharged on Mar. 6, 1915, on a diet of 25 gm. carbohydrate, 75 to 80 gm. protein (2.5 gm. per kg.), and 2400 calories (almost 80 per kg.). The regular weekly fast-days reduced the average to approximately 64 gm. protein and 2100 calories. The prescribed diet was thus below what she had proved able to tolerate.

Acidosis.—This was at no time threatening. The ferric chloride reaction diminished as usual and became negative with the low diets of mid-January. It will then be noted that increase of the total diet brought back well marked ferric chloride reactions, even though carbohydrate was decidedly increased at the same time.

Body Weight.—This was 31.2 kg. at admission. The undernutrition treatment brought it down to its lowest point of 27.2 kg. on Jan. 26. Thereafter the

higher diets produced a rise in weight, so that at discharge it was 30.7 kg.; *i.e.*, 0.5 kg. less than at admission.

Subsequent History.—The diet was faithfully followed. A few traces of glycosuria required a slight diminution of the carbohydrate allowance. On one occasion a trace of glycosuria followed excitement due to having seen a woman run over by a street car. The physical and psychic conditions remained good and the patient enjoyed life and kept herself interested in various occupations not involving exertion. Nevertheless, she tended to lose slightly in weight instead of gaining. Menstruation did not return, but none of the former symptoms of diabetes was present.

Second Admission.—Oct. 4, 1915, the patient returned to the hospital by arrangement, for purposes of observation and for testing the effect of exercise. Height 156.2 cm. Weight 28.8 kg.

The urine was still sugar-free, but showed a trace of ferric chloride which disappeared with a single fast-day on Oct. 5. A tolerance test was then begun in routine manner with 10 gm. carbohydrate in the form of green vegetables on Oct. 6. A trace of glycosuria appeared with 130 gm. carbohydrate on Oct. 19, and persisted with the same intake the next day and with increased intake on the following days, notwithstanding the introduction of exercise at this point in the attempt to raise tolerance. After the clearing up of glycosuria by a sharp reduction of food on Oct. 24 to 25, a diet was gradually built up, with the usual weekly fast-days. In the week of Nov. 22, a ration of 55 gm. protein, 15 gm. carbohydrate, and 2200 calories was tolerated without glycosuria, but with ketonuria. With the same protein and carbohydrate, an increase of fat to 2400 calories in the following week brought on well marked continuous glycosuria, and the damage thus done resulted in a continuance of glycosuria and ketonuria, notwithstanding a sharp reduction of diet in the succeeding week (Dec. 6 to 11). Low nutrition beginning Dec. 12 was continued throughout the remainder of the stay in hospital. From Dec. 15 to Jan. 22, the protein was kept at 60 gm. daily. The calories at first were 1200, but beginning Jan. 3 were diminished to 850. Though all carbohydrate was omitted at the same time, this diminution in total calories brought a complete clearing up of the ferric chloride reaction. Beginning Jan. 24 another carbohydrate tolerance test was made. The assimilation was found to be 140 gm., a gain of 20 gm. over the previous test. The patient was discharged Feb. 26 on a diet of 30 gm. carbohydrate, 60 gm. protein (2.26 gm. per kg.), and 1000 calories (nearly 36 calories per kg.). This was reduced one-seventh as usual by the regular fast-days, making the average daily intake approximately 1.9 gm. protein and 33 calories per kg.

Acidosis.—The most striking feature is that well marked ferric chloride reactions were produced by high calory diets in every instance, irrespective of whether these diets contained carbohydrate. On lower diets suited to the patient's actual tolerance there has been no difficulty in keeping this test continuously negative. The ammonia excretion is also kept at a low level. The carbon dioxide capacity

of the plasma tended to remain near or below the lower normal limit, but was within normal limits at the time of discharge.

Blood Sugar.—Though this must have been high with the glycosuria resulting from the carbohydrate test of Oct., yet, as usual when hyperglycemia is produced only by carbohydrate, it fell quickly, for on Oct. 25, after 2 days of low diet, it was down to 0.13 per cent. It promptly rose to 0.26 per cent in the plasma on the next day with continuance of a diet of 1200 calories and 15 gm. carbohydrate. On the morning of Nov. 1, following the fast-day of Oct. 31, it was down to the former approximately normal level. The curve ran similarly through Nov., with hyperglycemia on feeding and lower values following fast-days, but with a general upward tendency. The diet up to 2400 calories, ending Dec. 4, had produced such injury that the reduction to 1500 calories did not prevent the occurrence of the highest blood sugars of the series; *e.g.*, 0.32 on Dec. 9 and 0.29 on Dec. 11, with glycosuria. This was one of the reasons for the ensuing sharp reduction of diet. After 2 days of fasting on Dec. 12 and 13, the sugar in the plasma on the morning of Dec. 14 was down to 0.155 per cent, and in the whole blood down to 0.125 per cent. Thereafter the curve ran nearly within normal limits, except for the sharp terminal rise on Feb. 25 to 0.224 per cent. This occurred on 40 gm. carbohydrate, and the patient was sent home with only 30 gm. carbohydrate in the diet.

Body Weight.—At the second admission this was 2 kg. less than at the previous discharge, and at the second discharge it had been brought down still lower. The net result of treatment from the first admission to the second discharge was a reduction of weight by 4.9 kg. At home the patient's weight has been constantly reported as approximately 60 pounds; *i.e.*, about 27 kg., or 4 kg. less than at her first admission. There has been no appreciable growth in height, but the patient was already almost as tall as her mother. She is noticeably emaciated, but the graphic chart well illustrates that every gain of weight brought on glycosuria and acidosis. In order to live, the patient must keep her weight down. It is not only inadvisable but impossible to force the weight up, for any diet exceeding her tolerance as respects food and weight will quickly bring on active diabetic symptoms, which of themselves would lead to loss of weight.

Exercise.—The second period in hospital was devoted largely to a clinical test of exercise in this patient. During the carbohydrate tolerance test in Oct. she was kept at rest until the first trace of glycosuria appeared. She was then exercised to the limit of her strength, chiefly by climbing stairs and walking, also by roller-skating and tossing the medicine ball. The glycosuria did not cease, and no gain in tolerance could be demonstrated. Subsequently high diets were given, as stated, from the latter part of Oct. to the forepart of Dec.; and the patient, who was moderately strong, was exercised regularly to her utmost capacity in the attempt to burn off the surplus calories. The low plasma bicarbonate during this time is doubtless due in part to exercise. It proved impossible to

prevent hyperglycemia and finally glycosuria by this means, and the ferric chloride reaction became positive when exercise was thus taken to burn up the fat, though on lower fat intake it was negative even without exercise. Accordingly in Dec. the diet was reduced as above mentioned. Exercise was still continued.

From Dec. 12, 1915, to Jan. 23, 1916, three influences were present, namely, carbohydrate abstinence, undernutrition, and hard muscular exercise. Nevertheless, the absence of any noteworthy acidosis is demonstrated by all tests. The rise of 20 gm. in tolerance shown by the carbohydrate test in Feb. is merely what might be expected from the undernutrition treatment, and there is no indication that the 4 months of hard systematic exercise had served specifically to increase tolerance.

Subsequent History.—At the time of discharge the patient was advised to discontinue severe exercise and take only as much as she could enjoy. She has found pleasure in spending much of her time in walking, bicycling, and various forms of active play. What has actually been accomplished by exercise is a decided gain in strength, general health, and happiness. The change, as compared with the first admission when she was kept nearly at rest, is evident at a glance, and friends complimented her on her improved color and appearance. Nervousness and worry are also controlled, and she is enabled to derive some real enjoyment from life.

Glycosuria has remained absent except for rare traces due to unintentional excesses; *e.g.*, traces resulted from the use of cream cheese or sugar cured ham. By June 19 she had lost three quarters of a pound in weight, but this was slightly more than regained by Sept. In the fall she undertook light school work. In Nov. and Dec. she had two colds and showed traces of sugar several times in consequence, so that carbohydrate had to be entirely eliminated from the diet on some occasions. In Apr., 1917, the patient reported having finished the first year of high school and having easily obtained the highest mark in every subject. Her diet has been modified to consist of 40 gm. protein, 10 gm. carbohydrate, and 1000 calories. She keeps herself sugar-free without difficulty and knows how to treat herself if accidental causes bring on traces of glycosuria.

Remarks.—This patient, when received, presented a case of juvenile diabetes of 2 years standing and considerable severity. The subsequent treatment illustrates especially two points. One is the effect of exercise. The case was of such severity that the deficiency of the pancreas could not be balanced to any appreciable extent by improved function and activity of the muscles. Accordingly the carbohydrate tolerance was not perceptibly improved, but the general health was greatly benefited. Second is the question of growth and nutrition. Here the clinical experiment was performed of taking this patient, clearing up her condition radically by undernutrition, so that about the middle of Jan., 1915, she was entirely free from both glycosuria and acidosis, and then making the attempt to have her grow and develop. The diets in the latter half of the first

hospital period were planned to this end. The weight rose, but symptoms simultaneously returned. The diet at this discharge represented approximately 2.25 gm. protein and 80 calories per kg. of body weight. Fasting and modifications of diet required by the occasional traces of glycosuria absolutely prevented gain or growth. It is not known whether a specific diabetic deficiency also may be concerned. The net result of this attempt to put on weight was, as stated, that the patient returned to the hospital 7 months later, weighing 2 kg. less than at discharge.

After the undernutrition represented by the Oct. carbohydrate test, the diet was gradually built up, the weight rose with it, and the maximum of weight and the onset of urinary symptoms coincided (Dec., 1915). Subsequently undernutrition diminished the weight and removed all active symptoms. It is obvious throughout that the total diet was the essential governing factor, and the relative proportions of protein, carbohydrate, and fat were of minor influence. The net result to date is that the patient is alive 3 years from the beginning of this treatment, and 4½ years from the onset of her diabetes. There is no evidence of any spontaneous downward progress; neither has there been any fundamental¹ improvement. The cumulative effect of slight strains and accidents may bring bad results sooner or later. Meantime, the patient is holding her own and is actually deriving enjoyment from life and carrying on limited activities. The one requisite is close control of her diet.⁴

CASE NO. 27.

Male, married, age 42 yrs. American; clerk. Admitted Jan. 15, 1915.

Family History.—One sister died of cardiorenal disease at 23. Family history otherwise negative. Patient has been married 18 years and has one healthy son, aged 15. Wife healthy; one miscarriage about 13 years ago.

Past History.—Healthy life. Good hygienic surroundings. Measles and chicken-pox in childhood; mild diphtheria at 8; mumps at 18, complicated by unilateral orchitis. At about 20 there was an attack of jaundice with clay-colored stools lasting 2 or 3 days. At 26 one attack like acute appendicitis, which passed off under ice applications in a hospital. There have been indefinite minor attacks since. At 27 patient had fever every night for 28 days, with one hard chill at the end; then given medicine by family physician and has had nothing like malaria since. Occasional sore throats; never tonsillitis. Venereal disease or exposure denied. Habits regular; no excesses in alcohol, tobacco, or food.

⁴ Word has been received of the patient's death in Feb., 1918. The child herself was faithful and contented, but the parents concluded to try an independent experiment to "build her up." The child was kept in ignorance of the glycosuria which quickly followed the increased diet, and the fatal outcome was due solely to this folly of the parents.

Present Illness.—8 years ago patient began to feel rather poorly, also had serious trouble with his teeth. Numerous teeth had to be extracted, and he developed an infection of the mandible, some of which sloughed away. His physician diagnosed diabetes. The carbohydrate in his diet was diminished but other foods were not restricted. Since that time he has had occasional attacks of polydipsia, otherwise no diabetic symptoms, except more or less continuous trouble with his teeth. Some recent worries apparently made the condition worse, but he remained in fair health and able to work until Jan. 3, 1915, when his neck began to pain and swell. He was immediately taken in charge by an eminent New York surgeon who had been an old-time friend. The pain required morphine, and the fever and progressive advance of the border of infection were so threatening that the surgeon contemplated complete excision of the infected area and brought the patient to this Institute with the intention of operating the same or the following day.

Physical Examination.—Height 169 cm. Weight 59.6 kg. A well developed, fairly well nourished man, with fever, flushed face, unduly bright eyes, and appearance of prostration. Numerous teeth missing; much caries and pyorrhea. On the left side of the neck behind, there is a very large carbuncle with its apex about midway between the postaural line and the posterior median line, and with marked redness and induration extending past the posterior median line behind and to the internal border of the sternocleidomastoid in front. The whole area is intensely tender and movements of the neck are prevented. Physical examination otherwise negative.

Treatment.—Fever was continuous, but the highest temperature was 102.5°. Morphine was required to control pain, particularly at night. There was a heavy ferric chloride reaction, and the urine on the 1st day contained 36.4 gm. sugar, on the 2nd day 32.4 gm. The diet on this day (Jan. 16) was 87 gm. protein, 11 gm. carbohydrate, and 1400 calories. The general condition was critical, and the surgeon felt impelled to operate by the approach of the infection to the plane of the great vessels of the neck; but in view of the acidosis and negative carbohydrate balance it was advised that operation be postponed for at least a day or two until the influence of fasting could be brought to bear. Accordingly, fasting was begun on Jan. 17, with as much whisky as could be comfortably taken for the sake of keeping up strength. The quantity of alcohol thus taken was from 700 down to 500 calories daily. After 1 day of fasting the glycosuria had fallen to 9.75 gm. and the general condition was at least no worse. The glycosuria continued to diminish on the following days and was absent on the 4th day of fasting. Meanwhile the general condition improved, pain diminished, the apex of the carbuncle began to discharge pus, and the night of Jan. 21 was the first on which morphine was not required. 2 days of complete freedom from glycosuria were allowed to pass before the addition, on Jan. 22, of 9 gm. carbohydrate in the form of tomatoes, celery, and lettuce to the daily allowance of whisky. On Jan. 23 this was raised to approximately 20 gm., and on Jan.

24 to 30 gm. On account of traces of glycosuria it was diminished on the following days to 6 gm., and following that both whisky and carbohydrate were increased, so that from Feb. 7 to 27 the diet was usually just below 40 gm. carbohydrate and 100 gm. alcohol daily. The fever had gradually fallen, but the temperature remained between 99° and 100°F. until Jan. 31, after which it was normal. The core of the carbuncle was extruded on Jan. 30, but full healing of the large local inflammation was not complete until Mar. 1. With continuance of the diet mentioned, the traces of glycosuria became less frequent as the infection cleared up, so that the allowance of 40 gm. carbohydrate and 100 gm. alcohol was fully tolerated.

Beginning Mar. 1 a diet was gradually built up, at first containing only some 20 gm. protein and 500 non-alcohol calories, but rising by Apr. 8 to 115 gm. protein, 40 gm. carbohydrate, and 2650 calories. Whisky was then discontinued and, except for the fast-day of Apr. 11, was not used again even on fast-days. A regular diet was planned consisting of 90 to 100 gm. protein, 25 gm. carbohydrate, and 2000 to 2200 calories; this was in the neighborhood of 2 gm. protein and 40 calories per kg. of body weight, reduced one-seventh by the weekly fast-day, so that the actual average was nearly 1.5 gm. protein and 35 calories per kg.

After the initial critical infection was overcome, the patient had been left weak and debilitated, complaining of pains in the legs and other parts of the body. The blood pressure on Feb. 11 was down to 90 systolic, 70 diastolic. He gained strength while losing weight, and still more as his weight was slightly built up. He was encouraged to begin exercise as soon as strength permitted, and this was increased until at the time of discharge he was taking long walks daily. He had not only regained the condition present before the carbuncle, but had reached a state of health better than at any time during the previous years of diabetes. He was discharged to undertake his regular work.

Acidosis.—This was measured at the outset only by the ammonia excretion, which was modified by alkali dosage. As a measure of precaution against the acidosis to be feared with an infection, sodium bicarbonate was given beginning Jan. 16. On this day the total taken was 15 gm., on the next day 40 gm., and this daily quantity was continued with scarcely any change until Feb. 3, when it was diminished to 10 gm. On Feb. 7 it was increased to 20 gm., on Feb. 10 to 30 gm., and on Feb. 19 to 40 gm. This was continued until Feb. 23, when it was abruptly stopped. On Mar. 3, 10 gm. soda were begun and continued to Mar. 13, after which soda was permanently discontinued.

The chart gives the impression that the patient had been threatened with a serious acidosis. The low ammonia value shown on the day of admission represents only part of a day. The excretion of approximately 1.4 to 1.6 gm. ammonia nitrogen Jan. 17 to 21 occurred in spite of the considerable alkali dosage mentioned. The carbon dioxide capacity of the plasma was kept within normal limits during this alkali treatment, at least after Jan. 29. High normal values were present on Feb. 18 to 22 with 30 to 40 gm. bicarbonate daily, and the am-

monia nitrogen was also down to the low figure of 0.25 to 0.35 gm. Promptly with the omission of soda on Feb. 23 the plasma bicarbonate fell sharply and the ammonia began a corresponding steep rise. On Mar. 2 the CO₂ capacity touched its lowest point of 43.6 vol. per cent, and the ammonia N on the same day had risen to 2.8 gm. The use of 10 gm. sodium bicarbonate daily, beginning Mar. 3, produced a rather prompt rise of the plasma bicarbonate. The ammonia fell only slightly, then rose to an actually higher level on Mar. 8. The increase of protein in the diet was presumably one factor. By Mar. 13, however, the ammonia nitrogen was down to 1.68 gm. By this time the strength of the acidosis seems to have been broken. On Mar. 24, without alkali, the ammonia was slightly lower (1.4 gm. N). The next day it fell sharply to 0.56 gm., and almost simultaneously the ferric chloride reactions became light for the first time. The ammonia was equally low on the fast-day of Apr. 4. With the high diets of Apr. 5, 6, and 7 it was higher, and fell again on the fast-day of Apr. 11. After that it varied between 0.4 and 1.25 gm. N. Likewise, following the discontinuance of alkali on Mar. 13, the plasma CO₂ capacity remained little changed until Mar. 19. The tests on Mar. 24 and 30 showed it falling rapidly, but it stopped at 44.2 per cent, and then rose spontaneously within normal limits without the aid of alkali.

The impression is given that alkali was a useful temporary aid in this case. The milder grades of acidosis may be ignored, and the severer ones also can frequently be treated successfully without alkali, but when there is a tendency to serious acidosis overtaking the defenses of the alkaline reserve of the body, both comfort and safety are apparently served by the use of sufficient quantities of alkali, which are discontinued when proper treatment has overcome the essential condition underlying the acidosis.

The ferric chloride reaction was heavy at admission and became intense following the use of soda. It proved very persistent, in conformity with the other manifestations of the tendency to acidosis. The condition being satisfactory in other respects, this reaction was left to wear itself out with time and improvement of tolerance. As stated, it became negative some months after discharge, and has not reappeared.

Blood Sugar.—Analyses were made during the latter part of the hospital period, and the relatively low values found constituted one feature of the favorable picture.

Weight and Nutrition.—The steep fall in weight, which was intentionally reduced from 59.6 kg. on Jan. 16 to 47 kg. on Mar. 4—a loss of 12.6 kg. in 48 days—is one of the noticeable features of the treatment. It was necessary first to control radically the diabetes which was responsible for the susceptibility to infection. Second, it was necessary to build up tolerance for carbohydrate and other foods, in order to save the patient from the persistent acidosis and weakness. These objects were accomplished by rigorous undernutrition. The patient with acute infection and fever was subjected to 5 days of fasting with alcohol. After that, nothing but a little green vegetables was added up to Mar. 1, the idea being

to continue undernutrition while combating acidosis by the use of carbohydrate to the limit of tolerance under the conditions of highest tolerance; *viz.*, exclusion of other food. Except for these green vegetables, there was complete deprivation of solid food for the 42 days from Jan. 17 to Mar. 1. The fall in weight was therefore to be expected, and from the urea and ammonia curves it is also possible to estimate a considerable loss of body nitrogen. It is to be emphasized that under these conditions the resistance to infection apparently, and the general strength certainly, improved. Weakness and lowered resistance are to be regarded as due more to the specific diabetic disorder than to depletion of food materials, and the policy of trying to strengthen diabetic patients by feeding in excess of the tolerance is an injurious one.

After the crisis was past, the condition gradually began to assume its proper proportions as a comparatively mild case of diabetes. In view of the patient's age and the demonstrated food tolerance, a fairly liberal diet was built up, sufficient for health and efficient work, and a moderate gain of weight was also permitted. At discharge, however, the weight was only 50.4 kg.; *i.e.*, 9.2 kg. below the weight at entrance. The patient has since obeyed the injunction not to put on much flesh, and is now thin, wiry, and strong.

Subsequent History.—The patient adhered to his diet and remained free from glycosuria except for a trace on June 18, after 150 gm. strawberries for breakfast. A moderate ferric chloride reaction was still present on Dec. 27, 1915, but cleared up not long after that. He later undertook work which made difficult the accurate weighing of food, and he was therefore allowed to estimate the quantities from his previous experience. He has since remained free from glycosuria, ketonuria, and all symptoms. He feels as well as at any time in his life and has risen to the position of cashier.

The carbuncle made the diabetes worse, but the mouth condition was seemingly the result rather than the cause of the diabetes; for after the therapeutic control of the diabetes, the patient now with ordinary dental care remains free from tooth trouble.

Remarks.—This was one of the difficult cases of serious infection which may cause even mild diabetes to turn suddenly severe, incidentally illustrating the functional as opposed to the organic element in human diabetes. Numerous fatalities are inevitable with such a combination. The favorable outcome in this case must undoubtedly be attributed largely to the fact that the carbuncle was near the point of discharging spontaneously, so that a few days of fasting are not to be credited with radical cure of the infection. On the other hand, good evidence is afforded that the resistance was not lowered by fasting, and the belief is that it was raised. Likewise the subsequent treatment by undernutrition has not made the patient susceptible to infections and other mishaps, but has on the contrary relieved him of these and all other diabetic complications.

CASE NO. 28.

Female, age 11 yrs. American; schoolgirl. Admitted Jan. 19, 1915.

Family History.—A paternal granduncle died of tuberculosis some years ago. No other disease in family. Father, mother, and one brother of patient entirely well.

Past History.—Healthy life. Whooping-cough at 5, measles at 6, and mumps at 10. A strong, active child, living under good hygienic conditions in a small town in New York. In Aug., 1913, she had fever for 24 hours. Temperature was as high as 104°, and the physician could make no diagnosis. There were a few cases of poliomyelitis in the neighborhood about that time. For a short time afterward, the patient was subject to nervous movements and had pain in ankles without objective signs of inflammation. Habits always regular. Disposition not nervous. She has been on the honor roll at school, but has been kept from overstudy.

Present Illness.—While visiting in New York City after New Years day this year, polyuria was noticed, and when this continued several days the patient's mother suspected diabetes, and the diagnosis was made by her physician. The nervous movements noted after the previous illness were now increased. A diet was prescribed excluding most ordinary carbohydrates, but including gluten bread, toast, and milk.

Physical Examination.—A healthy looking girl, well nourished and rather large for her age. The face appears nervous, and there are twitching or choreiform movements of the head and arms. Teeth in good condition. Tonsils hypertrophied. Enlargement of epitrochlears but not of other lymph nodes. Knee and other reflexes exaggerated. Examination otherwise negative.

Treatment.—The glycosuria of 1.65 per cent present when patient was brought to the hospital ceased immediately on a carbohydrate-free diet of 600 to 650 calories, but the ferric chloride reaction, which had been negative, developed in moderate intensity on the second day of this diet. 2 fast-days were then imposed (Jan. 21 and 22), and the ferric chloride color became intense. Green vegetables were begun in the usual manner on Jan. 23 and increased until the limit of tolerance seemed to be reached with 133 gm. carbohydrate on Feb. 1. Instead of a fast-day on Feb. 2, the vegetables were merely diminished to 36 gm. carbohydrate. Under this program the ferric chloride reaction had become much paler, the ammonia nitrogen had fallen from 0.85 gm. on Jan. 25 to very low figures, and the plasma bicarbonate had risen from 47 per cent on Jan. 25 up to the lower normal limit. Carbohydrate-free diet was begun on Feb. 3 with two eggs, 20 gm. butter, and 250 gm. thrice cooked vegetables. This diet was rapidly increased and carbohydrate introduced. On Mar. 1 to 3 the patient proved able to tolerate 80 to 90 gm. protein, 50 gm. carbohydrate, and 3000 calories, without glycosuria but with persistence of a slight ferric chloride reaction. She was discharged Mar. 5 on a diet of 72 gm. protein, 30 gm. carbohydrate, and 2500 calories (approximately 2.5 gm. protein and 90 calories per kg.).

lation was actually diminished. Carbohydrate up to 140 gm. was tolerated perfectly, then heavy glycosuria occurred. The child was brought to confess that this was due to stealing bread, and that the difficulties in the preceding months had been due to the same cause. By Oct. 12 she was taking 75 gm. protein, 30 gm. carbohydrate, and 1500 calories, weighed 86 pounds, and had grown $2\frac{1}{2}$ inches since leaving hospital. On Jan. 10, 1917, the first menstrual period appeared in normal manner, but none has appeared since that time. The report on Jan. 18, 1917, showed that she was taking 80 gm. protein, 24 gm. carbohydrate, and 1625 calories, and weighed $90\frac{1}{2}$ pounds.

In Mar., 1917, she went through German measles without glycosuria. There have been occasional traces of glycosuria, the trouble being partly due to indulgent management, but these traces are always cleared up immediately and completely by fasting. The patient feels and appears entirely well and is continuing normal activities.

Remarks.—The history suggests that this is a case of diabetes resulting from an acute infection. If so, the damage produced was not transitory. The patient remains diabetic, and is liable to take an unfavorable turn from some accidental disturbance at almost any time; spontaneous downward progress is not noted. There is a definite improvement, but not to any extent suggesting a complete cure. If such improvement can continue the ultimate outcome may be very favorable. Actual recuperation to this degree, especially on rather high diets, is unusual, and possibly stands in relation to an exceptional etiology. If diabetes is caused by a transitory infection, the repair of the damage may sometimes be partial instead of complete. Possibly childhood may actually favor repair under the special conditions. In the absence of complete recovery, there is no doubt that neglect of diet will entail rapid downward progress. Dietetic treatment may save in proportion as it is early and effective. If the improvement can continue, the ultimate outcome in this particular patient may be very favorable. Thus far at any rate, in this case of juvenile diabetes, taken at an early, fairly mild stage, it has been possible through $2\frac{1}{2}$ years to obtain improvement rather than downward progress, along with seemingly normal growth and development.⁵

CASE NO. 29.

Female, unmarried, age 26 yrs. Finnish; domestic. Admitted Jan. 27, 1915.

Family History.—Parents are living; both have heart trouble. One brother is well. Two sisters died of tuberculosis and three others of unknown causes in adult life. Family history otherwise negative for tuberculosis, cancer, syphilis, and diabetes.

Past History.—Healthy life, spent in comfortable circumstances on farm in Finland up to 3 years ago, since then patient has been employed as domestic

⁵ A relapse has occurred, and the patient has been referred elsewhere for treatment. The experience is a further warning of the pernicious effect of high diets.

in the better parts of New York. For the past 8 months she has been a cook. No illness remembered, except whooping-cough in childhood. Occasionally patient spits a little bright red blood. Diet has been rich in starch but not in sweets. No excesses or bad habits.

Present Illness.—Just after the recent Christmas holidays the patient first noticed weakness, weariness, polyphagia, polydipsia, and the loss of 15 pounds weight. A physician immediately diagnosed diabetes.

Physical Examination.—A well appearing, fairly well nourished young woman. Teeth in good condition. Throat slightly congested; tonsils show neither hypertrophy nor exudate. Cervical, epitrochlear, and inguinal lymph nodes not palpable. Axillary glands are shot-like. General examination negative. Blood pressure 110-90.

Treatment.—The partial urine specimen on the day of admission showed 1.69 per cent, or 7.52 gm. sugar. On the next day (Jan. 28), on a carbohydrate-free observation diet of 68 gm. protein and 1350 calories there was glycosuria of only 2.1 gm. Anorexia had come on before admission, so this diet was all the patient cared to take. On Jan. 29 fasting was begun, and on the subsequent days as much as 100 cc. whisky were allowed; larger quantities could not be taken because of nausea. The urine immediately became sugar-free, but a well marked ferric chloride reaction persisted, partly perhaps because of the use of sodium bicarbonate. Because of the slightly subnormal CO_2 capacity of the plasma and the seeming tendency to weakness and nausea, 50 gm. sodium bicarbonate had been given on the first day of fasting (Jan. 29) and 100 gm. on the second fast-day (Jan. 30). The clinical condition was not perceptibly altered, and gave no indication of either benefit or injury. On Jan. 31, after the urine had been sugar-free over 72 hours, green vegetables were allowed containing 5 gm. carbohydrate. This quantity was increased up to 100 gm. carbohydrate on Feb. 4 and 5. This was tolerated without glycosuria. But with the protein-fat diet of 1200 to 1700 calories (Feb. 8 to 12), traces of glycosuria occurred with an intake of only 9 gm. carbohydrate.

Owing to the persistence of ferric chloride reactions, another period of alcohol and green vegetables was given up to Feb. 25. Thereafter only traces of glycosuria resulted from very high diets; e.g., 90 gm. protein, 35 gm. carbohydrate, and 3600 calories on Mar. 8 to 10. The diet was then adjusted so that at discharge on Apr. 21 it consisted of 90 gm. protein, 50 gm. carbohydrate, and nearly 3000 calories (approximately 2 gm. protein and 70 calories per kg.). The weight, which had been markedly reduced during undernutrition up to Feb. 25, increased on the higher diets, so that at discharge it was almost at the admission level.

All symptoms had disappeared and the patient felt entirely well. Radiographs and repeated sputum examinations failed to reveal any tuberculosis.

In Apr. the patient received word that her only brother had died of tuberculosis. She therefore insisted upon returning to Finland. The bad news and the preparations for departure brought on no glycosuria. She was given a letter to a professor in Helsingfors, and was warned to remain free from glycosuria under all conditions.

Remarks.—The case is not instructive. Even with allowance for the weekly fast-days the diet was too high for permanently good results. The patient was ignorant of the gravity of her condition and it was judged that she would not adhere to any serious restrictions, and this became more certain when she decided to return to Finland. Rather than have her break away from restrictions altogether, it seemed advisable to plan a diet adequate to permit her to work and feel well for the present and not attempt a more ideal result. Nothing has been heard of the patient since discharge.

CASE NO. 30.

Female, married, age 45 yrs. American; housewife. Admitted Jan. 30, 1915.

Family History.—Father is living, aged 72. Mother died at 47, following operation for fibroids. One sister died at 35, following operation for an old traumatic hip; three sisters are well. No diabetes or other special diseases known in family. Patient has been married 25 years and has had seven children; three are alive and well, the others died in infancy when the mother was in bad condition or suffering from grippe or typhoid.

Past History.—Usual childhood diseases (history indefinite). Typhoid fever 25 years ago. Grippe at several times; no sore throat. Appendicitis 8 years ago; operation. 7 years ago curettage for menorrhagia. Operation for mastoiditis 6 years ago. For some years past the patient has been nervous and suffered from nervous indigestion. Feces have also been pale, but never showed blood. Habits have been regular, diet simple; no excesses.

Present Illness.—First symptom was pruritus vulvæ 7 months before admission, followed by marked polyphagia, polydipsia, and polyuria. She sought no treatment for 4 months, then was placed on a diet, carbohydrate-free except for green vegetables and one slice of toast. She has lost 35 pounds weight. During 2 days prior to admission to hospital her physician had placed her on absolute fasting with whisky and sodium bicarbonate.

Physical Examination.—Woman without dyspnea or acute symptoms, moderately weak. Body shows evidence of considerable loss of weight, but still carries fair quantity of fat. Eyes react normally and ophthalmoscopic examination is negative. Teeth are in good repair. Throat congested; tonsils free from exudate or hypertrophy. Cervical and inguinal glands not palpable, axillaries and epitrochlears slightly enlarged. Knee jerks obtained only on reinforcement, and then sluggishly. Achilles jerks present. Blood pressure 110 systolic, 85 diastolic. General examination negative.

Treatment.—Patient seemed in fair condition and in no danger when admitted. Only slight glycosuria was present, and only a moderate ferric chloride reaction. She was admitted in the afternoon and received supper consisting of soup, 100 gm. steak, and 100 gm. raw and 100 gm. thrice cooked vegetables. She was menstruating, and had slight diarrhea. A phenolphthalein tablet and 15 gm. mag-

nesium sulfate produced small liquid or soft movements which continued under small doses of cascara on the following days. On the first full day in hospital (Jan. 31) the diet consisted of 81 gm. protein, 5 gm. carbohydrate, and 1650 calories. Glycosuria was entirely absent, the ferric chloride reaction still only moderate, and the condition apparently satisfactory. The next day, Feb. 1, the diet consisted of 50 gm. protein, 12 gm. carbohydrate, and 1250 calories. The patient showed slight nausea. On Feb. 2, the diet consisted of coffee, soup, one egg, and 600 cc. milk, representing 27 gm. protein, 30 gm. carbohydrate, and 500 calories. Nausea had increased, and on this day the patient vomited once a little undigested food. She said she had often had such attacks with her indigestion in the past. With small doses of chloretone, also a Seidlitz powder followed by a saline enema which removed considerable feces, the nausea seemed greatly diminished. Meanwhile a trace of glycosuria had appeared from the carbohydrate, and the ferric chloride reaction had become intense, but the highest ammonia nitrogen output (Feb. 2) was 1.9 gm. On Feb. 3, the diet was limited to 300 cc. clear soup, 300 cc. milk, and 90 cc. whisky. The patient also received 3 cc. aromatic cascara, 30 cc. Pluto water, and 10 gm. sodium bicarbonate. On Feb. 4, as glycosuria and ketonuria were well marked and the patient was slightly nauseated, a fast-day was given, the entire intake being 150 cc. coffee, 130 cc. whisky, 15 gm. sodium bicarbonate, 3 cc. aromatic cascara, and 30 cc. Pluto water. Though the urine remained acid, the glycosuria diminished to a trace, ammonia fell to 0.87 gm. N, and the CO₂ capacity of the plasma, which had been only 35.8 per cent on Feb. 2, rose to 57.7 vol. per cent on Feb. 4. Feb. 5 was also a fast-day, the intake being 140 cc. whisky and 15 gm. sodium bicarbonate. The urine remained acid. In the morning the patient felt well; toward evening she was slightly dizzy and nauseated. Feb. 6 was also a fast-day with 125 cc. whisky and 25 gm. sodium bicarbonate. The symptoms were more alarming; the temperature was 99.2°F., the pulse 90, the respiration 20; the pulse was weak, and the patient complained of dizziness and vomited several times. Two doses of 0.5 gm. chloretone were given for the vomiting, and 2 gm. compound jalap powder to empty the bowels further, though there had been one or more defecations every day.

On Feb. 7 only 25 cc. whisky could be taken because of nausea. Vomiting continued notwithstanding the use of a variety of routine measures, and weakness was becoming serious. The temperature first was as high as 99.8°, but fell by the close of the day to 96°. The pulse ranged 100 to 130, the respiration 28 to 44. Caffeine was administered at intervals subcutaneously, and later camphorated oil. An attempt also was made to feed, and milk, eggs, and beef juice were given and partly vomited. 1 liter of 4 per cent sodium bicarbonate solution was successfully given by the rectal drip method. The patient had become very drowsy, almost unconscious.

On Feb. 8, eggs and beef juice were continued, as also the caffeine and camphorated oil. Levulose was also given in small doses totaling 140 gm.; it was

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retained but had no evident effect. At 4 p.m., 700 cc. 4 per cent sodium bicarbonate were given intravenously. At 10 p.m. 100 cc. were likewise given. The temperature had slowly risen, and continued to rise, reaching 101° F. at 7 p.m. on Feb. 8, 101.8° at 1 a.m. on Feb. 9, and 104° at 5 a.m. The pulse remained about 140, the respiration 40 to 48. Toward the close the picture was that of fully developed diabetic coma. Death occurred at 6:45 a.m. on Feb. 9.

Remarks.—This was the first case seen at this Institute showing development of fatal acidosis on fasting, and the treatment was mistaken because the condition was unexpected. The very rapid loss of weight, from 56.8 kg. on Jan. 31, down to 52.2 kg. on Feb. 7, is a significant feature apparently present in all such cases. One error in treatment is the low fluid intake and correspondingly low output as shown in the graphic chart. Salts should also have been more liberally supplied. But the chief lesson for such cases is to break off fasting when the first warning symptoms appear, and after a period of some days of feeding to repeat the fast, which then is well borne. Suitable preparatory feeding preceding the initial fast will doubtless also prevent all or nearly all such mishaps.

CASE NO. 31.

Male, unmarried, age 35 yrs. American; real estate agent. Admitted Feb. 12, 1915.

Family History.—Mother is well except for occasional rheumatism. Father died of sarcoma at 62. One brother and two sisters are well; two died in infancy. No knowledge of any family disease.

Past History.—Patient has lived all his life in New York City in good health and hygienic surroundings. Measles and whooping-cough in childhood. Gonorrhoea 10 years ago. Syphilis denied; two Wassermann tests in the past have been negative. In 1889, after exposure to a great blizzard in winter, the patient suffered from inflammatory rheumatism in the spring. This returned almost yearly until 1895, when he received treatment by medicine, which ended the rheumatism permanently but left him with persistent bad digestion. 12 years ago he had St. Vitus' dance, which was cured in a German sanitarium by rest and arsenic. He has sore throats every year. No excesses in food, drink, or tobacco. Since becoming diabetic he has lost about 35 pounds weight. For about a week past he has had pain in the great toe of the right foot.

Present Illness.—3 years ago debility without other symptoms began. The urine was found to contain 5 per cent sugar. This gradually cleared up on carbohydrate-free diet with addition of one slice of bread at each meal. In 1913 he became worse and was placed in a hospital, where 3 green days cleared up glycosuria. Since leaving the hospital he has constantly had 3 to 5 per cent sugar in the urine. He continued work up to 4 months ago; since then he has been physically and mentally incapacitated.

Physical Examination.—Sallow color; only moderate emaciation; acetone odor present. Teeth in good repair. Tonsils and throat normal. Axillary glands

palpable, but not cervical, epitrochlear, or inguinal. Arteries are palpably sclerotic. Blood pressure 90 systolic, 75 diastolic. Knee jerks sluggish; Achilles jerks active. The great toe of the right foot shows a slight abrasion. The toe is bluish in color, cold to the touch, and the skin between it and the next toe is lifted up by exudate. Examination otherwise negative.

Treatment.—There were 2 days of observation diet. On Feb. 13, the first full day in hospital, this consisted of 84 gm. protein, 6 gm. carbohydrate, and 1830 calories. The glycosuria on this day was 31.3 gm., and the ferric chloride reaction was strong. Fasting was then begun, particularly with a view to the incipient gangrene. Whisky was permitted in quantities up to 500 calories of alcohol. On Feb. 17, whisky was diminished to 30 cc., and 9 gm. carbohydrate were added. Glycosuria, which had been absent, returned in traces and continued for 2 days longer, though the carbohydrate on Feb. 18 was diminished to 4 gm., and on Feb. 19 only whisky and 350 gm. thrice cooked vegetables were given. These traces of glycosuria were accidental, or else continued undernutrition brought rapid improvement; for beginning Feb. 20, 40 to 50 gm. carbohydrate in the form of green vegetables were given daily without glycosuria, until Feb. 25. On Feb. 26, the carbohydrate was diminished to 10 gm. The whisky was now 170 cc. Glycosuria ceased, but reappeared Mar. 3 on a diet of 70 gm. protein and 1700 calories without carbohydrate. It became heavier as the calories were increased to 2300, stopped with the fast-day of Mar. 7, reappeared with the carbohydrate-free diet of 2300 calories on Mar. 8, and ceased when the diet was cut down to 1200 calories Mar. 9 to 11. There were no vegetables of any kind in these later diets, so the glycosuria was evidently due to the protein-fat intake. Thrice cooked vegetables were then added and were at first tolerated, but glycosuria reappeared on Mar. 13, 14, and 15, on diets lower in protein and calories than those formerly assimilated. Though the vegetables on these days consisted only of 150 gm. string beans and 100 gm. celery, both thrice boiled, the glycosuria was evidently due to this trifle of carbohydrate. This very low tolerance improved with continued undernutrition and the diminution of other elements in the diet. Thus, beginning Mar. 17, the same thrice boiled vegetables were tolerated, the protein now being 30 gm. and the total calories 400. This diet was gradually built up and on Apr. 3 a trace of glycosuria appeared with 75 gm. protein, 200 gm. thrice boiled vegetables (string beans and asparagus), and 1700 calories. This stopped on the fast-day of Apr. 4; and on Apr. 5, 5 gm. carbohydrate in the form of asparagus, celery, and lettuce, without other food, were tolerated without glycosuria. Beginning Apr. 6 the protein was diminished to 40 gm. and the calories to 1400. With this reduction in protein, not only did the same quantity of thrice cooked vegetables cause no glycosuria, but also on Apr. 9 and 10 the addition of 10 gm. carbohydrate was tolerated. The attempt during the ensuing week (Apr. 12 to 17) to raise the carbohydrate to 20 to 30 gm. and the calories to 1800 resulted in slight glycosuria. The tendency to glycosuria gradually diminished, and by July 7 the patient had

become able to tolerate 80 gm. protein, 25 gm. carbohydrate, and 2150 calories (over 1.5 gm. protein and 40 calories per kg. for a weight of 50 kg., but diminished one-seventh by the weekly fast-days). He was dismissed on this diet in good condition.

Acidosis.—This was never acutely threatening. The ferric chloride reaction was fairly persistent. It cleared up with the undernutrition at the close of Mar., and returned with the higher diets in Apr., even though carbohydrate was soon added to these diets. Then, without special change in the diet, the ferric chloride reaction gradually disappeared and was absent at discharge. 20 gm. sodium bicarbonate were given daily Feb. 15 to 22. On Feb. 23, it was diminished to 5 gm., and then stopped. The carbon dioxide capacity of the plasma, as far as observed after Mar. 18, was within or near normal limits, and was high at discharge.

Blood Sugar.—This fluctuated, but hyperglycemia was the rule. The last analysis on June 24 still showed 0.165 per cent. It is evident that hyperglycemia did not prevent continued improvement in tolerance and symptoms. Nevertheless, this hyperglycemia is an unfavorable feature. It could doubtless have been brought lower, but the patient was unintelligent and untrustworthy. For this reason an ideal result was not considered possible in his case, and a fairly satisfying diet was therefore permitted, with some hope that improvement might still be possible, if he remained continuously free from glycosuria.

Weight and Nutrition.—The rise of 5 kg. in weight from Feb. 15 to 23 was due to edema resulting from the sodium bicarbonate. The weight fell rapidly on stopping the bicarbonate. Beginning May 31 there was another onset of edema independent of bicarbonate or other known cause. Albumin and casts were absent from the urine. The entire gain in weight from May 31 to June 16 was 6 kg. That this was wholly due to fluid retention, apparently from renal cause, is shown by the prompt fall following June 16, when salt-free diet was instituted. The entire period in hospital represented undernutrition such that the weight was diminished by 4 kg. There was clinical benefit instead of injury. Under the fasting and subsequent treatment the threatened gangrene cleared up smoothly. Strength was regained, the appearance and color improved, and at discharge the patient was able to resume his work, in contrast to the state of incapacity at the time of admission with higher weight and active diabetes present.

Subsequent History.—The patient followed diet and showed normal urine for several months. In Aug. he passed through a severe bronchitis without showing sugar. Toward Oct. he had much business worry, and analysis showed 0.204 per cent sugar in the whole blood and 0.278 per cent in the plasma (probably more dietetic than psychic in origin, however). The patient rejected the advice to return to the hospital at this time because of business emergencies which he must meet. He again reported at the hospital on Nov. 29. Meantime he had been traveling through other states under conditions which prevented following diet. The blood sugar was 0.227 per cent, plasma sugar 0.244 per cent. He was

instructed as to becoming sugar-free at home, and on Dec. 5 reported that glycosuria had stopped with 1 day of fasting and had remained absent on his regular diet. The urine on this date was normal, the blood sugar 0.208 per cent, the plasma sugar 0.250 per cent. On Dec. 12 a trace of glycosuria appeared, and the patient therefore fasted on Dec. 13. The urine was normal, the blood sugar 0.178 per cent, the plasma sugar 0.213 per cent. The patient was continually inclined to carelessness, but felt worse when showing sugar and therefore made some attempts at following diet. On Dec. 28 he returned to the hospital.

Second Admission.—The urine showed slight sugar and ferric chloride reactions. On the observation diet of Dec. 29, comprising 77 gm. protein, 15 gm. carbohydrate, and 2000 calories, a trace of glycosuria persisted in the early hours but cleared up before the close of the day. A fast-day was nevertheless imposed on Dec. 30, followed by a routine carbohydrate test, which fixed the tolerance at 70 gm. carbohydrate. On the subsequent diets entirely unaccountable traces of glycosuria occurred, and the patient finally proved to be repeatedly violating diet. On account of his persistent carelessness and disobedience, he was dismissed and was referred to a local specialist, with the idea that he might appreciate treatment more if he had to pay for it.

Remarks.—On the fast-day of Dec. 30 the blood sugar was 0.111 per cent and the plasma sugar 0.122 per cent. It is seen that the body weight at the second admission was identical with that at the former discharge. Notwithstanding repeated indiscretions in carbohydrate, the patient had kept down his total diet approximately as directed, and the tendency to a lowering of the hyperglycemia, as hoped for at the previous discharge, had actually shown itself. The case had been characterized by very low tolerance in the initial period of the first admission, but, in consequence of the undernutrition then imposed, had become easy to manage. The only difficulty was the light-mindedness of the patient. He was discharged in favorable clinical condition, with prognosis governed by behavior.

CASE NO. 32.

Female, married, age 21 yrs. Russian Jew; housewife. Admitted Feb. 18, 1915.

Family History.—Father died when patient was an infant. Mother well at 51. One brother and one sister well. No heritable disease known.

Past History.—Considerable sickness in infancy. Diphtheria complicated by measles at 2½ years. Pneumonia at 3 years. Healthy life since then. Habits regular. Diet largely carbohydrate, but no sugar. Married 3 years, has a healthy 2 year old child. The only recent illness was a 2 day attack of tonsillitis 2 years ago.

Present Illness.—Last June began polyphagia, polydipsia, polyuria, weakness, headache, and pains in legs. Recently pruritus vulvæ. Menstruation stopped last Oct. Patient supposed all the symptoms due to pregnancy, and was surprised when a physician found pregnancy absent and diagnosed diabetes. She was sent to this hospital for impending coma.

Physical Examination.—Height 168.5 cm. A well developed and nourished young woman, with flushed face and drowsy expression. Dyspnea is present; respiration about 30 per minute. Teeth in fair condition; some pyorrhea. Tonsils moderately hypertrophied; the left axillary and epitrochlear glands palpable; cervical and inguinal not palpable. Knee jerks not obtainable; Achilles jerks present. Blood pressure 100 systolic, 65 diastolic. Faint albuminuria.

Treatment.—Because of the imminent danger of coma, fasting was begun immediately, with some 400 to 600 calories of whisky daily. The patient was conscious though sleepy, and not nauseated. On Feb. 18 she received 10 gm. sodium bicarbonate and 2 gm. compound jalap powder; 30 gm. sodium bicarbonate on Feb. 20 and 21, 10 gm. on Feb. 22. She was thirsty, and was able to drink as much as 3 liters of water daily, but the main reliance was placed on fasting. Both the glycosuria and the clinical symptoms rapidly cleared up. The urine became neutral on Feb. 21. Glycosuria was absent on Feb. 23, but the first food was allowed on Feb. 26. This consisted only of 12 gm. carbohydrate in the form of green vegetables. By Mar. 6 it had been increased to 50 gm. carbohydrate without glycosuria. The whisky meanwhile was continued at 500 calories daily. It might have been well to have pushed the carbohydrate to the point of glycosuria, with a view to clearing up the remaining slight ferric chloride reaction. But after the fast-day with whisky on Mar. 7, protein-fat diet was begun. On Mar. 10 whisky was permanently stopped. The diet was gradually built up to 118 gm. protein, 25 to 27 gm. carbohydrate, and 2600 to 2800 calories (approximately 2.4 gm. protein and 52 to 56 calories per kg. on 50 kg. weight, reduced one-seventh by the weekly fast-days), with only transient traces of glycosuria. She was dismissed Apr. 7 on a diet of 85 gm. protein, 20 gm. carbohydrate, and 2500 calories (1.7 gm. protein and 50 calories per kg. reduced by weekly fast-days to 1.5 gm. protein and 43 calories average). This was well below what she had seemed able to tolerate. At discharge she was to all appearances entirely healthy.

Acidosis.—The carbon dioxide capacity of the plasma was only 26.4 vol. per cent at admission. Fasting was evidently the most important factor in raising it, for on Feb. 19, after only 10 gm. sodium bicarbonate, it had risen to 38.5 per cent. Under the larger doses of bicarbonate it rose still more rapidly to the high normal figure of 64.6 per cent on Feb. 22. This was an artificial elevation resulting from the alkali dosage, for with discontinuance of alkali the CO_2 capacity fell steeply to 45 per cent on Feb. 25. Under the influence of the small quantities of carbohydrate it rose spontaneously within normal limits, reaching 62.2 per cent on Mar. 4, without the aid of alkali. It fell on the fast-day of Mar. 7, alcohol alone being apparently unable to hold it up. It continued to fall, on addition of protein and fat, down to 46.5 per cent on Mar. 10. The steep rise to 56 per cent on Mar. 11 and 60 per cent on Mar. 12 is perhaps explainable by the introduction of 75 gm. protein in the diet. From this time the curve tends to run near or slightly below the lower normal limit, and was barely at this limit at discharge. The ferric chloride reaction was intense at the outset, diminished

rapidly during the fast, and was down to traces during the ensuing carbohydrate period. The later diet being a high one, this reaction did not become permanently negative in hospital. Notwithstanding the use of alkali, the ammonia nitrogen on Feb. 19 was up to 3.54 gm. It fell as steeply as the plasma bicarbonate rose. Its general course was still downward after discontinuance of alkali, but with the beginning of protein-fat diet, as the CO₂ capacity fell, the ammonia again rose, up to 1.9 gm. N on Mar. 11, with a fall thereafter, perhaps partly because of introduction of carbohydrate, perhaps partly because of the improved condition. No clinical symptoms were associated with the persistent traces of ferric chloride reaction and chronically low CO₂, and the use of alkali was not indicated.

Blood Sugar.—This was down to 0.128 per cent on the morning of Mar. 22, following the preceding fast-day. On Apr. 3, at the close of a week of high diet, it was up to 0.192 per cent. Following the fast-day of Apr. 4, the blood sugar on the morning of Apr. 5 was found to have returned promptly to the normal level of 0.117 per cent. At discharge on Apr. 7 it was 0.133 per cent. It could have been kept rigidly within normal limits, but a gradual fall was hoped for with continued improvement under suitable diet.

Weight and Nutrition.—The initial fall in weight during fasting was moderate, amounting to 2 kg. in 8 days. The bicarbonate did not produce edema, but beginning Feb. 26 the green vegetables produced a definite water retention, as often happens, so that the weight on Mar. 2, after practically continuous fasting, was 1 kg. higher than at admission. This slight but visible edema cleared up spontaneously and did not return. It will be noted that the initial fasting treatment, which cleared up the impending coma, consisted in 18 days of total abstinence from food, except the moderate quantities of alcohol and trifle of green vegetables. The weight fell from 53.2 kg. on Feb. 18 to 49 kg. on Mar. 9, a loss of 4.2 kg. Later with higher diets it tended to rise slightly, but was only 50 kg. at discharge; *i.e.*, 2.3 kg. less than at admission. It was hoped that the case was mild enough to permit a moderate gain in weight, and as the patient had to work, a liberal diet was allowed as described.

Subsequent History.—This patient, though poor and uneducated, adhered strictly to dietary instructions. The urine was continuously free from sugar and the ferric chloride reaction had disappeared, therefore 10 gm. carbohydrate were added to the diet on May 26. On June 4, the blood sugar was 0.105 per cent; on June 11, 0.122 per cent in the whole blood, 0.143 per cent in the plasma. The weight had risen to 56.3 kg. By Oct. 12, it had risen to 62.3 kg. The blood sugar then was 0.130 per cent and the CO₂ capacity of the plasma 66.2 vol. per cent. The diet was then increased by 200 cc. milk, as the patient reported herself not yet quite up to full working strength. On Nov. 3, the sugar in the blood was 0.149 per cent, in the plasma 0.175 per cent, and the CO₂ capacity was 56.3 per cent.

On Nov. 22, the sugar in the blood was 0.130 per cent, in the plasma 0.143

per cent, and CO₂ capacity 42.5 per cent. The first trace of sugar was reported in the urine.

On Dec. 6, the patient reported having had cold and cough for 10 days. The urine remained normal, and she probably ate less than usual, for the sugar was found to be 0.100 per cent in the blood, 0.105 per cent in the plasma; the CO₂ capacity 65.5 per cent.

On Dec. 23, the patient reported at the hospital with fever of 100°, complaining of pains in joints and chest. She continued to feel badly and lost a few pounds in weight. The urine remained normal. Her menstruation, which had returned in the autumn, had again ceased.

On Dec. 27, she was readmitted because of her cold or grippe, though diabetic symptoms were absent.

Second Admission.—Coryza was present, but the general appearance was good. Temperature was never above 99.8°F. The body weight was now 58.3 kg., as compared with 53.2 kg. at the first admission. Glycosuria was present Dec. 29 to 31, on a diet of 90 gm. protein, 50 gm. carbohydrate, and 2075 calories (1.54 gm. protein and 35.6 calories per kg.). The low blood sugars recorded mornings before breakfast show the absence of any continuous hyperglycemia. The ammonia nitrogen was 0.73 gm., and the total acidity (Henderson) 205. A carbohydrate tolerance test was instituted in the usual manner, beginning with a fast-day on Jan. 2. The increase in carbohydrate was made more rapidly than usual because of the high tolerance, which was found to be approximately 180 gm. carbohydrate. The patient was discharged on Jan. 16, 1916, weighing 57.8 kg., with a prescribed diet of 100 gm. protein, 50 gm. carbohydrate, and 2000 calories (1.7 gm. protein and 35 calories per kg., reduced one-seventh by the weekly fast-days). She was advised this time to take as much open air exercise as possible in order to build up her strength and relieve her chronic neurasthenia. The blood sugar had now come down to normal, so that all tests were normal in all respects, and the physical condition was entirely favorable.

Subsequent History.—The patient remained free from glycosuria and acidosis, notwithstanding an attack of tonsillitis in Mar. Normal menstruation returned in Apr. In July she again had fever and a grippe-like illness.

Third Admission.—On account of this she was readmitted on July 13, 1916, with definite tonsillitis and temperature of 100.5° F. This cleared up in a few days. The general condition was good, and the weight 54.5 kg. A carbohydrate test at this time showed a tolerance of 190 gm.; *i.e.*, practically identical with the 180 gm. half a year before. The patient was discharged on Aug. 15, 1916, weighing 52.2 kg., with a prescribed diet of 90 gm. protein, 60 gm. carbohydrate, and 2300 calories.

Subsequent History.—The urine remained normal. On Aug. 29, the blood sugar was 0.2 per cent, the plasma sugar 0.204 per cent, CO₂ capacity 65.1 per cent. On Sept. 6, the blood sugar was 0.167 per cent, the plasma sugar 0.181 per cent, the CO₂ capacity 65.8.

Fourth Admission.—On Oct. 24, 1916, the patient was again admitted to hospital because of cold and sore throat. The urine was normal, but a carbohydrate test showed a tolerance of only 130, as compared with the former 190 gm. She was again discharged on Dec. 5, 1916, in good physical condition, on a diet of 75 gm. protein, 30 gm. carbohydrate, and 1750 calories. Her weight was 51.6 kg. The blood sugar was 0.164 per cent.

Fifth Admission.—Feb. 20, 1917. The trouble again was tonsillitis with fever. There had been increasing tendency to glycosuria following repeated attacks of sore throat, and the patient had recently carried out a carbohydrate test in the regular manner at home, which showed a tolerance of only 90 gm. carbohydrate. A test prior to this had shown a tolerance of only 70 gm. carbohydrate. The general condition was still good, but the patient was kept in hospital for some time in order to prepare her for tonsillectomy under the most favorable conditions.

Tonsillectomy was performed under local anesthesia on Mar. 19, 1917, and was followed by no glycosuria, acidosis, or complication of any kind.

The patient was discharged Apr. 6, 1917, on a diet of 50 gm. protein, 10 gm. carbohydrate, and 1200 calories, weighing 46.5 kg.

Subsequent History.—On a low diet, made still lower by weekly fast-days, the urine remained normal and the patient felt well except for weakness. There were no more sore throats, but occasional joint pains returned as in the previous attacks.

By May 22, the diet was increased to 55 gm. protein, 10 gm. carbohydrate, and 1500 calories. On June 5, it was further increased to 60 gm. protein, 10 gm. carbohydrate, and 1600 calories. The weight was 46.5 kg.

On June 19 the blood sugar was 0.161 per cent and the CO₂ capacity 61.7 per cent. On account of complaints of persistent weakness and recurrent attacks of so called rheumatism, the diet was further increased to 75 gm. protein and 1800 calories (1.6 gm. protein and 38.5 calories per kg.). On July 3, the weight was 47.3 kg., the blood sugar 0.172 per cent, the CO₂ capacity 58.4 per cent. The general condition seemed slowly but steadily improving.

Remarks.—This result, 2½ years after the patient was first received on the verge of coma, is not bad under the circumstances. Downward progress, though not rapid, has been perceptible in the presence of two distinct causes.

The first to be considered is diet. In the light of later experience a severely diabetic patient, aged 21 years, ought not to receive an average ration of 43 calories per kg. as prescribed for this patient at the first discharge. One of the hopeful features of the earlier stage of diabetes is the ability to react energetically and to carry even unduly high diets with apparent safety for a considerable length of time. The most discouraging feature of the later stage resulting from these high diets is the apparent breakdown of recuperative power, so that lower diets may then spare the weakened assimilation, but can no longer raise it. This patient at her first discharge had good flesh and color, but was hindered in earning her living by slight neurasthenia and subjective weakness. The familiar

attempt was therefore made to build her up by liberal feeding. For a time she displayed the ability, characteristic of this incipient stage, to carry the increase of both diet and weight; but the neurasthenia was not cured, nor the recurrent infections prevented. It is apparent that the high diet had the usual effect of lowering the assimilation and weakening the power of recovery. Evidence is seen in the marked hyperglycemia on certain occasions between the first and second admissions, and in the persistent traces of glycosuria, Dec. 29 to 31, 1915, on diets lower than had been tolerated at the close of the first admission. At the second admission the blood sugar was kept normal. In contrast to the former 2500 calories, she was discharged this time on the wiser diet of 2000 calories (30 calories per kg. daily average). The third admission was 7 months later, and the carbohydrate tolerance test proved that no loss of assimilation had occurred during this interval. The diet was then raised to 2300 calories. Marked hyperglycemia was found within 2 weeks; and in the interval of only 2 months between the third and fourth admissions there was a demonstrated loss of 60 gm. carbohydrate tolerance. The hyperglycemia at the fourth admission was not overcome, and though the diet at discharge was only 1750 calories, traces of glycosuria recurred and downward progress accordingly became more rapid. It is the familiar story that high diet first fails to accomplish the intended purpose, and subsequently forces the employment of lower diets than would have been proper in the first place.

A second and highly important factor was that of infection. The attacks recurred at all periods. The history shows, first, that high feeding did not prevent the infectious attacks; second, that glycosuria and lowering of tolerance from these attacks were most marked when the diet was unsuitable. Even if the diet, however, had been perfectly planned, downward progress might still be expected from the repeated infections. The comparative safety with which operations can be performed with suitable preparation renders them advisable in preference to a continuance of the infectious injury.

CASE NO. 33.

Female, married, age 51 yrs. Russian Jew; housewife. Admitted Feb. 18th 1915.

Family History.—Not much known. One sister died of consumption. Patient has been married 32 years; had eight children; one died after tonsillectomy; others are well.

Past History.—Patient was born in Russia. For past 9 years has lived in New Jersey in good environment. Healthy life. Measles and typhus in childhood. Had nervous breakdown at time of her son's death, and about that time all her teeth became loose and were pulled out. During her first pregnancy she appears to have had an acute nephritis following a cold; another such attack occurred last year. Occasional indigestion and constipation. No alcoholism. Much starch and sweets in diet. She has been obese throughout her adult life.

Present Illness.—Over 2 years ago, because of nervousness, weariness, cold feet, headache, and pains in limbs, she consulted a physician and diabetes was diagnosed. Glycosuria cleared up on carbohydrate-free diet; she did not relish it and lost 25 pounds. Toast was then added to the diet, and later she was allowed even cake. She regained 7 pounds weight and glycosuria returned. She was then restricted to three slices of bread at each meal, but as glycosuria continued, the suffering from the above symptoms was so great and continuous that she was eager to submit to the most radical treatment if relief were obtainable.

Physical Examination.—Height 130 cm. A short, obese woman without acute symptoms. General sensitiveness to touch. Skin of face pits slightly on pressure. Teeth all false. Throat normal. No lymph node enlargement. Slight emphysema. Systolic murmur at heart apex, transmitted to axilla. Blood pressure 190 systolic, 100 diastolic. Knee jerks exaggerated. Ankles pit slightly on pressure. Faint albuminuria without casts.

Treatment.—The patient was first placed on a low diet of approximately 52 gm. protein, 5 gm. carbohydrate, and 750 to 800 calories. With this intake the glycosuria on Feb. 18 was 6.1 gm., and on Feb. 19, 5.95 gm. On the first day of fasting (Feb. 20) it fell to 1 gm. and after a trace on Feb. 21, cleared up entirely. For the purpose of reducing the excessive weight, plain fasting was continued for 1 week, with only 150 cc. coffee and 150 cc. soup daily (Feb. 20 to 26). On Feb. 27 and 28, nothing but whisky was given (250 to 400 calories), and then green vegetables added, containing 12.5 gm. carbohydrate on Mar. 1 and increasing to 50 gm. carbohydrate on Mar. 6. A fast-day with 300 calories of whisky on Mar. 7 cleared up the resultant trace of glycosuria. Eggs and a trifle of crisp bacon were then added to the whisky, but the total intake was not above 850 calories (Mar. 9). The trace of glycosuria which appeared on this day was probably attributable to 100 gm. string beans and 150 gm. cabbage, both thrice boiled. This glycosuria cleared up on the following day on practically the identical diet. After Mar. 12 no more whisky was used, except on the fast-day of Mar. 21. On Mar. 12 to 13, a diet of 25 to 40 gm. protein and approximately 300 calories was tolerated. But on Mar. 14, 68 gm. protein, 9 gm. carbohydrate, and 1200 calories caused glycosuria, which continued on the subsequent days with reduced caloric intake; the glycosuria was, however, very faint and ceased spontaneously on Mar. 20. The plan was pursued of giving a diet adequate in protein, with carbohydrate to the limit of tolerance, but poor in fat and calories. Thus, toward the early part of Apr. this diet contained about 120 gm. protein, 20 to 45 gm. carbohydrate, and 1000 to 1100 calories. Fast-days, sometimes doubled, were given almost every week for reducing weight. Toward the close of Apr. the patient had become able to assimilate as much as 118 gm. protein, 30 to 50 gm. carbohydrate, and 2000 calories. She never complained much of hunger and was well satisfied on the later diets.

There was a general gain in clinical condition, but still many complaints of headache and pains in abdomen and various parts of body. Weakness and ner-

vousness were also persistent. About the middle of Mar. occurred the first menstruation since 8 months before admission to hospital. In Apr. there was another menstruation, with undue hemorrhage. Gynecological examination failed to reveal fibroids or other cause of hemorrhage, but some abnormality was suspected because of the history of a similar trouble in the past. The patient was discharged May 8, with the idea of having her reduce her weight further at home and find something to divert her attention from her symptoms, which were of the sort called neurasthenic. She was well pleased with the improvement and could be trusted to continue treatment.

Acidosis.—A salient point is the absence of any threatening symptoms in this obese woman during a week of complete fasting without special preparation. The ferric chloride reaction, which had been negative, became positive on the low diet of Feb. 19 and grew heavy during the fast. Alkali was not employed. The ferric chloride reaction subsequently diminished, but was not permanently negative during this period in hospital. In the latter part of the stay in hospital the ammonia followed a fairly low curve, and the plasma bicarbonate held a low normal level.

Blood Sugar.—There is little to remark except the downward tendency. Evidently radical measures might have brought it within normal limits rather quickly, but in view of the general condition it was deemed preferable to allow the hyperglycemia to be taken care of in the course of long improvement.

Weight and Nutrition.—The most important therapeutic purpose was to diminish the excessive body weight. The abdomen was very pendulous, and the question arose whether there might not be benefit from a surgical operation which should correct the diastasis of the recti and tighten up the abdominal wall, perhaps thereby relieving some neurasthenic complaints, and at the same time amputate some 10 or 15 pounds of fat which were sufficiently in the patient's way that she would have welcomed surgical relief. It was decided not to venture this, but to depend entirely on dietary measures. The weight fell rapidly on fasting, and continued to fall on the subsequent diet which conformed to the above mentioned standard of adequate protein, carbohydrate to the limit of tolerance, and restriction of fat. The weight at admission was 83 kg., at discharge 70.6 kg.; *i. e.*, a loss of 12.4 kg. in 2½ months. The discharge diet represented 92 gm. protein, 30 gm. carbohydrate, and 1800 calories (approximately 1.3 gm. protein and 25 calories per kg., reduced one-seventh by the weekly fast-days). As usual, the clearing up of diabetic symptoms by reduction of weight had resulted in actual gain of strength. In this instance the reduction of the obesity was in itself a relief to the patient.

Subsequent History.—The presence of a somewhat elevated blood pressure and the occasional uterine hemorrhages raised a question in regard to exercise in this patient. She was advised to practice walking and to work 3 or 4 hours every day in her garden. The urine continued to show negative sugar and slight ferric chloride reactions. On June 11, the diet was increased by 50 gm. meat, 2 eggs,

and 10 gm. carbohydrate. The weight was 70 kg. On July 21, the carbohydrate intake was increased to 50 gm., and at the same time the fat was diminished by omitting 25 gm. olive oil. Though the condition in respect to diabetes remained uniformly good, the patient's neurasthenia made her a nuisance to a devoted family, and she was therefore readmitted to the hospital on Aug. 25 for observation.

Second Admission.—The sugar was down to 0.112 per cent in the blood, 0.118 per cent in the plasma. A slight ferric chloride reaction still persisted. None of the organic disorders suggested by the patient's numerous complaints could be found. She was again kept on very low diet, the fat being particularly low, the protein low but adequate as before, and in this instance the carbohydrate was also made low with the idea of maintaining a normal blood sugar. This was also the diet prescribed at discharge; namely, 100 gm. protein, 10 gm. carbohydrate, and 1000 to 1100 calories. The patient was now some 7 kg. below the weight at her former discharge, and the loss was expected to continue.

Subsequent History.—The progress was as before. Glycosuria remained absent, and on Oct. 6 the ferric chloride reaction was also found negative. Hyperglycemia was, however, found to be present after eating, the sugar being 0.156 per cent in the whole blood and 0.182 per cent in the plasma. The varied neurasthenic complaints had diminished but were still upsetting the patient herself and her entire household. There had been no recurrence of the former uterine hemorrhages, and the patient was readmitted to hospital on Oct. 11 to try more vigorous exercise under supervision.

Third Admission.—The weight was down to 59.2 kg.; *i.e.*, a loss of 24 kg. since the first admission. The patient was far stronger and more cheerful. Both sugar and ferric chloride reactions were negative. A carbohydrate test was now begun in routine manner with a fast-day on Oct. 11, then green vegetables with increase of carbohydrate by 10 gm. daily. A slight ferric chloride reaction quickly reappeared and persisted until abolished by increase of carbohydrate; *i.e.*, with the ingestion of 80 gm. carbohydrate on Oct. 21. The trace of glycosuria appearing with the 150 gm. carbohydrate on Oct. 29 was evidently accidental, for it disappeared with further increase of the ingestion, and the true limit seemed to be reached with 250 gm. carbohydrate Nov. 7 to 13. This assimilation is in striking contrast to the almost complete absence of tolerance shortly after the first admission. One contributing factor in it seemed to be exercise (see Chapter V). The slight glycosuria was cleared up by a fast-day on Nov. 14, which promptly brought the high blood sugar of the carbohydrate test down to 0.119 per cent in the whole blood and 0.125 per cent in the plasma. Thereafter a trial was made of a diet of 75 gm. protein, 150 gm. carbohydrate, and 2500 calories. Persistent traces of glycosuria resulted, evidently from the carbohydrate, inasmuch as the blood sugar curve shows normal values in the morning before breakfast. The carbohydrate was therefore diminished to 100 gm., and the intake of 2500 calories maintained by substituting fat. The patient was discharged on Nov. 26, 1915, weighing 55.6 kg., a total loss of 27.4 kg. since her first

admission. Her diet now represented approximately 1.3 gm. protein and 45 calories per kg., reduced one-fourteenth by fortnightly fast-days. The exercise had been strenuous during this period in hospital, and it proved wholly beneficial. She had reached a point where she could walk 8 miles and climb 40 flights of stairs daily in addition to an hour or two of jumping rope and tossing the medicine ball. A fairly liberal diet was therefore allowed at the close to maintain strength and nutrition and furnish energy for exercise.

Subsequent History.—On Dec. 13, 1916, the weight was 60 kg., and the patient was doing her full housework and walking 5 miles and using a 6 pound medicine ball half an hour daily, with almost complete relief from neurotic troubles. In summer, gardening was largely substituted, and she spent 6 hours daily at this work.

On June 15, 1916, sugar was 0.141 per cent in the whole blood, 0.185 per cent in the plasma; CO₂ capacity 63.5 per cent; weight 52 kg. The patient complained somewhat of hunger, and on July 22 the diet was changed to 100 gm. protein, 50 gm. carbohydrate, and 2750 calories. On this diet the sugar was 0.159 per cent in whole blood, 0.192 per cent in plasma, CO₂ capacity 57.9 per cent. Blood pressure 130 systolic, 90 diastolic.

In Sept., the weight was 54 kg. Occasional doubtful traces of glycosuria were reported, but on examination at the hospital such reactions were found to be false, the slight sediment not representing a true copper reduction. Progress has continued in this manner to the present. Neurasthenic symptoms still persist to some extent, pain being complained of at different times in head, abdomen, legs, and fingers. The quantity of the diet is fully satisfactory. Monotony is sometimes complained of. Active work is still continued with pleasure, and in general the patient is entirely transformed in health and appearance as compared with her first admission.

Remarks.—There are three salient points. First is the good toleration of fasting by an obese woman without symptoms of acidosis, and the improvement in strength with undernutrition. Second is the transformation produced in the sugar tolerance by reduction of weight, an increase from practically zero to 250 gm. Third is the beneficial effect of exercise in a patient apparently showing some contraindications. The dangers feared did not materialize, and even the blood pressure came down to normal. There is still an abundant supply of body fat, but undoubtedly a larger proportion of the weight is now muscle. The neurasthenia was benefited more than the carbohydrate tolerance, and without exercise it is doubtful if permanently favorable results could have been achieved.

CASE NO. 34.

Male, unmarried, age 26 yrs. Jew; clerk. Admitted Feb. 19, 1915.

Family History.—Father well at 55. Mother died with diabetes and cardiovascular disease at 51. Two brothers and three sisters are well; one brother died in infancy; one sister died this year in diabetic coma, aged 19. No knowledge of other heritable disease.

admission. Her diet now represented approximately 1.3 gm. protein and 45 calories per kg., reduced one-fourteenth by fortnightly fast-days. The exercise had been strenuous during this period in hospital, and it proved wholly beneficial. She had reached a point where she could walk 8 miles and climb 40 flights of stairs daily in addition to an hour or two of jumping rope and tossing the medicine ball. A fairly liberal diet was therefore allowed at the close to maintain strength and nutrition and furnish energy for exercise.

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Family History.—Father well at 55. Mother died with diabetes and cardiovascular disease at 51. Two brothers and three sisters are well; one brother died in infancy; one sister died this year in diabetic coma, aged 19. No knowledge of other heritable disease.

Past History.—Healthy life in fair environment. Measles in childhood, the only sickness. Venereal denied. No excesses in alcohol or tobacco. Diet moderate without much sweets, but has consisted largely of bread and meat; few vegetables.

Present Illness.—In Nov., 1911, the patient consulted a physician for pains in his arms. Local examination revealed nothing, and a liniment was prescribed which accomplished nothing. An osteopath was then consulted and gave electrical treatments without result. In the latter part of 1912 the patient returned to the original physician, who this time discovered glycosuria. On carbohydrate-free diet plus one slice of Graham bread daily, glycosuria diminished. The physician sent the patient to a sanitarium, where he remained 5 weeks. Glycosuria was absent only on green days, but the patient returned home with sugar diminished and strength improved. He resumed work as a clerk, but gradually became worse, and in 1913 was again sent to the sanitarium. Glycosuria did not cease and the result was less favorable. He attempted light work after returning home, but becoming alarmed by the downward progress, with polyphagia and polydipsia, he spent 5 weeks under the care of Carl von Noorden in the summer of 1914. He was free from glycosuria only on 1 fast-day, but felt improved in strength on leaving. He resumed light work on carbohydrate-free diet with addition of 250 to 300 calories carbohydrate.

Physical Examination.—A well developed young man, thin, but not seriously emaciated. No acute symptoms or distress. Flush of cheeks and slight yellowish color about nasolabial folds. Teeth in good repair; throat slightly congested; tonsils not hypertrophied. No palpable lymph node enlargements. Blood pressure 110 systolic, 90 diastolic. Knee jerks active. Examination otherwise negative.

Treatment.—On admission, the patient had glycosuria of 6.61 per cent or 150 gm. in 17 hours, with an intense ferric chloride reaction. There were no symptoms suggesting coma, and no hesitancy was felt in instituting carbohydrate-free diet. On Feb. 20 and 21 the diet was 75 to 80 gm. protein, 2 to 3 gm. carbohydrate, and 1650 to 1750 calories. The glycosuria fell to 33.2 gm. on Feb. 20, and 18.65 gm. on Feb. 21. Fasting was then begun with 500 to 600 calories of whisky daily. On Feb. 25 the urine was free from sugar and the ferric chloride reaction was much diminished. On Feb. 27, green vegetables were added to the whisky, and increased to 100 gm. carbohydrate on Mar. 7 to 8. A trace of glycosuria then appeared, while a slight ferric chloride reaction still persisted. After a fast-day with 600 calories whisky on Mar. 9, two eggs and 20 gm. bacon were added, and increased to a total of 1300 calories on Mar. 11. Whisky was then dropped and carbohydrate introduced; but the diet of 91 gm. protein, 25 gm. carbohydrate, and 1740 calories on Mar. 13 to 15 proved decidedly in excess of the tolerance. After a fast-day on Mar. 16, a low carbohydrate-free diet was again begun. On Mar. 24, it became possible to introduce 10 gm. carbohydrate. The diet was then progressively built up until before

discharge on May 8, it represented 95 gm. protein, 50 gm. carbohydrate, and 2900 calories. The diet prescribed at discharge was 80 gm. protein, 10 gm. carbohydrate, and 2500 calories (nearly 1.6 gm. protein and 50 calories per kg., reduced one-seventh by weekly fast-days). The patient looked entirely well and described himself as feeling better than at any time since the onset of diabetes. He was discharged to rest in the country during the summer.

Acidosis.—There were no threatening symptoms, either on carbohydrate-free diet, or during the initial fast. The carbon dioxide capacity of the plasma was slightly below the lower normal level at admission, but rose spontaneously and was normal toward the close of the stay in hospital. No alkali was employed at any time. The chief signs of acidosis were the ammonia nitrogen of 3.1 gm. at admission, and the intense ferric chloride reactions. The ammonia fell rapidly to normal values. The beginning of a diet deficient in carbohydrate brought it up to 1.4 gm. N on Mar. 12, but later the curve ran lower. The ferric chloride reaction gradually diminished and was sometimes negative, but never remained so during this hospital period.

Blood Sugar.—On Mar. 24, without glycosuria, there was nevertheless a fasting blood sugar of 0.23 per cent. On Mar. 29, following the preceding fast-day, the morning blood sugar was 0.17 per cent. Thereafter the findings were all below 0.2 per cent. The normal blood sugar on Mar. 3, after the preceding fast-day, indicated a downward tendency, and showed that more rigorous treatment could easily have maintained a normal level.

Body Weight.—This was 51.6 kg. at admission. The lowest figure, on Mar. 29 and Apr. 5, was 48.2 kg., representing a loss of 3.4 kg. There was occasional slight edema, and particularly during the initial fasting and carbohydrate period up to Mar. 8 there was pronounced edema with gain of 0.5 kg. in weight. The weight rose on the higher diets in Apr. and May, and at discharge was 51.2 kg.; *i. e.*, 0.4 kg. less than at admission.

Subsequent History.—Intelligence and financial circumstances were in the patient's favor. He adhered to diet while resting in the country, but on May 18 showed glycosuria, and as the traces did not clear up he fasted 48 hours. On May 25, his urine showed positive sugar and negative ferric chloride reactions. The diet was quantitatively reduced, and thereafter glycosuria remained absent except for traces appearing at the close of each week and cleared up by the routine fast-days. He was therefore readmitted to the hospital on July 28.

Second Admission.—Almost 1 kg. had been gained since the former discharge, so that the patient now weighed 0.4 kg. more than at the previous admission. The urine was sugar-free but showed a well marked ferric chloride reaction. A carbohydrate tolerance test was first instituted. Beginning with a fast-day on July 28, 20 gm. carbohydrate in the form of green vegetables were given on July 29 and increased 20 gm. daily until well marked glycosuria occurred with an intake of 120 gm. After a fast-day on Aug. 5, the diet on Aug. 6 and 7 consisted of 100 gm. protein, 30 gm. carbohydrate, and 2580 calories. Glycosuria

resulted; also the ferric chloride reaction, which had become negative during the carbohydrate test, returned. A lower diet was then begun, of 50 gm. protein, 10 gm. carbohydrate, and 1300 calories. It became possible to increase the carbohydrate to 20 gm., and the ferric chloride reaction became negative. Sept. 9 to 11 the patient was at home on this same diet. Sept. 12 was a fast-day. A diet of 50 gm. protein, 70 gm. carbohydrate, and 1200 to 1400 calories then caused well marked glycosuria. The fast-day of Sept. 18 was spent at home. The same carbohydrate was given for the following week and strenuous exercise begun. Glycosuria remained absent during this week, though the protein was increased to 80 gm. and the calories to 2030. Sept. 27 to Oct. 9, a diet of 80 gm. protein, 100 gm. carbohydrate, and 2130 calories was tolerated without glycosuria. (For details of the exercise experiments, see Chapter V.) After the fast-day of Oct. 10 another carbohydrate test was instituted with heavy exercise. Potatoes and other high carbohydrate vegetables had to be used this time to avoid excessive bulk. Glycosuria appeared with 210 to 220 gm. carbohydrate on Oct. 28 and 29. Exercise was then increased, and glycosuria cleared up and did not return until an intake of 270 gm. was reached.

On Nov. 14, the patient was discharged in apparently excellent health, free from glycosuria and ketonuria, on a diet somewhat better balanced than before, namely 75 gm. protein, 75 gm. carbohydrate, and 2400 calories (over 1.5 gm. protein and 50 calories per kg., reduced by weekly fast-days to 1.3 gm. protein and 43 calories per kg.).

Acidosis.—The fluctuations shown in the blood bicarbonate were mostly connected with the exercise experiments. The ferric chloride reaction cleared up as stated when the carbohydrate intake reached 60 gm. on Aug. 1 without other food. It remained absent on the fast-day of Aug. 5, but reappeared promptly with the subsequent diet. During Aug. it became entirely negative, doubtless on account of the low calory diet rather than the introduction of the small quantities of carbohydrate. The subsequent occasional traces were perhaps associated with the heavy exercise, but continued exercise produced no continuance of this reaction. Alkali was not used.

Blood Sugar.—There is little to remark except the tendency to slight continuous hyperglycemia. Some of the fluctuations stand in connection with the exercise experiments. On the high diets allowed it is evident that exercise failed to keep the blood sugar below about 0.15 per cent. This accords with other experience that it cannot be used as a substitute for caloric restriction.

Body Weight.—From 52 kg. at entrance, this was reduced to 49 kg. on Aug. 30. Thereafter it rose as high as 52.6 kg. on Oct. 10, partly by reason of slight edema. The carbohydrate tolerance test in Oct. produced first a sharp fall in weight due to undernutrition, followed by a rise to 51.6 kg. due to edema. With subsidence of the edema, the long undernutrition (29 days) of this carbohydrate test made itself felt by a sharp drop in weight. The patient was discharged weighing 47.4 kg.; *i.e.*, 4.2 kg. less than at the first admission.

Subsequent History.—The patient adhered to diet and exercise, and the urine remained normal. The health seemed perfect. On Feb. 10, 1916, sugar in blood was 0.141 per cent, in plasma 0.145 per cent, CO₂ capacity 65 per cent. Weight 51 kg. On Feb. 20, the patient slightly overstepped his diet at his brother's wedding, and brought on glycosuria which was checked by a fast-day. In Mar. he passed through an attack of grippe and bronchitis, and showed traces of glycosuria which required temporary reduction of diet.

Death occurred June 10, 1916. Inquiry elicited the information that there had been an attack of acute appendicitis. On account of the diabetes the family physician had attempted to avoid operation. Symptoms of perforation appeared on June 5, and glycosuria had also developed. On that day the patient was rushed to a hospital for an emergency operation. Anesthesia was given with nitrous oxide and oxygen. Perforation of the appendix and free peritonitis were found. Following operation he seemed to do well and became free from glycosuria. The diet during this time was not stated. On June 9, coma was said to have developed in spite of alkali treatment and resulted in death the next day.

Remarks.—Undernutrition had the usual effect in raising tolerance, relieving symptoms, and improving strength. The diet toward the close of the first period in hospital was unduly high. The condition then, with sugar-free urine, rising weight, and only a trace of ferric chloride reaction and slight hyperglycemia, was one ordinarily considered highly favorable in a case of this type and was clearly superior to the results achieved by specialists who had treated this patient at earlier and milder stages of his condition. But the return of glycosuria while the patient was under favorable environment at home and adhering faithfully to treatment was not accidental nor an indication of spontaneous downward progress, but was the inevitable result of the high diet which was producing the gain in weight. A still more favorable condition was achieved during the period of undernutrition in the first half of the second stay in hospital. The diet was then increased to a less degree than before, and at the same time heavy exercise was employed to use up the surplus calories and if possible build up the assimilation. The effect upon both the tolerance and the general health was clearly beneficial and no ill results were observed. Nevertheless, exercise could not entirely replace caloric restriction, for hyperglycemia was persistent, whereas with exercise and a lower diet the blood sugar might have been normal. The ultimate outcome in this type of case probably could not have been favorable on a diet as high as that allowed. The observation upon this patient was interrupted by the untimely death from a cause bearing no definite relation to the diabetes. A noteworthy point is that the patient was on liberal diet, so that he was steadily gaining weight; otherwise critics might allege that susceptibility to such an accident was due to undernutrition. It so happens that the majority of serious infections and accidents in this series have happened to patients on high rather than to those on low nutrition. It is possible that suitable dietetic care before and after operation might have prevented the fatal result.

CASE NO. 35.

Male, married, age 61 yrs. American; lawyer. Admitted Feb. 20, 1915.

Family History.—Mother died of typhoid at 32, father of some paralytic condition at 57. Three sisters and two brothers are well; one other brother has arthritis. A first cousin died of cancer. No other heritable disease known. Patient has been married 34 years; wife healthy but never pregnant.

Past History.—Healthy life under excellent hygienic conditions. Grippe, measles, whooping-cough, and mumps in childhood. Probably mild typhoid at 13. A few attacks of grippe since. No sore throats or other minor infections. No venereal disease. Habits very regular and simple. No alcohol used until prescribed for diabetes. No excesses in diet or indulgence in sweets. Bowels regular. No nerve strain. Patient has been a prosperous lawyer and official in a small New York city under seemingly ideal conditions of health.

Present Illness.—11 years ago persistent backache was the first symptom. Within a year thereafter more or less polyuria was noticed. Glycosuria was then found, but ceased with simple abstinence from bread and potatoes. During the ensuing year, however, glycosuria became more stubborn and 20 pounds weight were lost. 9 years ago, on his physician's advice, the patient spent 30 days under the care of Carl von Noorden. He received the usual treatment with green days, oatmeal days, etc., and was told that it was impossible for him to be free from glycosuria. He returned with glycosuria diminished and strength increased, with a gain of 5 pounds in weight. He adhered for 1½ years to the diet prescribed in Vienna, which contained liberal amounts of carbohydrate. 10 pounds weight were lost. He then returned to Vienna for 33 days of treatment. He again gained 5 pounds and felt better. The glycosuria was still present on leaving. He again followed the prescribed diet until 1909, when he returned to von Noorden for 31 days. This time the trouble was more persistent and there was little improvement. The patient still carried on his regular work. In 1911 he was treated by von Noorden for 33 days with more stringent measures than before, 2 fast-days being employed. He continued in slightly reduced health until Apr., 1914, when a bull knocked him down and broke four ribs. Dangerous acidosis came on. His medical advisor knew of the fasting treatment, and withheld all food for 4 days. The symptoms of impending coma passed off. Since then he has remained subjectively in tolerable health, and came for treatment only because his physician advised that the persistent glycosuria and acidosis should be cleared up if possible.

Physical Examination.—Height 170 cm. A well developed, adequately nourished, unusually rugged looking man for his age. No acute symptoms, but a marked odor of acetone. Mouth and throat normal. Only insignificant lymph node enlargements. Blood pressure 120 systolic, 80 diastolic. Liver edge palpable 4 cm. below costal margin in mammary line. Knee jerks obtained only slightly with reinforcement. Ankle jerks sluggish. General examination is that of an unusually healthy man.

Treatment.—On the first full days in hospital, Feb. 21 and 22, the patient received an observation diet of 95 to 130 gm. protein, 5 to 8 gm. carbohydrate, and 1900 to 2000 calories, and excreted 25 to 22 gm. sugar, with evidently considerable diacetic acid. Beginning Feb. 23 he was given an 8 day fast, with 150 to 200 cc. whisky, 300 cc. soup, and 300 cc. coffee daily; no alkali. The glycosuria diminished, but the ferric chloride reaction became intense; the carbon dioxide capacity of the plasma remained approximately normal. The patient began to complain of malaise and nausea, and appeared drowsy. On Mar. 2 he vomited. 10 gm. sodium bicarbonate on this day failed to alter the symptoms. Therefore on Mar. 3 the fast was broken off, and a diet of 48 gm. protein, 5 gm. carbohydrate, and 1300 calories was given. This was increased on the following days, so that on Mar. 10 the intake was 90 gm. protein, 5 gm. carbohydrate, and 2450 calories. 30 gm. sodium bicarbonate were given on Mar. 3, and the same on Mar. 4. The ketonuria continued heavy and the glycosuria increased, but not to anything like the previous figure. Mar. 12 to 16 the diet was strictly carbohydrate-free. The symptoms which had developed on fasting had disappeared immediately on feeding, and the patient remained entirely comfortable on carbohydrate-free diet. Mar. 17 fasting was resumed with whisky, soup, and coffee as before. The glycosuria promptly fell to traces. Alkali was not given. On Mar. 17 the patient was subjectively comfortable. On Mar. 18 he complained of slight nausea. Therefore, without waiting for absolute freedom from glycosuria, on Mar. 19 the 630 calories of alcohol were augmented with an egg, 25 gm. bacon, and 250 gm. thrice boiled vegetables. The clinical symptoms were thus relieved, and the glycosuria also cleared up on Mar. 20, while the ferric chloride reaction was diminished. Traces of glycosuria returned on certain of the ensuing days. Another single fast-day with whisky, soup, and coffee was given on Mar. 28. The protein-fat diet was gradually built up, until on Apr. 2 and 3 it represented 72 to 82 gm. protein and 1750 calories, nearly half of which was alcohol. As symptoms of danger were apparently past, it became feasible to proceed to raise the tolerance and attack the persisting acidosis. Therefore Apr. 4 was a fast-day with 700 calories of whisky. On the following 2 days, 10 gm. carbohydrate were added to the whisky. On Apr. 7 whisky was diminished, and thereafter discontinued. A routine carbohydrate test (Apr. 8 to 17) established the tolerance as about 100 gm. carbohydrate. At the same time the ferric chloride reaction became much paler. A diet was then begun with inclusion of 15 gm. carbohydrate. Traces of glycosuria were too frequent, and on May 12 to 14 the patient fasted 3 days; nothing but 300 cc. coffee and 300 cc. soup daily was given. Undernutrition was then continued, with persistent low diet and a routine fast-day every week. After the fast-day of May 23, glycosuria was permanently absent, but slight ferric chloride reactions continued. The patient was discharged June 22, on a diet of 78 gm. protein, 15 gm. carbohydrate, and 2120 calories (slightly less than 1.5 gm. protein and 40 calories per kg., diminished one-seventh by the weekly fast-days). He had become accustomed to the simple

low diet, and could be depended upon to continue it accurately at home. The general appearance was distinctly not so good as at admission; but in addition to the altered laboratory findings, the patient insisted that he felt better and his mind was clearer than before.

Acidosis.—The case illustrates the difficulties and possible danger of fasting sometimes in long standing diabetes, when the patient perhaps appears in very favorable condition. This patient had previously undergone fasting with benefit after the accident with the bull. His physician considered that at that time the fasting saved him from dying in coma. On the present occasion in hospital he showed no symptoms either on mixed diet or on the change to carbohydrate-free diet. But toward the close of an 8 day fast the typical warning symptoms developed, and were not prevented by the rather liberal use of whisky, nor relieved by 10 gm. sodium bicarbonate. The carbon dioxide capacity of the plasma at this time was within normal limits and gave no warning of the critical condition, which was recognized by clinical symptoms alone. As usual when this condition is taken in time, feeding cleared up the symptoms immediately. Other experience confirms the view that the use of soda was not essential, nor was it necessary to give carbohydrate. The mere giving of food, even though this consisted chiefly of fat, was sufficient to relieve the intoxication of this fasting acidosis. Also as usual in such cases, the sensitiveness disappeared later, so that modifications of diet were made at will without clinical disturbance. Corresponding to the normal blood alkalinity, the ammonia nitrogen was never above 2 gm. It diminished, but did not reach normal limits until the carbohydrate tolerance test in Apr. The intense ferric chloride reaction was the only laboratory index which corresponded to the clinical intoxication, yet this remained equally intense when carbohydrate-free diet had cleared up the clinical symptoms completely. This reaction gradually faded out, but did not become permanently negative during this period in hospital.

Blood Sugar.—The only normal blood sugar was 0.108 per cent in both whole blood and plasma on the morning of June 14, following the preceding fast-day. The persistent hyperglycemia was the reason for the rigorous undernutrition period (May 11 to 15) comprising 2 days of very low diet and 3 fast-days. This entirely failed to reduce the hyperglycemia, which was 0.2 per cent on May 15. The treatment had been rigorous, and it was deemed advisable not to push undernutrition further in an attempt at a rapid reduction of such a stubborn hyperglycemia, but rather to leave it, like the ferric chloride reaction, to take care of itself in the course of gradual improvement.

Weight and Nutrition.—The patient was received appearing in unusually robust health for his age, weighing 66.4 kg. At discharge his weight was 54 kg.; *i.e.*, a loss of 12.4 kg. in consequence of the undernutrition treatment. The only tangible sign of improvement was from the laboratory side. He claimed to feel such benefit subjectively that he was firm in continuing treatment, but his appearance was noticeably thin and haggard, compared to that on admission. The

diet at discharge was sufficiently liberal that he could be expected to hold weight or perhaps gain slightly.

Subsequent History.—Glycosuria remained absent, and by the end of July the ferric chloride reaction had become negative. On Aug. 21, his local physician (not the consultant who had sent him to the hospital) called at the Institute to report that the patient's family and friends were worried about him, and that although he was doing his work after a fashion, his working power and apparent strength were not equal to what they were before treatment. Information was otherwise obtained that the home opinion of the effect of the treatment was decidedly unfavorable, and only the loyalty of the patient himself and his medical consultant kept him strictly to the program. His local physician was assured that a considerable period of subnormal weight and strength was unavoidable, and the results would appear later. With continued diet and exercise the progress continued favorable. On Oct. 13, 1915, the sugar in whole blood was 0.178 per cent, in plasma 0.185 per cent. The weight was 57.4 kg. An increase of carbohydrate to 25 gm. was permitted. Steady and obvious improvement continued, and the patient reentered the hospital Feb. 5, 1917, on request for observation, having never shown glycosuria since discharge.

Second Admission.—The weight was 61.6 kg.; *i.e.*, 7.6 kg. more than at discharge, but 5.2 kg. less than at the first admission. The urine was negative for both sugar and diacetic acid. Following the fast-day of Feb. 6, the blood sugar on the morning of Feb. 7 was 0.115 per cent. A carbohydrate test ending Feb. 26 showed a tolerance of 240 gm. carbohydrate, as compared with the 100 gm. in the previous Apr. Chiefly by the undernutrition in the carbohydrate test the weight was reduced, and was 57.2 kg. at discharge on Mar. 3. The mixed diet of Feb. 29 to Mar. 3 contained 50 gm. carbohydrate. The diet prescribed at discharge consisted of 100 gm. protein, 35 to 40 gm. carbohydrate, and 2500 calories.

Remarks.—The case illustrates the feasibility and desirability of effective treatment even in long-standing cases of diabetes in advanced life. Probably no diabetic of 61 years could appear more healthy and less injured by glycosuria than this patient, according to superficial appearances at his first admission. There was a serious question whether it was worth while to undertake to clear up the condition. This was done partly on advice of Dr. S. J. Meltzer, who urged that the patient might at any time meet some accident and go into coma, or develop gangrene and die from it. The known difficulties of such cases were encountered; namely, first, the serious symptoms during fasting, and second, the period of several months of lowered weight and impaired strength from undernutrition. Not only, however, was relief from diabetic symptoms and the attendant dangers ultimately achieved, but also the physical condition even at a slightly reduced weight came back to a decidedly better state than before treatment. The patient could think better, work better, and enjoy life more than at any time since the first onset of his diabetes, and the objective evidences were such that his family and neighbors were fully convinced.

The primary treatment of such a case is fully as difficult as that of young patients. In a case of this severity, halfway measures are wholly inadequate and often injurious. The ultimate prognosis is undoubtedly better than in younger patients. The slow improvement may be expected to continue, so that further relaxation of diet and increase of weight may be expected. Barring accidents, there should be no further trouble from the diabetes.

CASE NO. 36.

Male, unmarried, age 30 yrs. American; electrical engineer. Admitted Mar. 8, 1915.

Family History.—Father died of Bright's disease 5 years ago. Mother alive, has myxedema. Three sisters are well. One brother died of diphtheria at 4 years. Another died of diabetes at the age of 15. 13 years ago a paternal first cousin died of diabetes at 16. No tuberculosis, cancer, syphilis, or nervous disorders known in family.

Past History.—Healthy life, mostly spent in Canada, always under excellent hygienic conditions. Measles and diphtheria in childhood. A large peritonsillar abscess at 27 years, which lasted 2 weeks and caused fever and obstruction of breathing.

Present Illness.—During 1913, trouble occurred with a wisdom tooth, resulting in an abscess, and a dentist in several attempts was unable to extract it. Thirst, polyuria, and loss of weight were noticed shortly thereafter. In Jan., 1914, the diagnosis of diabetes was made in Toronto. He was in hospital 10 days under dietetic treatment, when another abscess developed about the same wisdom tooth. This was extracted after 3 days, but necrosis of the jaw and septicemia ensued. There was fever and delirium, and more or less infection persisted until the end of Apr. From his normal weight of 140 pounds he declined to 90 pounds, but during May came back to 130 pounds. At the end of May there was an attack of acute appendicitis with pain and fever for 2 days. Another attack came on July 28, and appendectomy was performed on July 30. There was a colon bacillus infection of the wound, which did not heal until Sept., 1914. Meanwhile there were three abscesses in the neck, treated by vaccine; the last one did not heal until Oct. The weight was now down to 115 pounds. The patient dragged along with glycosuria and diminished weight and strength, but was not bed-fast, until the time of admission to this hospital.

Physical Examination.—A well developed, moderately emaciated young man with no urgent symptoms. Acute coryza present. Teeth in good repair except lower left third molar, of which only the root is present. Throat normal; no tonsillar hypertrophy or exudate. Very slight enlargement of superficial lymph nodes. Blood pressure 100 systolic, 60 diastolic. Reflexes normal. General examination negative.

Treatment.—The observation diet on Mar. 9 and 10 consisted of 75 to 80 gm. protein, 3 gm. carbohydrate, and 1670 to 2300 calories. On Mar. 10, the sugar

excretion was 14.6 gm., the ammonia nitrogen 2.25 gm., and the ferric chloride reaction intense. 4 days of fasting with whisky cleared up the glycosuria and diminished the ferric chloride reaction and the ammonia output. Green vegetables were then begun, 20 gm. carbohydrate being thus added to the whisky on Mar. 15, after which whisky was stopped. Increase of vegetables in the form of a carbohydrate test established the tolerance as 175 gm. carbohydrate, this quantity being tolerated on Apr. 3, but causing slight glycosuria on Apr. 4. A mixed diet was then rather rapidly built up, with the usual weekly fast-days. At discharge on July 15 the diet consisted of 80 to 90 gm. protein, 50 gm. carbohydrate, and 2500 calories (1.6 to 1.8 gm. protein and 50 calories per kg., diminished one-seventh by weekly fast-days). The only special incident in hospital was the removal of the root of the left lower third molar tooth on Apr. 28, after a rather difficult half hour operation under local anesthesia. Glycosuria followed this operation, though it will be noticed that both carbohydrate and total diet were less than had been tolerated on former days. The slight glycosuria ceased with a single fast-day on Apr. 29, and there was no further trouble. The patient at discharge was not up to full normal strength, but was improved to the point where he felt able to undertake light work.

Acidosis.—This was never threatening, and the carbon dioxide capacity of the plasma remained normal. The ferric chloride reaction was not negative for any considerable period except during the carbohydrate tolerance test, Mar. 24 to Apr. 5. The persistence of this reaction, though slight, was one indication of the need of more thorough treatment in a patient of this type.

Blood Sugar.—In conformity with the rule that glycosuria or hyperglycemia resulting from carbohydrate alone is brief, the blood sugar on the morning of Apr. 1 was 0.11 per cent notwithstanding the large carbohydrate ration. The normal figure on Apr. 30, following the single extra fast-day of Apr. 29, shows how easily hyperglycemia might have been abolished. The actual tendency of the curve, as far as analyses were made, was progressively upward. Traces of glycosuria also became more frequent toward the close. These points confirmed the indication of the ferric chloride reactions, that the tolerance was being slightly overtaxed.

Weight and Nutrition.—Slight undernutrition was practiced at first, then liberal diets allowed, and the weight at discharge was almost exactly identical with that at admission. The patient was over-eager for quick results. He complained of hunger on slight restrictions, and found fast-days very hard. His neurotic temperament was one excuse for the attempt to feed with a view to maintaining the highest possible weight and strength.

Subsequent History.—Sugar remained absent and the ferric chloride reaction slight. On July 27, an increase of carbohydrate to 60 gm. was permitted. In Aug. the patient reported having found congenial light work, and as sugar was still absent the carbohydrate ration was increased to 75 gm. Glycosuria remained completely absent except for one trace in Nov. from an unintentional mistake in

diet, and another in Dec. from nervousness (on the usual basis of dietary hyperglycemia). After Christmas, 1915, he stopped weighing food and became interested in Christian Science. He began to add cautiously to his diet, and whenever sugar appeared was frightened out of his trust in Christian Science and fasted sufficiently to clear it up temporarily. In May, 1915 he began to disregard diet and urinary tests altogether. The rapid loss of weight and strength convinced him of his mistake, but he did not report to the Institute. He was at a mineral water resort for a short time, and became so weak that he had to telegraph his sister to assist him home. He arrived in New York on June 6 with indigestion, and was obliged to fast almost completely from inability to take food, until readmitted to the hospital on June 9.

Second Admission.—Emaciation had brought the weight down to 42.2 kg. The patient was semistuporous, bordering on coma. Knee and Achilles jerks were normal. June 10, the first full day in hospital, on a carbohydrate-free diet of 63.5 gm. protein and 1450 calories, he excreted 68 gm. glucose and 4.55 gm. ammonia nitrogen, with urinary acidity of 611 cc. N/10 (Folin). The ferric chloride test was black, the CO₂ capacity of the plasma 30.3 vol. per cent, the sugar in whole blood 0.270 per cent and in plasma 0.385 per cent. The plasma during the entire former period in hospital had been clear; it now appeared like cream, and showed 8.2 per cent fat. The feeding of June 9 and 10 had been employed because of the possibility that coma symptoms had resulted from fasting. Feeding did not clear up the symptoms. On the contrary, on June 10 the ammonia was higher and the CO₂ capacity lower than at admission the day before, and the clinical condition appeared more critical. Accordingly, absolute fasting was begun June 11, with nothing but 450 cc. coffee and 550 cc. clear soup daily; no alcohol and no alkali. The fluid intake was not forced; the patient was merely encouraged to drink rather freely, and actually took only 2500 to 2800 cc. total fluids daily. 9 days of absolute fasting diminished the lipemia to 4 per cent, the ammonia to 1.34 gm. N, the urinary acidity (Folin) to 230 cc. N/10, and the glycosuria to 5.88 gm. The CO₂ capacity of the plasma rose with equal steepness to normal limits. The hyperglycemia showed one of the peculiarities sometimes observed in fasting; for after the sugar had gone down to 0.25 per cent in the whole blood and 0.3 per cent in the plasma, it suddenly rose to 0.38 per cent on June 14, and was still 0.325 per cent on June 16, though the glycosuria had greatly diminished. All symptoms of danger had cleared up in the early days of fasting. Though the patient was not dangerously weak, it was deemed expedient to interrupt the long fast by a few days of low diet. Accordingly, on June 20, 35 gm. protein and 683 calories were given, and on June 21 to 23, 50 gm. protein and 1000 calories daily. The glycosuria increased, the blood sugar rose from 0.2 to 0.28 per cent, the ammonia excretion increased slightly, and the plasma bicarbonate fell from 58.6 to 55.4 per cent. Fasting was resumed June 24 to 27, thus making 13 fast-days in all. Glycosuria ceased, the ferric chloride reaction became negative, the ammonia fell low, the CO₂ capacity reached its highest point, and sugar in both blood

and plasma dropped to 0.2 per cent. The ensuing carbohydrate test revealed a tolerance of not over 70 gm. carbohydrate in green vegetables. In this test the ammonia reached its lowest level. After the fast-day of July 9, mixed diet was begun, consisting first of 72 gm. protein, 5 gm. carbohydrate, and 1450 calories increased on July 24 to 85 gm. protein, 15 gm. carbohydrate, and 1700 calories. The urine was now normal, and the patient, though not so strong as at his former discharge, felt able to do light work, and was discharged on July 26 on the last mentioned diet, with addition of 3 bran muffins and 400 gm. thrice boiled vegetables.

Acidosis.—The salient point is that both the clinical and laboratory signs of a very imminent coma were cleared up promptly and completely by fasting without alcohol or alkali. Presumably alcohol would have accomplished nothing unless to maintain strength. Soda might have been given if the blood alkalinity had not risen spontaneously. No clinical tendency to acidosis was left behind. The CO_2 capacity remained fully normal. The ferric chloride reaction cleared up completely during the second fast and remained negative. The ammonia fell steeply during both fasts, reached its lowest level during the carbohydrate test, and rose as high as 0.8 to 1.1 gm. N on the subsequent mixed diet, it being at this time the sole indication of slight acidosis. It is noteworthy that even though the diabetes was clearly worse than at the former admission and the carbohydrate in the diet so much less, the markedly low diet as respects fat and calories now prevented the excretion of diacetic acid which was almost constantly present during the former period in hospital.

Blood Sugar.—The peculiarities during fasting were mentioned above. On the carbohydrate test the fasting blood sugar remained stationary at 0.2 per cent and the plasma sugar rose to 0.228 per cent. On mixed diet the tendency of the blood sugar was downward, the normal value on July 24, following the fast-day of July 23, showing that the hyperglycemia was still readily capable of control by a low caloric diet. The slight increase in diet at discharge brought a return of moderate hyperglycemia.

Body Weight.—The difference between loss of weight produced by underfeeding for therapeutic benefit and the injurious emaciation resulting from unchecked diabetes is exemplified.

This brief period in hospital gives an unusually striking illustration of the possible fluctuations in water content of the tissues of diabetics, as shown by the contour of the weight curve. As usual it fell slightly during the first days of fasting. The slight rise due to edema toward the close of the fast is not uncommon. The unique feature is the continued steep ascent on the low protein-fat diet of June 20 to 23. It reached 50 kg. and remained there during the 4 day fast; *i.e.*, a gain of 8.4 kg. in the week June 16 to 24. The edema was so intense that there were pressure pains in the legs. It was presumably of renal (no albumin or casts) or obscure metabolic origin, possibly standing in some relation with the peculiar leap of the blood sugar, and evidently associated with chloride reten-

tion, for salt-free diet brought a fall almost as rapid as the rise. Though the diet beginning June 10 was low, the weight rose again without visible edema. The increase (45.7 kg. at discharge as compared with 42.2 kg. at admission) probably represents largely water retention by tissues formerly abnormally dried.

Undernutrition.—The following calculation can be made for 46 days of the second hospital period (June 9 to July 25):

	46 days.	Per day (average).
Protein in diet.....	1,535.2 gm.	33.4 gm.
Nitrogen " "	245.6 "	5.34 "
Total nitrogen excreted.....	334.64 "	7.27 "
Nitrogen deficit (output—intake).....	89.04 "	1.93 "
Total calories in diet.....	29,737	647

Subsequent History.—On Aug. 23 the patient reported that he was feeling constantly better. The urine was uniformly negative for both sugar and ferric chloride reactions. The sugar in whole blood was 0.117 per cent, in plasma 0.128 per cent, CO₂ capacity 51.8 per cent. Weight 46.8 kg. An increase of 5 gm. carbohydrate was permitted and tolerated. In Sept. an increase of fat, so as to make the total calories 1830, was permitted. The weight was then 48 kg. The patient was at work and professed himself contented with his condition and diet. On Nov. 26, a letter was received expressing deep gratitude, and stating that he had followed diet but wished to relieve himself of his former pledge; though he intended to make no radical changes, he nevertheless proposed to follow his own discretion. The next report received was a telegram on Feb. 2, 1917, announcing that the patient had died at 8 o'clock that day.

Remarks.—The case presents two possible etiologic factors; namely, heredity and infection. Diets to the verge of tolerance were permitted, partly because of the unstable temperament, but largely because their injurious effects were not properly understood. They were fairly well borne for a number of months as usual, but did not serve to prevent the patient from breaking treatment. They perhaps did more harm than the record indicates. It seems possible that on the basis of a mild or moderate inherited tendency, active diabetes had been developed and maintained by a series of acute infections. With the clearing up of the infections and of diabetic symptoms there was seemingly a marked tendency to improvement, as indicated by the rapidly acquired tolerance for high diets. Possibly under sufficiently careful treatment the diabetes might to some extent have become latent. The tendency to improvement was probably crippled by the high diets employed. It is certain that seemingly brilliant success often masks irreparable injury. After months or years of overdriven function a permanent and hopeless lowering of assimilation is found, which is blamed upon "spontaneous downward progress." In this instance the actual disaster was precipitated by Christian Science; but in any case with acute infectious etiology,

there is always the possibility that early thorough relief of dietary strain may permit a degree of recovery sufficient to protect against such a misfortune.

On the second admission to the hospital the patient had learned a severe lesson and was amenable to discipline. The results show that although his case had become more severe, it was still readily controlled by radical treatment, and on better treatment than before the laboratory findings were somewhat better, though the weight and strength were less. After discharge the tendency to a slow recovery of tolerance and weight was still manifest. This time New Thought literature overcame the patient's fears, when he began to feel like himself once more. He was of the neurotic nature predisposed to such aberrations, and they were responsible for his death.

CASE NO. 37.

Male, unmarried, age 16 yrs. American; high school student. Admitted Mar. 19, 1915.

Family History.—Mother, father, two brothers, and one sister well. No special disease in family.

Past History.—Healthy life under excellent conditions in New York City. Measles and chicken-pox in infancy. No venereal or other diseases. Never used alcohol or tobacco. No excesses in diet. Up to 2 years ago his family complained that he did not eat enough. Since then he has been "always ready to eat." Has the usual appetite for candy, but has not taken more sweets than most boys. Never nervous or overstudious. Has been content to stand about the middle of his class, has taken part in athletics and is now captain of the basket-ball team of his high school. Lately he has had toothache, and just before admission to hospital an abscess about one molar.

Present Illness.—3 weeks before admission patient caught a severe cold in connection with a hard game of basket-ball. The following day he felt considerable thirst, which he attributed to the fever accompanying the cold. Polydipsia and polyuria continued, and his family noticed a lack of energy. The symptoms progressed until, about a week ago, he was drinking water and passing urine approximately every 40 minutes. Appetite seemed to be unchanged. He has been sleepy the past few days. The family physician, who was then called, made an immediate diagnosis of diabetes, gave sodium bicarbonate, and advised coming to this hospital. The patient came unaccompanied, merely for examination. The signs of impending coma were such that he was put to bed immediately and his family notified.

Physical Examination.—A well developed, firm muscled boy, looking perfectly healthy except for the unnatural flush of the cheeks, noticeable dyspnea, odor of acetone, and marked sleepiness. Tongue red and slightly coated. Teeth show considerable caries and slight pyorrhea. Throat congested; tonsils enlarged to olive size. Small lymph nodes palpable in cervical, axillary, epitrochlear, and inguinal regions. Knee and other reflexes active. Blood pressure 120 systolic, 90 diastolic. Examination otherwise negative.

Treatment.—Owing to the urgent symptoms, fasting was begun immediately. The urine from 5 p.m., the hour of admission, to 7 a.m. showed 71.3 gm. sugar and intense ferric chloride reaction. The carbon dioxide capacity of the plasma was 25 vol. per cent at admission. 10 gm. sodium bicarbonate and 70 cc. whisky were given during the night. Mar. 20, the dosage was 30 gm. bicarbonate and 160 cc. whisky daily. By this time the threatening clinical symptoms had passed off. Mar. 22, the bicarbonate was diminished to 10 gm., and then discontinued. Whisky was not used after Mar. 24. Glycosuria was absent on Mar. 27, the ferric chloride reaction was slight, the carbon dioxide capacity of the plasma was approximately normal, and the ammonia nitrogen, which on Mar. 20 was 5.62 gm., had fallen to 0.73 gm. The blood sugar, which was 0.21 per cent at admission, fell steadily to 0.1 per cent on Mar. 31. On Mar. 29, 10 gm. carbohydrate in the form of green vegetables were given, and increased rather rapidly. On Apr. 12 to 14, 175 gm. daily were assimilated, but the increase to 200 gm. carbohydrate on Apr. 15 brought slight glycosuria. After the fast-day of Apr. 16, eggs, bacon, and vegetables were allowed on Apr. 17, representing 33 gm. protein, 15 gm. carbohydrate, and 770 calories. Slight glycosuria resulted, as sometimes happens with a diet following a fast-day. This cleared up, and higher diets were quickly tolerated with only bare traces of glycosuria. From the latter part of May to Aug., the diets were about 2500 calories, comprising 90 to 100 gm. protein and increasing carbohydrate up to 205 gm. On July 31, after the fast-day on Aug. 1, another tolerance test was instituted, and in order to give the requisite quantities of carbohydrate it was necessary to include such foods as potatoes, corn, lima beans, peaches, and bananas. On Aug. 6, 400 gm. carbohydrate with 83 gm. vegetable protein were assimilated. Glycosuria occurred on Aug. 7 with 500 gm. carbohydrate and 118 gm. vegetable protein. The glycosuria ceased with a green day on Aug. 8, representing 24 gm. protein and 103 gm. carbohydrate. The patient was dismissed Aug. 11 on a diet of 100 gm. protein, 100 gm. carbohydrate, and 2450 calories. He looked and felt entirely well and was permitted to resume school work. The only special incident in hospital was the necessary dental work to bring his mouth into good condition, including the extraction of three molar teeth, which was done without ill effects.

Acidosis.—The clearing up of the various signs of impending coma on fasting was noted above. The carbon dioxide capacity of the plasma fell slightly following the discontinuance of soda on Mar. 22, also following discontinuance of whisky on Mar. 24. In each case it readily rose again, and it is probable that neither alkali nor alcohol played an essential rôle. The ferric chloride reactions and the ammonia showed no such influence. On the carbohydrate test (Apr. 3 to 15) the ferric chloride reaction became entirely negative. On beginning mixed diet, nothing was definitely altered in the CO₂ capacity, and the ammonia was only slightly higher, but ferric chloride reactions began to recur as the caloric intake was raised, notwithstanding the fact that carbohydrate was similarly increased. Such reactions persisted up to May 22, with 50 gm. carbohydrate in

the diet. Further increase to 65 gm. carbohydrate abolished them, and they remained absent with further increase of carbohydrate, even though fat was also increased.

Blood Sugar.—The curve shows the characteristics of an early case, still in the mild stage. It returned quickly to normal, rose only slightly as the diet was built up, then became and remained continuously normal, notwithstanding the high diet.

Weight and Nutrition.—For nearly the first month in hospital there was under-nutrition. The practical abstinence from protein for 29 days is noteworthy, and there must have been a large loss of body nitrogen. The weight fell during the first part of the fast to Mar. 25, then began to rise on fasting with only 600 cc. soup and 300 cc. coffee daily, and continued to rise on green vegetables, until on Apr. 3 it was 1.2 kg. higher than at admission and there was visible edema of face and ankles. The weight then diminished spontaneously, but water retention evidently persisted, for the lowest point was gradually reached on May 10, when the diet was theoretically adequate. A slow continuous gain followed, and at discharge the weight was approximately the same as at admission.

The diet prescribed at discharge represented over 2 gm. protein and 50 calories per kg. of weight, diminished one-seventh by the weekly fast-days. Consideration was taken of the fact that the patient was a growing boy; also activity had been gradually increased, so that by July he was walking 7 miles daily in addition to other exercise. He was encouraged to develop his muscles, avoid mental strain, and plan a vocation in line with these purposes. In view of the normal results of all clinical and laboratory tests, the attempt was made to let him develop as nearly normally as possible, and the liberal diet was permitted to this end.

Subsequent History.—The urine remained normal, and the patient kept up with his school work and exercised by bicycling and skating. On Oct. 9, the weight was 50 kg., it having been kept down by exercise as ordered. The physical and subjective condition was excellent, but sugar was found to be 0.232 per cent in whole blood, 0.270 per cent in plasma. Increase of exercise was advised instead of reduction of diet. Competitive sports had been strictly forbidden for fear of excitement and strain. This was the only point in which the patient was disobedient, for he resumed basket-ball and participated in interscholastic matches. More dental work was necessary, and three trips to the dentist were followed by slight glycosuria each time. The carbohydrate was diminished to 40 gm., and the dental operations thereafter produced no glycosuria, illustrating the usual dietary factor. The blood sugar continued to rise, being 0.263 and 0.285 per cent in whole blood and 0.344 per cent in plasma on successive examinations. Undoubtedly exercise, by consuming surplus calories and keeping down weight, delayed the progress of the diabetes far beyond the period at which active symptoms would have developed at rest; but it was not able entirely to take the place of caloric restriction. By request, the patient returned to the hospital during his school holidays, after Christmas, for observation.

Second Admission.—The weight was now 53.8 kg.; *i.e.*, a gain of 6.2 kg. since the first admission. There were barely perceptible sugar and ferric chloride reactions. After 2 days of fasting a carbohydrate tolerance test was begun on Dec. 29. Glycosuria resulted with only 175 gm. carbohydrate on Jan. 2, 1916, and persisted when this intake was continued for 3 days. It ceased following the green day of Jan. 5, when only 41 gm. carbohydrate were taken. Also the blood sugar, which on Dec. 30 was 0.35 per cent, fell to 0.164 per cent on the morning of Jan. 6. The patient was discharged on Jan. 9 and allowed to return to school, on a diet of 100 gm. protein, 5 gm. carbohydrate, and 2100 calories (approximately 2 gm. protein and 40 calories per kg. on 52 kg. weight, diminished by the weekly fast-days). Clinically the condition was perfect, and laboratory findings were normal except for the hyperglycemia.

Subsequent History.—The patient did not do so well this time, showed traces of sugar frequently and lost weight by reason of the consequent fasting. Instructions were sent for him to return to the hospital, but he was unwilling to give up his school work. Early in Feb. there was constipation and an attack of colicky abdominal pain without fever or nausea, but with glycosuria. The patient hoped to fast himself sugar-free without stopping school. He fasted 8 days, attending school during the first 6. Glycosuria increased instead of diminishing. On Feb. 17 he was too weak to fast, and spent that and the following day lying down at home without nausea or vomiting, with increasing dyspnea and drowsiness. The only food eaten during the 8 days was four eggs and some bacon on Feb. 18. This seemed to give a little strength.

Third Admission.—The patient was readmitted at 3:15 p. m., Feb. 19, stuporous, but intelligent when roused, with deep noisy respirations, 25 per minute; typical odor; temperature 97.6°F., pulse 114, small and thready; cheeks unnaturally flushed and pinched; tongue dry and red; urine showing intense sugar and ferric chloride reactions, containing enormous numbers of casts, and turning to a solid curd of albumin with the heat-acetic test.

At admission, the CO₂ capacity of the plasma was 26.4 vol. per cent. In the absence of nausea, the bowels were moved by calomel in divided doses followed by 30 cc. 50 per cent magnesium sulfate solution and a colon irrigation. Plain fasting was imposed, with 150 cc. clear soup, and the patient was urged to drink as much water as possible, the fluid intake on this fast-day thus amounting to 1680 cc. By the next morning the clinical appearance was practically unchanged, but the CO₂ capacity of the plasma had fallen slightly, to 24.2 per cent. Because of this fact, and because the acidosis symptoms were said to have come on as a result of prolonged fasting, it was decided to feed as nearly a pure protein diet as possible, and to give moderate doses of sodium bicarbonate such as would probably not derange the stomach. The diet consisted of 600 cc. clear soup, 600 cc. coffee, 300 gm. thrice boiled vegetables, steak, and white of egg, with addition of 10 gm. sodium chloride daily. The record is summarized in Table X.

TABLE X.

Date.	Diet.			Weight. kg.	Sodium bicarbon- ate.	Fluid intake. cc.	Volume. cc.	Urine.			Blood plasma.				
	Protein. gm.	Fat. gm.	Calories.					Sugar. gm.	Total nitrogen. gm.	D.N. ratio.	NH ₄ -N gm.	FeCl ₃ reaction.	Sugar. per cent	CO ₂ vol. per cent	
1916															
Feb. 20	162.8	19.0	843	44.9	30	3850	3774	100.0	28.50	3.53	6.62	++++	0.278	24.2	
" 21	93.9	22.8	598	44.8	40	4350	3980	87.0	32.32	2.72	5.71	++++	0.476	34.3	
" 22	93.9	22.8	598	44.6	20	3850	3620	79.0	28.92	2.72	5.44	++++	0.256	33.0	
" 23	93.9	22.8	598	44.6	40	4000	4005	103.0	31.69	3.24	5.36	++++	0.256	44.8	
" 24	63.0	15.2	399	45.0	40	4250	3395	67.9	26.85	2.69	3.96	++++	0.200	47.0	
" 25	63.0	15.2	399	46.0	40	4000	3375	59.0	19.55	3.02	2.95	++++	0.250	53.2	
" 26	63.0	15.2	399	47.0	40	5950	3580	53.8	19.82	2.71	2.55	++++	—	—	
" 27	31.5	7.6	200	48.4	25	6100	4180	48.1	21.40	2.24	2.39	++++	—	—	
" 28	31.5	7.6	200	49.0	—	6400	4460	28.6	17.96	1.59	2.66	++++	0.270	61.0	
" 29	31.5	7.6	200	49.8	—	6100	5608	35.8	—	—	—	++++	—	—	
Mar. 1	Fast-day.			48.0	—	5400	5590	23.9	12.85	1.74	1.25	+	0.285	60.6	
" 2	"			48.0	—	5800	5215	+	—	—	—	+	—	—	
" 3	"			47.4	—	4000	3450	+	—	—	0.87	0	*	54.8	
" 4	"			47.2	—	4400	3788	+	—	—	—	0	—	—	
" 5	"			47.2	—	3500	3725	0	—	—	—	0	—	—	

* Whole blood.

By Feb. 21, clinical improvement was perceptible and the albumin and casts had almost disappeared. Thereafter clinical betterment was rapid. The patient was kept in bed on account of weakness until Mar. 2, after which, notwithstanding the fasting, his strength permitted being up. The diet as shown represents first a high and subsequently diminished protein ration, with continuous undernutrition from the total energy standpoint. Glycosuria diminished but did not cease, and there was a still more marked subsidence of signs of acidosis. Beginning Mar. 1 fasting was instituted, with 300 cc. clear soup, 300 cc. coffee, and 10 gm. sodium chloride daily. The glycosuria cleared up uneventfully, also the ferric chloride reaction became entirely negative even during the fast. The diet was subsequently built up gradually in the usual way, and the patient was discharged July 29, 1916, weighing 39.6 kg., on a carbohydrate-free diet of 80 gm. protein and 1550 calories, without fast-days unless demanded by glycosuria (approximately 2 gm. protein and 39 calories per kg.). Not only was the carbohydrate tolerance practically nil, but the patient was now a thin semi-invalid, cheerful and able to be about, but contrasting strongly with the fully healthy appearing lad that he was at the former discharge. Though the urine was free from sugar and ferric chloride reactions, and the ammonia excretion and plasma bicarbonate were within normal limits, hyperglycemia was persistent. A bad prognosis was given.

Acidosis.—An example is afforded of the treatment of coma coming on during fasting, by means of protein feeding and moderate doses of alkali. Fat would presumably be harmful, both as furnishing acetone bodies directly and as detracting from the desired undernutrition. The value of carbohydrate is questionable with such high glycosuria, hyperglycemia, and D: N ratios. Protein presumably serves to protect body nitrogen, maintain strength, and supply material for ammonia formation, in addition to serving as a source of carbohydrate and to promote diuresis. In this instance such treatment was successful when prolonged fasting, aided only with alkali, probably would have ended fatally.

Subsequent History.—The patient remained free from glycosuria at home except for occasional traces cleared up promptly by fast-days. At the beginning of Sept. he developed a cold and simultaneous glycosuria. He was accordingly readmitted to hospital Sept. 5, 1916.

Fourth Admission.—The weight was 38.2 kg. The patient was not so strong as before, and had lost hope. No alarming symptoms were present, but a fast of 8 days was required to clear up the heavy glycosuria and ketonuria. A carbohydrate tolerance test with green vegetables alone showed a tolerance of 60 gm. carbohydrate under these conditions; but no carbohydrate was tolerated with mixed diet, and an intake of 60 gm. protein and 1200 calories was the maximum possible without glycosuria. The patient's appearance suggested tuberculosis, but the cold passed off readily with the clearing up of other symptoms by fasting, and there were no later symptoms or findings on examination suggesting tuberculosis. The patient was discharged on Oct. 4, 1916, weighing only 35.2 kg., on a diet of 50 gm. protein and 1000 calories (1.4 gm. protein and 28 calories per kg.). From the laboratory standpoint the condition was as before; *i. e.*, nearly normal urine with persistent hyperglycemia.

Subsequent History.—The patient passed through another cold late in Nov., for which he was treated by a private physician who did not attempt to abolish glycosuria and ketonuria. The cold passed off, but when seen Dec. 13 the patient was in very bad condition, with edema of face and legs, and too weak to rise from a chair without help. He was on a diet of 38 gm. protein, 10 gm. carbohydrate, and 1000 calories, with continuous glycosuria and ketonuria. By Feb. 2 the strength had slightly improved, and edema was absent. He was on a diet of 40 gm. protein, 10 gm. carbohydrate, and 1200 calories, with sodium bicarbonate. Death occurred suddenly and without special symptoms, Mar. 29, 1917.

Remarks.—This was an early case of diabetes in the best type of patient, with hereditary taint excluded as thoroughly as possible, and with the utmost intelligence and fidelity in respect to everything pertaining to the treatment. The early course was rapidly downward, threatening coma within 3 weeks, and the case was then of the type generally described in text-books heretofore as uncontrollable. These symptoms were promptly and easily cleared up, and a result was achieved which, according to former standards, was ideal. All clinical and urinary symptoms were abolished and a high carbohydrate tolerance was restored. Weight and strength were built up, and the blood sugar also was normal. The attempt was made to let the patient return to normal activities on a liberal caloric ration. The activity may have been permissible. The diet was calamitous. It is not to be supposed that the carbohydrate allowance was too high. There is not necessarily any harm in the fact that the protein at the first discharge was up to the Voit standard (1.7 gm. per kg.; one-sixth of total calories). But the average energy intake was 43 calories per kg. Vigorous exercise and moderate restriction of weight did not atone for this overload imposed upon a weakened metabolism. Efficiency and health are known to be possible on a far lower intake. With some reduction of weight, life could have been well maintained on half to two-thirds this number of total calories. As usual, the time actually arrived later when the boy was compelled to live on less than half this number of calories. The fatal mistake lay in imposing this strain upon his weakened function at the outset, so that it later broke down and was incapable of carrying adequately half this burden. The proper treatment would clearly have consisted in limiting the burden in the first place, so as to avoid such a breakdown. The case is a perfect example of what was formerly called "spontaneous downward progress" in diabetes.

By comparison with other cases taken under far worse conditions and treated on a different principle, it can be concluded that the downward progress in this case was due chiefly or solely to the treatment employed. Even in the later stages the diets permitted were such as taxed the weakened tolerance to the utmost. But the essential harm was done at the most favorable period, and the fatal outcome was assured by the methods employed at the very time when the prognosis seemed brightest.

CASE NO. 38.

Female, married, age 39 yrs. Russian Jew; housewife. Admitted Mar. 20, 1915.

Family History.—Father died at 65. Mother, one brother and sister are well; one brother died of phthisis. No other diseases known.

Past History.—No illnesses known. Said to have been treated at a hospital 2 years ago for "large liver and abdomen," cured by wearing a support. Habits, appetite, and bowel action normal. No excesses. Last menstruation was 5 months and 3 weeks before admission.

Present Illness.—Began with chilly sensations and malaise 1 week ago, followed by cough, fever, and pain, particularly in left lower chest.

Physical Examination.—A well developed and nourished woman, 5 or 6 months pregnant; flushed cheeks, slightly bluish lips; lying in bed breathing about 40 times per minute and groaning frequently. Tongue coated and dry; teeth false; tonsils and lymph nodes not enlarged. Pulse 110, temperature 102.8°. Blood pressure 150 systolic, 90 diastolic. Signs of pneumonia of left lower lobe. Liver edge 3 cm. below costal margin. Knee jerks not obtainable. Examination otherwise negative. Sputum was mucopurulent, yellowish gray, containing Gram-positive diplococci, not agglutinated by Pneumonia Serum I or II. Blood culture was sterile. Leucocytes 22,000, polymorphonuclears 91 per cent, lymphocytes 5 per cent, large mononuclears 4 per cent. Urine contained some albumin and casts and showed heavy sugar and ferric chloride reactions.

Treatment.—The patient was received on the pneumonia service, and the finding of diabetes was unexpected. The temperature fell to normal within 24 hours, but the pulse and respiration continued elevated.

After death a needle inserted in the third intercostal space close to the sternum, with the idea of obtaining blood from the heart, yielded an abundance of very turbid gray fluid, which clotted quickly on standing, showed leucocytes but no bacteria in films, and was sterile on culture—apparently a large pericardial effusion. Necropsy was not permitted.

Remarks.—This is another example of diabetes discovered during the course of an acute infection. Whether the infection produced it, or (more probably) made active a latent or mild diabetes, is undetermined. The severity of the acidosis is indicated by the low blood bicarbonate with large doses of alkali. In expectation of the use of such doses, cathartics were omitted, and, as anticipated, moderate persistent diarrhea was kept up by the bicarbonate, the discrepancy between fluid intake and output being thus accounted for. The impression was created that the alkali in such doses was definitely beneficial, and that smaller doses would not have sufficed. Notwithstanding the combination of infection and existing coma on Mar. 26, the acidosis symptoms passed off, and the blood bicarbonate on the day of death was nearly normal. It is possible that death was partly due to the diabetic intoxication, which may exist in the absence of some of the signs of acidosis, but there is entirely sufficient cause for death

TABLE XI.

Date.	Temperature.	Food.	Sodium bicarbonate.	Calcium carbonate.	Fluid intake.	Urine.		Blood.		Remarks.
						Volume.	Sugar.	Sugar.	CO ₂	
	°F.		gm.	gm.	cc.	cc.	gm.	per cent	vol. per cent	
1915 Mar. 21	101.3 98.4	Milk 920 cc. Celery soup 150 cc.	20	0	3000	975	30.4	—	—	
"	102.4 99	Orange albumin 1230 cc. Soup 600 cc. Whisky 110 cc.	20	0	3730	2520	75.6	—	—	
"	102 99	Orange albumin 450 cc. Soup 550 cc. Whisky 100 cc. Cream 60 cc.	20	0	2830	1795	64.0	—	—	Paracentesis for pain in right ear. Pus showed pure cul- ture pneumococcus. Pa- tient drowsy.
"	102.4 99.6	Orange albumin 820 cc. Soup 300 cc. Whisky 120 cc. Cream 60 cc. + Albu- min 2 eggs.	20	0	3790	1800	59.0	—	—	Very drowsy.
"	101.6 99.8	Orange albumin 200 cc. Soup 500 cc. Whisky 110 cc. Cream 60 cc. + Albu- min 2 eggs. Asparagus 100 gm. String beans 100 gm.	20	0	3200	3200	75.8	—	—	Dozes most of time.

CASE RECORDS

Jan. 26	100.4 98.6	Fasting. Whisky 160 cc.	125	90	5770	2620	48.5	0.161	19.5	Beginning coma. Patient can barely be roused. Typical Kussmaul breathing. High enema of 4 per cent bicarbonate expelled. In addition to 5770 cc. fluids by mouth, 600 cc. saline were given intravenously and 1450 cc. subcutaneously.
" 27	99.3 98.4	" " 120 "	110	110	6000	3420	56.8	0.285	30.5	Coma symptoms diminished.
" 28	99.5 97.8	" " 20 "	30	30	3700	3040	49.9	—	—	Nauseated from soda. Mind clear. Breathing normal. D : N 3.22.
" 29	99 98.4	" " 50 "	70	70	2800	2020	45.9	0.385	46.6	Morning blood. Nausea absent.
" 30	98.6 100	6 eggs with 30 cc. whisky.	40	30				0.365	64.5	9 p.m. blood. Premature delivery induced by insertion of bag without anesthesia with practically no disturbance. Fetus beginning to decompose.
								0.420	52.2	Considerable urine lost. Death.

without this assumption. It was not the intoxication sometimes attending upon fasting, because the typical nausea was absent, and the food retained on Mar. 29 brought no improvement. In summary, it may be said that pneumonia, middle ear infection, death of fetus with subsequent artificial delivery, and either pericarditis or empyema, constituted a sufficient explanation of the fatal result, and under these conditions 5 days of very low diet followed by 5 days of fasting failed to control the diabetes.

CASE NO. 39.

Female, unmarried, age 27 yrs. American; teacher. Admitted Apr. 3, 1915.

Family History.—A maternal grandfather died of cancer with suspicion of accompanying diabetes. A paternal aunt was insane 15 years ago, but has apparently recovered. Patient's mother died of diabetes at 37. Father is well, aged 70, but had nervous breakdown 25 years ago which kept him from work for 3 years. Strong neurotic element in family. A brother of patient is a young physician, of nervous temperament. A sister died of heart trouble within a few months after birth. No syphilis, tuberculosis, or other diseases known.

Past History.—General healthy life under good hygienic conditions in small New England towns. Several childhood diseases, including scarlet fever, said to have been followed by ear trouble and nephritis. No other illnesses. Habits regular; always nervous in disposition.

Present Illness.—About 4½ years ago headaches began and transitory polydipsia and polyuria. The patient was first dieted by a local physician, then beginning in the spring of 1913 she was under Dr. Joslin's care several times. He found her a model patient in hospital and the glycosuria was easy to stop, but the patient appeared mentally incompetent whenever she returned home and never had the will power to adhere to diet. On certain occasions she wandered from home in lapses of consciousness, and she was regarded by Dr. Joslin as definitely insane, though bright and active most of the time. In the summer of 1914, after heavy mental and physical strain, she suddenly lost consciousness for 1 day and was stuporous for 6 days thereafter. Her local physician called the condition diabetic coma. She recovered on fasting and bicarbonate. Thereafter she made some attempts to follow diet, but home conditions were difficult and glycosuria and ketonuria were continuous.

She was admitted to a New York hospital in Mar., 1915, with facial neuralgia of intense type. Here again glycosuria cleared up rather easily, but there was the same difficulty regarding adherence to diet, and here also the patient was considered mentally irresponsible to the point of insanity. The neuralgia, however, ceased with the improvement in the urinary symptoms. The patient was financially unable to remain longer under hospital expense, and was admitted to this Institute on Apr. 3, 1915, for the purpose of testing the effects of prolonged thorough treatment, not only upon the diabetes but also upon the nervous and mental condition.

Physical Examination.—Height 168.1 cm. A well developed and nourished, nervous appearing young woman. Hair thin, short, and dry. Eyes slightly prominent. Suspicion of slightly enlarged thyroid on palpation. Knee and ankle jerks normal. Examination otherwise negative.

Treatment.—Glycosuria and ketonuria were present. After a single fast-day on Apr. 4, notwithstanding faint traces of glycosuria, small quantities of green vegetables were begun. Glycosuria stopped even while they were increased, and remained absent until, on Apr. 15, the vegetable diet (including corn and peas) represented 42 gm. protein and 150 gm. carbohydrate. Although the fat in such diets was only 40 gm., marked ferric chloride reactions steadily persisted with this carbohydrate intake, and with 170 gm. carbohydrate on Apr. 16. Apr. 17 was a fast-day followed by diets of 800 and 450 calories on Apr. 18 and 19, and then 6 days of complete fasting, 150 cc. clear soup being permitted, except on Apr. 23 and 24, when nothing but water was given. The persistent glycosuria and elevated blood sugar strongly suggest surreptitious eating during this time. The usual diet was begun on Apr. 26 and rapidly increased, until for a short time after May 24, 90 to 100 gm. protein, 40 gm. carbohydrate, and 2300 calories were tolerated. On account of persistent slight glycosuria (June 3 to 7) fasting was imposed. No other interpretation seems possible than that this was due to forbidden food obtained in some manner not discovered; but the policy of fasting until glycosuria ceased was a salutary check to such practices. Thereafter a slightly lower diet was tolerated with occasional traces of glycosuria, some of which were confessedly, and others probably, due to candy or other prohibited foods. After fast-days on July 24 and 25, a carbohydrate test was instituted, and showed a tolerance of approximately 300 gm. carbohydrate in the form of green vegetables. The hospital discipline had benefited the patient, and this indication of improvement was a great encouragement to her.

She was discharged Aug. 13 on a diet of 100 gm. protein, 30 gm. carbohydrate, and 1900 calories (about 1.8 gm. protein and 34 calories per kg.), the weekly fast-days reducing the average to about 1.4 gm. protein and 30 calories per kg. She promised faithfully to adhere to this diet. There was unmistakable psychic as well as physical change in the patient, and though still nervous she was clearly more dependable and better fitted to take care of herself.

Acidosis.—At entrance the ammonia nitrogen was only 0.56 gm. and the ferric chloride reaction mostly no more than moderate; but the plasma bicarbonate showed the rather low level of 47 per cent on Apr. 5 and 45 per cent on Apr. 7. It thus fell slightly during the days of very low carbohydrate, which were almost equivalent to fast-days (10 gm. carbohydrate and 300 cc. soup daily). With continuance of undernutrition and slight increase of carbohydrate, it rose sharply within normal limits by Apr. 9, without the use of alkali. Thereafter the curve ran a normal course but seemed to tend to fall with fasting, being found slightly below normal on May 3, following the preceding fast-day, and again after fasting on July 26. The consistent course of the ammonia curve was low. A slight ferric

chloride reaction tended to persist. It gradually faded out and became negative in periods, and after the carbohydrate test in July and Aug. it became consistently negative.

Blood Sugar.—On Apr. 7, just as the glycosuria was clearing, the blood sugar was just below 0.2 per cent, indicating a normal renal threshold. With further days of low carbohydrate, it had fallen to normal on Apr. 9. The carbohydrate tolerance test led to hyperglycemia of 0.22 per cent with glycosuria on Apr. 16. The excessively high figure shown on Apr. 22 was not checked and therefore might have been a mistake. Thereafter the values tended to fall below 0.15 per cent. Other work made it necessary to stop the analyses on this case after May 18.

Weight and Nutrition.—The patient entered in a very well nourished condition weighing 59.2 kg. She was still well nourished at discharge, weighing 55.8 kg. The net result of treatment was thus undernutrition to the extent of a loss of 3.4 kg. With the clearing of diabetic symptoms there was the usual gain in strength and well-being, and the patient felt entirely well at discharge.

Subsequent History.—The patient resumed her regular work at home and followed diet surprisingly well. On three occasions she went on what she termed "sprees" of carbohydrate, but experienced symptoms of weakness and malaise within a limited number of hours after the onset of the heavy glycosuria, and cleared up her condition, generally after some delay, by fasting, on one or two occasions as long as 5 days. Against external as well as internal difficulties she kept up a continuous effort to remain sugar-free, and notwithstanding the lapses from diet, continued to gain in weight and subjective health. On account of sugar and ferric chloride reactions in urine specimens received, it became advisable to readmit the patient on Jan. 12, 1916, 5 months after discharge.

Second Admission.—The weight had now risen to 64.1 kg.; *i.e.*, 4.9 kg. more than at the former admission, and both the physical and mental condition appeared excellent. On the diet prescribed at discharge, the plasma sugar was 0.264 per cent and the CO₂ capacity 49 per cent. There was a heavy ferric chloride reaction, and 2.18 gm. ammonia nitrogen in the urine. Fast-days on Jan. 19 to 20 sufficed to clear up the glycosuria, but the tolerance on the ensuing days with green vegetables proved to be now only 50 gm. carbohydrate. Though diets lower in both carbohydrate and total calories were employed, it was difficult to obtain freedom from traces of glycosuria. During late Mar. and early Apr. there was decided intolerance for a diet of 65 gm. protein, 15 gm. carbohydrate, and 1500 calories. After Apr. 16, carbohydrate was excluded. Even on diets as low as 60 gm. protein and 1000 calories, traces of glycosuria recurred. But with continuance of this undernutrition they remained absent after May 2, and by May 12, 70 gm. protein and 1400 calories were tolerated. With reduction of one-seventh by weekly fast-days, this represented approximately 1 gm. protein and 20 calories per kg. of weight. The patient was discharged on this diet May 13, 1916.

Acidosis.—The CO₂ capacity of the plasma rose easily within normal limits without the aid of alkali, and remained so except for a single low reading on May 9. The ammonia excretion at the outset was much higher than before, *i. e.* 2.18 gm. N; also the ferric chloride reaction was heavier. Thus these signs indicated a higher acidosis than at the former admission, though the plasma bicarbonate was 2 per cent higher than then. Isolated determinations on Feb. 7 and 21 indicated about the same subsequent level of ammonia as at the previous period in hospital. The ferric chloride reaction cleared up much more easily and promptly than before, although the diets were so much poorer in carbohydrate than before and frequently carbohydrate-free. This result is explained by two causes, first, the previous treatment, and, second, the lower total caloric value of the diets at this admission. The ferric chloride reaction was thus negative on carbohydrate-free diet at discharge.

Blood Sugar.—An aggravation of the condition was indicated by the fact that even on low diets the blood sugar never became normal, but remained above, rather than below 0.15 per cent. More rigorous treatment could presumably have reduced the hyperglycemia even at this stage.

Weight and Nutrition.—The patient's gain in weight during her absence from hospital would once have been regarded as an improvement. Its real meaning is that the diabetes was sufficiently mild to permit a gain in weight even in the presence of glycosuria, and in this mild stage injury was wrought by exceeding the true functional power with respect to both diet and weight. After readmission to hospital, the weight at first fell from undernutrition, then fluctuated, and on two occasions, namely Mar. 7 and 8, and Apr. 28, rose higher than at admission, because of marked edema. This edema was not associated with any alkali administration, but may have been due to sodium chloride. The weight at discharge was 61.2 kg., being 2 kg. higher than at the first admission and 2.9 kg. lower than at the second admission. A portion of this weight may still have been abnormally retained water, which however was not apparent on examination. The diets in general represented undernutrition, and the diet at discharge meant further undernutrition and reduction of weight.

Subsequent History.—The patient undertook to support herself by visiting and other duties in connection with diabetic patients of a physician in New York, and one stay at a country place was also arranged. She remained free from glycosuria through the summer, but her diet became uncertain by reason of her preparing her own meals under irregular conditions and making trials of various modifications to suit herself. She finally undertook too heavy a load of work and took too high diets in the attempt to keep up with her ambitions. She managed to remain in fair condition as respects diabetes, and in good condition as respects general health, until readmitted Dec. 30, 1916.

Third Admission.—The weight was still 62.7 kg., partly due to edema. The general appearance, strength, and behavior showed no perceptible change. Downward progress was indicated by the fact that a 7 day fast was neces-

sary this time to bring the glycosuria under control. The subsequent history in hospital was uneventful. The patient broke diet on a few occasions, otherwise she was maintained sugar-free, and was dismissed Apr. 10, 1917, weighting 57.2 kg. on a diet of 60 gm. protein, 2.5 gm. carbohydrate, and 1300 calories. The patient's intentions in regard to work were now the principal difficulty. She was determined to carry a heavy load of work, and was not willing to undergo undernutrition to a point which would diminish her working capacity. As inevitable in such cases, the long abuse of the weakened assimilative power had now brought the point where maintenance of full weight and working power was impossible. The tolerance could be benefited only by undernutrition diets such as prescribed. Such reduction must continue for several months before any gain could be expected, and the damage already wrought was such that a full return to the former tolerance was undoubtedly impossible. The patient, though intelligent and grateful, was unwilling to accept life on these terms, and proposed from her knowledge of diets to nourish herself with a view to temporary working capacity as long as possible.

Subsequent History.—The patient took mixed diet with restriction of all three classes of food, but the period of ability to work was very brief. All her former symptoms quickly returned except the neuralgia. The mental abnormality again showed itself markedly. Though appearing bright and merely nervous in public, in private she tore her clothing, bit and otherwise injured herself, and made several attempts at suicide. She recognized symptoms of acidosis, and accordingly excluded fat almost completely from her diet. It was learned indirectly that she was in serious condition, and she was accordingly sent for and brought back to the hospital by a nurse on June 18, 1917.

Fourth Admission.—There was a history of edema a week before. The patient took two capsules of 8 grains diuretin, and edema is said to have disappeared rapidly, and epigastric pain began. Since then weakness and dyspnea have rapidly increased, so that she has remained lying down for the past 2 days. On the day before admission there was nausea and vomiting, and she took two teaspoonfuls of sodium bicarbonate; otherwise she has had no alkali. Also during these 2 days she claims to have fasted, partly from lack of appetite and partly in the attempt to treat herself for acidosis. Weight was 58.1 kg.; *i.e.*, 1.1 kg. less than at first admission. The patient lay in bed, evidently extremely weak. The general appearance was about as before. Neither emaciation nor edema was present, also the tissues were not perceptibly dry or flabby. There was a deep dusky flush of cheeks, involving lower eyelids. Air-hunger was intense; deep pauseless respirations 22 to 23 per minute as the patient lay in bed; so extreme on the slightest exertion that drinking and speaking were difficult. The patient dozed continually when undisturbed, but roused easily and rather nervously. Intelligence was fully clear, and she was entirely cheerful, while convinced that death was imminent. Physical examination was negative except for a row of herpes vesicles beginning to dry up under the left breast.

These and associated tenderness explained the epigastric pain still complained of, as due to intercostal neuralgia.

Inasmuch as symptoms of serious acidosis had begun and persisted while fat was diminished or even excluded from the diet, and signs of coma had appeared after 2 days of supposedly complete fasting, it was difficult to decide upon a line of treatment for the threatening crisis. It was feared that the existing nausea would be increased by alkali. An attempt was therefore made first with plain fasting with soup and coffee and water forced to the limit of capacity. The plasma bicarbonate was 30.5 per cent, the heart and kidneys were keeping up well, and there was no sign of immediate death. It therefore seemed most conservative to wait a few hours to learn the behavior under fasting alone. The actual progress was rapidly downward, perhaps partly on account of exhaustion from the trip to the hospital. Unmistakable progress into coma was evident. The patient was received at 4:30 p.m. By evening moderate doses of alkali by mouth were begun; by midnight there had been given 10 gm. sodium bicarbonate, 30 cc. whisky, and 2105 cc. total fluids. By 9 a.m. June 19, an additional 15 gm. sodium bicarbonate and 30 cc. whisky had been taken, yet the plasma CO_2 had fallen to 20.7 per cent, and the sugar and total acetone of the plasma were decidedly increased. During June 19, 1 gm. doses of sodium bicarbonate were given hourly with 5 gm. doses of calcium carbonate, in the hope that the latter would help settle the stomach and possibly have some acid-neutralizing power. Whisky was given in 15 cc. doses every 4 hours, 1800 cc. soup during the day, and 15 gm. sodium bicarbonate. The total fluid intake was 9805 cc. By 10:30 p.m. improvement seemed to have been obtained. The breathing seemed quieter, the consciousness clearer, and the CO_2 capacity had risen to 27.7 per cent. By the next morning the patient had begun to refuse bicarbonate because of nausea, and the coma symptoms showed increase. An attempt was therefore made to supply fluid and a moderate quantity of alkali intravenously. Accordingly, 500 cc. physiological saline solution containing 13 gm. sodium bicarbonate were given slowly through a needle. The breathing became quieter, but an attack of vomiting resulted and consciousness did not improve. It was then attempted to feed protein in the form of white of egg mixed in the soup. The small quantities thus given were retained several hours, then vomited. Complete unconsciousness came on, with continuance of the intense dyspnea, and nothing seemed left but to attempt to raise the blood alkalinity by larger doses of soda intravenously, notwithstanding the known danger. Accordingly 1 liter of saline solution containing 38 gm. sodium bicarbonate was given in an injection into the arm vein in half an hour. Dyspnea diminished. The pulse, which was strong, was unchanged. The flush of the cheeks became paler. Consciousness was not restored, and an attack of vomiting was excited. Unconsciousness with slight restlessness continued until 5 p.m., when there occurred the sudden death without warning which is rather characteristic following large intravenous doses of alkali. The principal data are contained in Table XII.

Remarks.—This was one of the cases with exaggerated protein catabolism, as indicated by the nitrogen excretion of 23.7 gm. on June 19. On June 20, an equal or higher quantity must have been eliminated, but large quantities of urine passed involuntarily were lost, and also death occurred at the end of 17 hours of this day. Any error of diet as an explanation of the high D : N ratios is excluded, as the patient was stuporous and isolated in a room with a special nurse. Only 2 days of fasting, according to the patient's report, had intervened since her period of liberal diet, including carbohydrate. The nutrition was well maintained as stated, and it must be assumed that with the rapid and intense change for the worse, body glycogen was being swept out.

Several lines of treatment are open in such a case, but death occurs in a great majority under these circumstances no matter what is done. Treatment without alkali and without food, but supplying fluid and salt, was first tried with ominous results. Another possibility would have been fasting with alkali from the outset. Dosage by mouth could have accomplished nothing more by reason of nausea. There might have been some real helpfulness in small intravenous doses of bicarbonate at intervals of a few hours, perhaps alternating with doses by mouth. It appeared, however, that considerable quantities of alkali were necessary to affect the blood alkalinity, and this excited nausea even when given intravenously. Another possibility lay in feeding with or without alkali. It is highly questionable if carbohydrate is of any benefit in the presence of a maximal D : N ratio. Fat would seem to promise nothing but harm. Protein might have been beneficial; but again it may be that an attempt to feed anything will sometimes aggravate a condition of impending coma. A noteworthy feature is the fact that the renal function was well maintained to the end, and large quantities of urine were passed involuntarily in the closing hours of life. It is now less common for patients received with impending coma to go into coma under treatment, but with the exaggerated protein catabolism and continued maximal D : N ratios, such a result is still often unavoidable.

In its general aspects the case illustrates the interrelation of diabetes and nervous disorder, and the actual symptomatic improvement of the latter under careful treatment of the former. Had either the psychic state or the environment been more favorable, something might have been accomplished; but with both adverse, the patient made a brave effort but lost in the end.

CASE NO. 40.

Male, unmarried, age 29 yrs. American; doorman. Admitted Apr. 12, 1915.

Family History.—Little known; no history of disease obtainable.

Past History.—Measles, whooping-cough, scarlet fever in childhood. Right-sided pneumonia 15 years ago. Neisser infection, also chancre some years ago; no secondary symptoms and no treatment. Frequent colds, but rarely sore

throat. Formerly used whisky to excess, but recent alcoholism denied. He smokes pipe and cigars in moderation, and takes two cups of coffee and three of tea a day. He sleeps well, has poor appetite, and regular bowels. No known loss of weight or other diabetic symptoms.

Present Illness.—Patient entered on the pneumonia service 24 hours after initial chill. He had a severe Type I pneumonia involving lower lobes on both sides, with positive blood culture. Leucocytes 24,800, polymorphonuclear 90 per cent. Highest temperature 104°. Blood pressure 125 systolic, 70 diastolic. Physical examination otherwise negative.

Treatment.—Urine was smoky red and showed heavy albumin, slight Benedict, and moderate ferric chloride reaction. He was treated on the pneumonia service with Type I pneumococcus serum. The blood became promptly sterile; the temperature, pulse, and respiration remained elevated. On Apr. 12, the diet consisted of 370 cc. milk, 150 cc. broth, and 150 cc. albumin water. On Apr. 13, 300 cc. albumin water, 150 cc. soup, and 150 cc. cocoa were given, and there was slight glycosuria and a slight ferric chloride reaction. On Apr. 14, 700 cc. albumin water and 150 cc. soup were the diet, and both sugar and ferric chloride reactions diminished to traces. Apr. 15 and 16, the diet was similar but included also 200 to 400 cc. milk. Traces of sugar and diacetic acid persisted. Meanwhile the temperature ranged from 101.2–103.6°F. Beginning Apr. 17, the patient was placed partly under the care of the diabetic service because of abnormal drowsiness and hyperpnea. On that day 15 gm. sodium bicarbonate were given, and the diet was changed to clear soup and whisky. On Apr. 18, 40 gm. sodium bicarbonate were given, and the previously acid urine turned neutral for part of the day. On Apr. 19 another 40 gm. sodium bicarbonate were given, and the urine was neutral throughout the day. On Apr. 20, the urine again turned acid, but another 40 gm. bicarbonate then turned it alkaline. Continuance of 40 gm. sodium bicarbonate on Apr. 21 and 30 gm. on Apr. 22 kept the urine neutral or alkaline. Meantime the ferric chloride reaction, from almost negative, had become intense. Under the influence of the alkali dosage the drowsiness cleared up. Apr. 23, 50 gm. carbohydrate in the form of green peas were tolerated, but 100 gm. in the form of peas and potatoes on Apr. 24 caused slight glycosuria. Beginning Apr. 25 a diet of soup, eggs, and vegetables was given, mostly about 1000 calories. Because of the stubborn ferric chloride reaction, fasting was imposed on May 2 and 3, and then a diet of vegetables up to May 6, containing a maximum of 75 gm. carbohydrate. On May 7, a low carbohydrate-free diet of less than 500 calories was given for the purpose of avoiding too long continued abstinence from solid food in a patient with infection. A mixed diet was then gradually built up, glycosuria appearing on May 16 with an intake of 67 gm. protein, 75 gm. carbohydrate, and 1700 calories. The diet nevertheless was still built up, and the tolerance rapidly improved with subsidence of the infection. The signs in the lungs persisted unduly long. Serum sickness with urticarial eruption was present Apr. 20 to 26. On May 10, the left seventh rib was resected

under local anesthesia for drainage of the empyema. It will be noted that glycosuria and a trace of ferric chloride reaction appeared on May 11, seemingly in consequence of this operation, and promptly cleared up without reduction in diet. The temperature subsided somewhat, but persisted in the neighborhood of 100°. Albuminuria had gradually diminished and was negative after May 10, but edema of the ankles persisted. On June 12, there appeared a fusiform swelling of three fingers of the right hand, and later also in joints elsewhere. The temperature rose at this time, but there was no glycosuria, and the ketonuria was only such as could be explained by the high fat of the diet. Thereafter the temperature gradually diminished and was normal after July 1. From the diabetic standpoint, the diet was built up to a high level, not only for the purpose of strengthening the patient, but also for the purpose of testing his tolerance. The latter proved to be almost unlimited. Carbohydrate was increased through the various classes of food, until the tolerance was found above 200 gm. in diets containing fruits, potatoes, cereals, and bread. Cane sugar was then permitted, beginning with 50 gm. on July 19, and glycosuria remained absent until a brief trace appeared on July 23 on an intake of 119 gm. protein, 380 gm. carbohydrate, and over 3900 calories. On July 22, he had tolerated such a diet, including 200 gm. cane sugar distributed throughout the day. On July 23, the carbohydrate allowance included this same quantity of sugar, but it was given all at once, and a trace of glycosuria was present for a few hours. The patient was therefore sent out on full mixed diet, on the presumption that the diabetes had been transitory.

Acidosis.—The case is an illustration of threatened coma under the influence of infection in a patient never known to have been diabetic, kept on very low diet because of the inability to take more, and with only slight sugar and ferric chloride reactions in the urine. The actual acidosis was revealed by the quantities of alkali required to turn the reaction of the urine, and by the intense ferric chloride reactions which resulted. Relatively few analyses had been made at the outset while the infectious features predominated. On Apr. 21, the first ammonia determination showed the low value of 0.59 gm. N under the influence of alkali. With omission of alkali, the ferric chloride reaction cleared up quickly but temporarily, and the ammonia nitrogen on Apr. 24 shot up suddenly to nearly 2.5 gm. By Apr. 26, adjustment had occurred under the influence of continued undernutrition and a little carbohydrate, and ammonia values thereafter never reached an alarming level. More or less ferric chloride reactions recurred until June 16, especially by reason of the high fat intake, but thereafter 75 gm. or more of carbohydrate in the diet sufficed to abolish ketonuria even with abundance of fat.

Weight and Nutrition.—The 1st month in hospital represented marked undernutrition, particularly in view of the fever. The body weight was kept up by edema. Beginning May 7, there was a sharp decline in weight with subsidence of edema, and after June 4 the weight rose rather rapidly under the liberal diets.

Remarks.—The case is an example of diabetes occurring with an acute infection under circumstances which make it appear that the infection had given rise to the diabetes. It is open to speculation whether the diabetes would have passed off if heavy glycosuria had been maintained by excessive carbohydrate feeding from the outset, especially as this might actually have been employed under former methods of treatment for the purpose of controlling acidosis. It was also important to determine whether the diabetes was actually transitory, presumably the result of direct or indirect involvement of the pancreas, or whether the infection merely brought into prominence a latent diabetes. The normal sugar tolerance at discharge would point to a genuinely transitory diabetes. On the other hand, the only decisive test would lie in following such a patient for many years. If diabetes ultimately became manifest, it might then mean either a latent diabetes, antedating an infection and temporarily made active by it, or it might represent injury of a previously normal pancreas by the infection, with temporary recovery to a considerable degree, with impairment and later breakdown of the internal function. None of these questions could be answered because the patient was lost sight of in spite of attempts to follow him up.

Among the features of the treatment, the most striking seems to be a definitely beneficial effect of alkali which cleared up symptoms threatening coma, when fasting and low diet were accompanied by dangerous acidosis and when the patient was in no condition to take much food. It is also worth noting that coma may threaten under such conditions with only slight sugar and ferric chloride reactions and with diabetes apparently of mild degree.

CASE NO. 41.

Male, married, age 52 yrs. Irish; politician. Admitted Apr. 23, 1915.

Family History.—Parents died in old age. One brother well; two died in infancy. One sister well; one died in infancy; one died of tuberculosis at 33. There was mental disorder running through several generations on the mother's side. Two of the patient's aunts died in insane asylums. No diabetes or other diseases in family.

Past History.—Healthy and checkered life. Measles, mumps, chicken-pox, scarlet fever, diphtheria in childhood; no sequelæ. Born in Ireland, ran away to sea at age of 20, and worked mostly as a stoker in the tropics for 7 years, but continued to enjoy good health. He then came to New York, worked at manual labor for a number of years, then gained influence in labor organizations and politics, and has since been occupied in official positions. There was cough and loss of weight shortly after his arrival in New York; tuberculosis was diagnosed, but there was apparently complete recovery. He also had pleurisy and "shingles" 20 years ago, but recovered rapidly, and has never been ill since. Venereal history consists in Neisser infection in 1883, followed by inguinal buboes treated by incision in hospital. Chancre in 1885, followed by slight rash 3 weeks later.

Habits have generally been good in view of hard life. Not more than 2 or 3 drinks a day, generally beer. Has never used tobacco. The diet on shipboard left him with more or less indigestion. Bowels usually regular. He has eaten rather liberally of sweet foods.

Present Illness.—4 years ago he was troubled with dry throat following a cold. Physician in routine examination found 2 per cent glycosuria. Shortly after this polyphagia, polydipsia, and polyuria set in, but disappeared on moderate restrictions of diet. There has been no attempt to make him sugar-free. 6 months ago he barked his shins; these were very slow in healing, and collections of pus required opening. Since Mar. 17, he has had a grippe infection and considerable impairment of general health, and his physician advised him to come to the Institute for diabetic treatment. The loss of weight has amounted to 15 pounds in the past 3 years.

Physical Examination.—Height 172 cm. A well developed, strong looking, somewhat obese man, showing no distress, but with cyanosis of face. Temperature 102° F., pulse 120, respiration in bed 36. Breathing not of air-hunger type. Teeth all false. Throat slightly congested; tonsils show slight hypertrophy without exudate. Lungs, slight bronchitis and emphysema. Slight generalized enlargement of lymph nodes. Blood pressure 125 systolic, 70 diastolic. Reflexes normal. Pigmented scars on shins; slight edema of ankles. Wassermann ++ in blood, negative in spinal fluid. Physical examination otherwise negative.

Treatment.—On admission there was a moderate sugar and slight ferric chloride reaction, and a heavy trace of albuminuria with large numbers of hyaline and finely granular casts. On Apr. 24, the first full day in hospital, the diet was 84 gm. protein, 3 gm. carbohydrate, and 2375 calories. Glycosuria entirely cleared up during the day, and the ferric chloride reaction was also negative. Fasting was begun, nevertheless, as the quickest means of undernutrition, and was continued for 8 days. The temperature and cough cleared up during this time, also the albuminuria gradually diminished to a trace. The patient was fully comfortable, and on 450 cc. soup daily had no special complaint of hunger. Green vegetables were the first food given, in the form of a tolerance test. The glycosuria with 20 gm. carbohydrate on May 4 was an accidental trace, not representing the true limit, which was reached with 100 gm. carbohydrate on May 8 and 9. This glycosuria ceased on cutting down the carbohydrate to 21 gm. on May 10. Beginning May 11, two eggs and 50 gm. bacon were given as the first substantial food in the 18 days since admission. 10 to 20 gm. carbohydrate were retained in the diet, which was gradually built up to 65 gm. protein and 1330 calories on May 16 and 17. That this diet was too high was indicated by the sharp rise in ammonia, and the high blood sugar on the morning of May 18. The fact that glycosuria was absent then, but traces were present on certain subsequent days, is possibly a phenomenon of renal permeability. Albumin and casts were absent from the urine after May 9, and renal function tests by Dr. McLean showed no abnormality throughout. It became possible to increase

all three classes of food rather rapidly. There was more feeling of hunger toward the close of May than on the fasting and lower diets previously. On May 13, 0.2 gm. salvarsan, and 0.5 gm. doses on May 24, and June 7 and 21, were injected intravenously. There were 30 mercury inunctions about this time. At discharge on July 7 the prescribed diet was 100 gm. protein, 95 gm. carbohydrate (including 20 gm. bread), and 2400 calories (approximately 1.4 gm. protein and 33 calories per kg., reduced one-seventh by the weekly fast-days). The recovery of subjective health was complete, in such manner that there was no question of the patient's future fidelity.

Acidosis. Ferric Chloride Reaction.—First may be noted the fact that a slight ferric chloride reaction was present along with glycosuria on the lax diet at admission, and on the carbohydrate-poor diet of Apr. 24 this cleared up completely. It then reappeared on the second day of fasting and became heavy, but this was no reason for discontinuing the fast. The reaction diminished to traces on May 8 and 9, but the ingestion of 100 gm. carbohydrate without other food was unable to abolish it completely on these days. With the diminished carbohydrate intake and the gradual addition of fat on the succeeding days, it again became heavy, but showed the usual tendency to fade out, irrespective of diet, as the general condition improved. After becoming negative, it still showed the same tendency to reappear with fasting, being present on June 21 after a fast-day (but not on the fast-day itself), absent with the fast-day of June 27, and present on the fast-day of July 4. The trace of glycosuria which appeared on June 23 was supposedly the result of slight excitement, and, as frequently happens, a trace of ferric chloride reaction appeared with the sugar.

Blood Bicarbonate.—No CO_2 estimations were made during the first few days. The low level of 45 per cent on Apr. 30 was probably the result of fasting. No alkali was given, and the curve tended to rise rather than fall. Particularly the allowance of a little carbohydrate brought it well up to normal limits on May 6. With undernutrition and predominantly fat diet on May 12, the CO_2 was again down to 46.4 per cent. On the morning of May 18, following the increased diets of May 16 and 17, it was again within normal limits. It may be noted that this rise was not prevented by the febrile attacks mentioned below. On May 24, following the preceding fast-day, it was again barely above 45 per cent. With the higher diets and higher carbohydrate ration prior to discharge, the CO_2 capacity was at a high normal level.

Ammonia.—In conformity with the absence of other signs of acidosis, the ammonia nitrogen on carbohydrate-poor diet on Apr. 24 was only 0.63 gm. It steadily rose on fasting, showing the development of acidosis, and on Apr. 30 had reached 2.27 gm. The 100 gm. carbohydrate on May 8 and 9 brought the ammonia down to a low normal level. Thereupon, with little carbohydrate, and undernutrition with a predominance of fat, the ammonia rose slightly. On May 13, 0.2 gm. salvarsan in 150 cc. saline was injected intravenously. On May 14, there was temperature of 100.8°F ., with slight albuminuria and a few casts.

Toward evening there was a chill with temperature of 104°, leucocyte count 14,000, polynuclear 75 per cent; no malaria parasites; blood culture sterile; influenza bacillus and Pneumococcus IV in sputum. On the following days there was pain and swelling of the left leg from knee to ankle. By May 18, the temperature was down to 99.2°, and thereafter was normal. Aside from the hyperglycemia shown, this infectious attack made itself felt strikingly in the ammonia output. This climbed steeply to the astonishing figure of 5 gm. ammonia nitrogen on May 17, then fell abruptly as the temperature fell. Relatively low values were present with the undernutrition and fasting of May 19 and 20. In consequence of protein-fat feeding, the ammonia rose as feeding was continued to nearly 3.36 gm. N on May 26 and 30. Thereafter, with increasing carbohydrate intake and improved general condition, the ammonia proceeded to fall to a permanently normal level.

Blood Sugar.—The hyperglycemia doubtless present at admission was replaced by the normal figure of 0.120 per cent as early as Apr. 27. The rise to 0.167 per cent on Apr. 30 is one of the curious fluctuations which occur sometimes in fasting. Hyperglycemia of 0.168 per cent was present with the febrile attack on May 18. Subsequent determinations showed fully normal values (mornings before breakfast).

Weight and Nutrition.—The patient was obviously overnourished, and treatment consisted primarily in reducing weight and relieving the overburdened metabolism. The sharp fall in the weight curve during the early undernutrition is shown in the graphic chart. It was noted above that only benefit was felt subjectively, and the existing gripe infection and albuminuria both cleared up promptly. Even during the period of low diets the patient said he felt as if 10 years had been subtracted from his age. He lost 10.2 kg. in hospital, but the weight of 72 kg. at discharge was abundant for his stature, and he stated that he had never felt better in his life. It is obviously bad practice to allow a diabetic patient to carry abnormal weight. The good prognosis of fat diabetes belongs to the mildness of the diabetes and not to the obesity, and the prognosis is better when the obesity is properly reduced.

Subsequent History.—The patient took long vacation trips to Michigan and California, exercised heavily in walking, swimming, etc., and remained free from glycosuria. On Oct. 8 the diet was increased by two eggs and 20 gm. bread. The weight was 72.6 kg. On Jan. 1, 1916, it was the same. On Apr. 8, 1916, 25 gm. glucose were given at 11 a.m., and specimens of urine at 12, 1, 2, and 3 p. m. were negative for sugar. Weight 80 kg. On Apr. 24, the patient came to the hospital fasting for the purpose of a glucose test. 100 gm. Merck anhydrous dextrose were ingested at 9:55 a.m. The record was as follows:

Hr.	Blood Sugar.	Plasma Sugar.	Urine Sugar.
	<i>per cent</i>	<i>per cent</i>	
9:50 a.m.	0.125	0.135	0
10:50 "	0.179	—	0
11:50 "	0.156	0.164	Faint.
12:50 p.m.	0.123	0.110	0
2:05 "	0.083	0.084	0

Up to this time the patient had received a total of 9 intravenous injections of 0.5 gm. salvarsan and 30 mercury inunctions. The Wassermann reaction remained consistently + + + +. With the idea that the diabetes might have been of luetic origin and might have been cured by the specific treatment, permission was given on the basis of this glucose test for the patient to relax his diet to the extent of ceasing to weigh food, and merely take the same general type of diet as before so as to avoid much carbohydrate. Up to June 1, 1916, three more doses of salvarsan had been given, also three mercurial injections outside this Institute. He was seen at the Institute July 14, weighing 86.2 kg.; *i. e.*, a greater obesity than at the time of the first admission. He looked tired and overstrained. Glycosuria was present. He had not been performing urine tests, and showed blood sugar 0.270 per cent, plasma sugar 0.294 per cent, CO₂ capacity of plasma 62 per cent. He was instructed to resume a weighed diet of 93 gm. protein, 75 gm. carbohydrate, and 2300 calories, and to take measures to reduce his excessive weight. With swimming and other heavy exercise he lost 2 kg. in the following week, and became free from glycosuria and ketonuria on July 20. On July 21 the sugar in whole blood was 0.182 per cent, in plasma 0.204 per cent, CO₂ capacity 54.7 per cent. The urine has since remained normal and the patient has retained subjective health. The management of the diet at home is probably not accurate, for with continuous exercise he has never brought his weight below 80 kg. Vigorous treatment with salvarsan and mercury has been continued under the care of a competent private practitioner, but the Wassermann reaction is still + + + in the serum.

Remarks.—The case is of special interest in connection with the possible luetic origin of the diabetes. There has been no tendency to progress downward even though the Wassermann reaction remained strongly positive. The state of health was transformed by diet alone, before any antisiphilitic treatment was employed. If specific treatment checked the syphilitic damage, it did not repair it. The combined treatment did not cure the diabetes, notwithstanding the excellent result of the glucose test of Apr. 24. It could then have been noticed that the patient at his elevated weight showed hyperglycemia even on fasting, and the blood sugar curve following the dose of glucose was unduly high. This warning was not heeded; and with further gain of weight, without carbohydrate excess, the inevitable glycosuria returned in due season.

The case was a typical example of so called "spontaneous downward progress" when the treatment was wrong; but progress was upward when the treat-

ment was right. The patient's treatment of himself at home is evidently not sufficiently stringent. He keeps his weight too high, and although he is in excellent subjective health and carries on his work without difficulty and the urine remains normal, more rigid treatment is necessary or there may ultimately be trouble.⁶

CASE NO. 42.

Female, age 11 yrs. American; schoolgirl. Admitted Apr. 30, 1915.

Family History.—Patient is the only child of apparently healthy parents, with no heritable disease anywhere in family as far as known.

Past History.—Measles and whooping-cough in infancy. Scarlet fever at 7 and again at 9. No sequelæ. Has been a strong, healthy, well grown child, though living in tenement environment. She has attended school in the usual grades. During the past 2 years she has been nervous, the mother stating that "the higher she gets in school the more nervous she gets." About the average indulgence in candy. A curious feature of diet is that she has never eaten vegetables, not even potatoes. The food has been mostly eggs, bread, and milk. Appetite has been notably small and she has had to be coaxed to eat.

Present Illness.—3 weeks before admission polyphagia, polydipsia, and polyuria began acutely. After 2 weeks she was taken to a physician who first prescribed carbohydrate-free diet with addition of milk, then as glycosuria continued he advised bringing her to this Institute.

Physical Examination.—A thoroughly well developed and nourished, normal appearing girl. Tonsils protrude and show deep crypts, with pus on pressure. Very few small lymph nodes palpable. Reflexes normal. General examination fully normal. The child is a splendid physical specimen, brimming over with life and spirits.

Treatment.—Patient was admitted at 11:45 a.m. Apr. 30, and received no food on that day. Castor oil was given as a laxative. The blood sugar was 0.286 per cent at 3:30 p.m., but probably diminished rapidly, for the glycosuria in the mixed urine up to the next morning was only 0.3 per cent. On May 1, nothing was given but two eggs and 450 cc. clear soup. May 2 and 3 were fast-days. The glycosuria was only slight on May 1, and immediately cleared up, the whole picture being characteristic of an early, still mild stage in which glycosuria and hyperglycemia had been kept up essentially by carbohydrate. On the other hand, the ferric chloride reaction was well marked at admission and became heavy on fasting. The child also vomited on the 1st fast-day and was weak on

⁶ Continued specific treatment finally reduced the Wassermann reaction to \pm . At the same time continuous glycosuria gradually developed, followed within a few weeks (Feb., 1918) by a rather threatening infection of the right foot. This cleared up promptly with fasting and rest, and a more rigid dietetic régime has since been pursued.

the 2nd. On May 4, she received 16 gm. carbohydrate without glycosuria. With 40 gm. carbohydrate on May 5 in the form of green vegetables and 150 gm. strawberries, a trace of glycosuria appeared, increased with 60 gm. carbohydrate on May 6, and disappeared with a reduction of carbohydrate to 12 gm. on May 7. By this time the ferric chloride reaction was diminished, and a diet of eggs and sugar-free milk (Whiting's) was begun, with 5 gm. carbohydrate in the form of celery and asparagus. The caloric intake was below 650, and with this undernutrition the ferric chloride reaction and all other signs of acidosis were cleared up by May 13. Traces of glycosuria were frequent, and accordingly, without further trouble from acidosis, the diet from May 16 to 21 was kept so low as to represent almost continuous fasting. Beginning May 22, the attempt was made to feed approximately 1200 calories daily; but glycosuria promptly appeared, and continued notwithstanding withdrawal of carbohydrate and a partial fast-day on May 27 and a complete fast-day on May 30. This being an impossible state of affairs, the child was brought to confess that the glycosuria was due to her stealing small quantities of bread. Though always a rather unmanageable patient, she was tractable after learning that glycosuria meant fasting, and soon became contented under hospital discipline.

On June 2 partial, and on June 3 complete fasting was given. Beginning June 4, a carbohydrate tolerance test was continued until June 26. A deceptive trace of glycosuria appeared with 180 gm. carbohydrate on June 17, but the true tolerance proved to be 260 gm. carbohydrate on June 25 and 26, in contrast to the 40 to 60 gm. carbohydrate which had caused glycosuria on May 5 and 6. The benefits of the 2 months of undernutrition and liberal carbohydrate supply were now apparent in a greatly increased tolerance for mixed diets. This was rapidly built up, with routine weekly fast-days, and glycosuria was absent until the increase reached 84 gm. protein, 110 gm. carbohydrate, and 2250 calories on July 21. The ration was immediately reduced to a lower figure than had been tolerated before, nevertheless glycosuria continued for 3 days. The child was now clinically and subjectively entirely well, and the urine remained normal except for the traces of glycosuria on Aug. 19 and 20, due to stealing food. Oct. 11 to Nov. 3, another carbohydrate test showed a tolerance of 240 gm., as compared with 260 gm. in June. In Nov. a diet of 75 gm. protein, 75 gm. carbohydrate, and 1500 calories was assimilated without glycosuria. In Dec. the attempt to replace part of the fat with carbohydrate, making the diet 75 gm. protein, 100 gm. carbohydrate, and 1500 calories, was endured for about 2 weeks, then caused glycosuria on Dec. 15 and 16, so that the former diet with 75 gm. carbohydrate was resumed. She was discharged on this, after having been 232 days in hospital.

Acidosis.—This was an instance of the production of acidosis by fasting. The tendency was already present, as shown by the ferric chloride reaction and slightly subnormal blood alkalinity at admission; but the nausea and weakness developing early in fasting were characteristic, and on the morning of May 4

the CO₂ capacity of the plasma was found to have fallen to the ominous level of 27 per cent. No alkali was given, but only the 16 gm. carbohydrate in green vegetables as mentioned. With small carbohydrate intake the CO₂ capacity rose quickly to 44 per cent on May 6; then on a protein-fat diet of 600 calories with only 5 gm. carbohydrate it rose still further. On May 18, which was a green day with 20 gm. carbohydrate in the form of celery, asparagus, tomato, and cucumber, the CO₂ was as high as at admission. With the carbohydrate tolerance test in June it reached a high normal level. It tended to fall below normal on the ensuing mixed diet. The tendency toward acidosis on fasting was displayed in the tests made on the morning of the fast-day of Sept. 12 and the following morning, but the steep drop in plasma bicarbonate as a result of this fast was partly explainable by the lively exercise which the patient was now taking. The later values, with the exception of the low figure of 48.8 per cent on Nov. 17, were normal for a child.

Blood Sugar.—The quick fall to normal is characteristic of an early case. Normal values were still present on Sept. 12 and 13, after a long period of adequate nutrition; but increase of the carbohydrate allowance from 82 to 100 gm. on Sept. 23 without change in the total calories resulted in a rise of blood sugar to 0.26 per cent on Oct. 7. There was hyperglycemia of 0.25 per cent on Oct. 22 during the carbohydrate test. Thereafter the general tendency of the curve was downward. Notwithstanding the increase of carbohydrate on Nov. 30, which subsequently resulted in glycosuria, the analysis before breakfast on Dec. 4 showed normal sugar in the whole blood and only slight elevation in the plasma. At the close of the following week, on Dec. 11, there was definite hyperglycemia, giving advance warning of the glycosuria which appeared on Dec. 15.

Weight and Nutrition.—Though the patient was a growing child, undernutrition was employed to obtain control of the threatening condition present when admitted. The degree of undernutrition thus enforced for 2 months can be shown as follows. The quantity of bread obtained surreptitiously was so small as to be negligible in this calculation.

	58 days.	Per day (average)	Per day per kg.
Total calories in diet.....	37,132 0	640.0	24.0
“ protein “ “	1,769.9 gm.	30.5 gm.	1.13 gm.
Animal “ “ “	850.3 “	14.6 “	0.54 “
Vegetable “ “ “	919.6 “	15.8 “	0.58 “
Carbohydrate “ “	3,190.0 “	55.0 “	2.03 “

The child was cross and rebellious at first because of having been spoiled at home, so that trouble resulted not merely from hunger but from any matters in which her will was thwarted. The greatest loss of weight was 3 kg. The increase of weight during the carbohydrate test in June represented the usual slight edema. By reason of the subsequent diets, the weight at dismissal was the same as at entrance. It was not learned whether any growth in stature occurred

in hospital. At discharge, with weight of 27 kg. and height of 129.8 cm., the child appeared splendidly developed and nourished and her strength and spirits were of the highest.

The diet at discharge represented approximately 2.8 gm. protein and 56 calories per kg., reduced by the weekly fast-days to 2.4 gm. protein and 48 calories average per kg. Along with this, heavy exercise had been employed and was evidently one reason for the failure to gain weight. The child had certainly gained in muscle, for her muscles were large and hard at discharge, and presumably she had lost some fat. Exercise was in the form of strenuous sports, and because of her strength and boisterous disposition she enjoyed these thoroughly.

Subsequent History.—This was an instance in which more reliance had to be placed on the child than on the parents, for they would not control her effectively. Though spoiled and rebellious at first, she had become obedient and convinced of the necessity of remaining free from glycosuria. Though in tenement environment, she was able to obtain the required food, and remained free from glycosuria, except for 1 day in Jan. with a bad cold. She continued exercise and also attended school, leading a thoroughly normal child's life except for diet. On Mar. 2, 1916, the height was 130.6 cm. On Apr. 18, the blood sugar was 0.156 per cent, plasma sugar 0.164 per cent, CO₂ capacity 52.6 per cent. As the urine was consistently normal, 150 cc. milk were added to the diet. On June 13, the blood sugar was 0.123 per cent, plasma sugar 0.130 per cent, CO₂ capacity 52.1 per cent. On July 17, the health and urine remained as before. The blood sugar was 0.192 per cent, plasma sugar 0.227 per cent, CO₂ capacity 50.5 per cent. Weight 26.8 kg. Height 131 cm. The diet was diminished to 1400 calories with only 50 gm. carbohydrate, and the patient was allowed to go to the country until fall. In Nov. traces of glycosuria began to appear frequently, the urine and subjective condition having been normal up to this time. The patient was therefore readmitted Nov. 17, 1916.

Second Admission.—The weight was 27.8 kg. There was slight edema of feet, but the apparent physical condition was still very good, though the child was obviously not so strong as before. Only a trace of glycosuria was present, but this persisted on a diet of 60 gm. protein, 15 gm. carbohydrate, and 800 calories. It cleared up with 1 fast-day. A carbohydrate tolerance test was then instituted in the usual manner, and the tolerance was found to be only 90 gm. Thereafter a diet was given consisting of 40 gm. protein, 10 gm. carbohydrate, and 800 calories. Any attempt at an increase above this diet caused glycosuria. She was discharged on this diet Dec. 18, 1916, weighing 25.5 kg. On the basis of this weight, with allowance for the weekly fast-days, the prescribed diet represented 1.3 gm. protein and 27 calories per kg.

Subsequent History.—Traces of glycosuria still recurred, and on this account the patient was out of the hospital only a little over 2 weeks.

Third Admission.—Jan. 4, 1917. Weight 27.5 kg., evidently explainable by edema, as the diet had not been high enough for gain in weight. Only a trace

of glycosuria was present, and the prescribed diet was continued for 3 days in hospital to determine whether it resulted from violation of diet at home. The sugar, however, slightly increased instead of decreasing, and 2 fast-days were then necessary to stop it. The trace of ferric chloride reaction present at admission persisted on fasting, but the ammonia nitrogen, which had been 1 gm., fell to 0.36 gm. A carbohydrate test was then given in the usual manner, and the tolerance was found to be only 50 gm., indicating steady downward progress. The blood sugar on admission was 0.332 per cent, and at the end of a fast-day following the carbohydrate test it was 0.176 per cent. Frequent traces of glycosuria and acidosis persisted on a diet of 36 gm. protein, 10 gm. carbohydrate, and 750 calories. In Feb. the condition changed for the worse. There were gastric upsets, edema of face and legs, mental depression, and loss of weight and strength. The diet was gradually diminished to 25 gm. protein and 350 calories without carbohydrate, but traces of glycosuria continued, while acidosis was absent or slight by all tests. There was no cough, but pain particularly with breathing appeared over the precordia. The temperature did not go above 98.9° F. Physical and x-ray examinations gave only suspicious and not positive signs in lungs. The continuance of pain made tuberculous pleurisy probable. On Feb. 27, the CO₂ capacity of the plasma was down to 44 per cent. A trace of ferric chloride reaction returned on Mar. 5. At the beginning of Mar. the attempt to maintain sugar-freedom was abandoned, and heavy glycosuria was thenceforth present on a carbohydrate-free diet of 30 gm. protein and 450 calories. By Mar. 8, the ammonia nitrogen was up to 1.1 gm. The ferric chloride reaction gradually became heavy. By Mar. 14 the ammonia nitrogen was 1.5 gm. The CO₂ capacity of the plasma was 18.9 per cent on that day. 15 gm. sodium bicarbonate were given, and the CO₂ capacity fell to 16.9 per cent. The patient died in diabetic coma on Mar. 15, 1917.

Remarks.—The patient was received with diabetes acute and severe in type, but yet early and mild in degree. She was treated for 2 months with rigorous undernutrition, and all threatening symptoms cleared up and a high carbohydrate tolerance was developed. Undernutrition was then abandoned and the attempt was made to feed a high calory diet suitable for a normal child, while at the same time gain in weight was prevented by means of heavy exercise. A splendid physical condition was attained.

The child was kept alive for 2 years, during the greater part of which she enjoyed a high degree of health and led an approximately normal existence. The outcome shows that exercise cannot wholly replace restriction of total calories. While downward progress may be unavoidable with severe diabetes under the metabolic strain of youth and growth in children, a longer and better course in other children more rigidly treated is an indication that at least part of the downward progress in this case was attributable to the unduly high diet. It is better to make a less severe reduction in the earliest stage when so much greater benefit is attainable, than a more extreme reduction after downward progress has

resulted. As usual, the attempt to maintain the highest possible level of vigor did not prevent and probably predisposed to infection. With the onset of tuberculosis, a quickly fatal termination in such a case was assured.

CASE NO. 43.

Female, unmarried, age 27 yrs. American; nurse. Admitted May 31, 1915.

Family History.—Father died at 70 of Bright's disease. Mother died of unknown cause during menopause at 45. Possible diabetes in a maternal aunt. Maternal grandmother died of tuberculosis. No other heritable disease known.

Past History.—Patient has spent her life under favorable conditions in two southern states. In childhood, measles, mumps, whooping-cough, chicken-pox, diphtheria. Pneumonia at 7 and again at 17; both light. In the spring of each year she has had so called malarial attacks with slight fever and malaise, but without chills. Menstruation has been irregular. General health good. Habits and diet normal. 3 years ago she accidentally plunged a hypodermic needle into her hand and broke off the point, which was not extracted for 24 hours. Severe sepsis resulted. The whole arm was swollen and blackened, and three incisions were made for drainage. There was delirium, and at one time her recovery was not expected. The hand has only partially recovered function. There was also albuminuria during the attack, and treatment with diet and other measures for nephritis was followed for many months. Albuminuria finally cleared up.

Present Illness.—In Jan., 1915, marked polyphagia, polydipsia, and polyuria were noticed, and the weight fell from the usual 118 to 97 pounds. About the first of Mar. she concluded she had diabetes, and this was confirmed by a medical examination. Beginning late in Mar. she was under treatment in hospital for several weeks on the von Noorden plan with green days, oatmeal days, and occasional fast-days. She was sugar-free during the last week, but relapsed on leaving hospital. Since the middle of Apr. she has been on protein-fat diet with addition of green vegetables, a little potato, and two slices of bread at each meal. Pruritus vulvæ troublesome.

Physical Examination.—Poorly developed, thin young woman. Pale complexion. Skin dry. Considerable loss of hair. Mouth and throat normal. A few barely palpable lymph nodes. Reflexes normal. Trace albuminuria. Examination otherwise negative.

Treatment.—On June 1, the first day in hospital, the diet was 83 gm. protein, 5 gm. carbohydrate, and 2530 calories. The sugar excretion was 14.88 gm. On the next day 2071 calories were taken. June 3 and 4 were fast-days with no food of any kind. On June 5 and 6, 300 cc. clear soup, 150 cc. coffee, and 3550 cc. whisky were permitted. Glycosuria cleared up, but signs of acidosis became marked. On June 7, green vegetables containing 10 gm. carbohydrate produced prompt glycosuria. This carbohydrate was continued, and eggs, butter, and

bacon were added to build up a diet approximating 1600 calories. Glycosuria diminished when the carbohydrate was halved, but did not cease until the fast-day of June 13. Thereafter a similar diet was tolerated up to June 21. Beginning June 22, a carbohydrate tolerance test was instituted, and ignoring insignificant traces of glycosuria on July 5 and 8, the tolerance was reached with 230 gm. carbohydrate on July 17 and 18. Thereafter a mixed diet of 80 to 100 gm. protein, 100 gm. carbohydrate, and 2200 to 2500 calories was taken, with only occasional traces of glycosuria. The weight having risen to equal that at entrance, another carbohydrate test was begun on Oct. 11, and the limit of tolerance was reached with 170 to 190 gm. carbohydrate. Mixed diet was then resumed, and though 2500 calories were tolerated, the permanent level, beginning Nov. 5, was fixed at 2000 calories. Green days with 25 gm. carbohydrate were substituted for the previous weekly fast-days. Though glycosuria was absent, the carbohydrate allowance beginning Nov. 26 was diminished to 25 gm. Nevertheless, a decided glycosuria appeared in the middle of Dec. It was then learned that this, and also the preceding appearances of glycosuria (Nov. 6 to 24) had been due to the patient's buying and eating 10 cents worth of cheese when on walks away from the hospital. After reduced diet and fasting (Dec. 17 to 20) the glycosuria was cleared up, and the former diet resumed on Dec. 21 without glycosuria. The patient was dismissed on a diet of 80 gm. protein, 25 gm. carbohydrate, and 1800 calories (1.92 gm. protein and 43 calories per kg., reduced by weekly fast-days to an average of 1.65 gm. protein and 37 calories per kg.). She felt well at discharge, except on fast-days, which always left her temporarily weak and depressed. She proposed to undertake diabetic nursing, and was instructed also to continue regular exercise.

Acidosis.—At admission there were no acidosis symptoms, the ferric chloride reaction was slight, the ammonia output was low, and the first carbon dioxide determinations only slightly subnormal. Acidosis was produced by fasting. The ferric chloride reaction promptly became heavy. Before breakfast on the morning of June 7 the CO₂ capacity of the plasma was down to 35 per cent, and the ammonia nitrogen by that day had risen to 2.35 gm. Alcohol up to 350 calories had not prevented this acidosis. On June 8, 20 gm. sodium bicarbonate were given, with the low calory diet and 10 gm. carbohydrate above mentioned. The result was a prompt rise in CO₂ and fall in ammonia. But with simple increase of protein-fat diet without any more alkali, the CO₂ capacity rose still more sharply to a fully normal level, and the ammonia output correspondingly fell. The acidosis was also manifested by the usual clinical symptoms of nausea, vomiting, and malaise; these also cleared up promptly on feeding. The CO₂ capacity was unaccountably low on July 8, probably in consequence of undernutrition and exertion, while on the next day the usual high normal value was found present. On mixed diet the curve had descended by Sept. 12 to the lower normal limit. The tendency toward acidosis on fast-days persisted. Sept. 12 was a fast-day, and the CO₂ capacity that morning was 54.8 per cent, whereas the next morning,

after 24 hours with only 300 cc. soup and 300 cc. coffee, it was down to 46.6 per cent; while after 3 days of feeding it was 57 per cent on the morning of Sept. 16. It was also within normal limits on Oct. 29, at the close of a carbohydrate test; but on the morning of Nov. 1, after the previous fast-day, it was down to 47.4 per cent. On the other hand, on Dec. 19 the high normal value found after fasting is perhaps one indication of the improved condition, notwithstanding the existence of a positive ferric chloride reaction in the urine at that time. It is also worth noting that the ferric chloride reaction became negative on June 28 with nothing in the diet but vegetables representing 70 gm. carbohydrate. But after the carbohydrate test it reappeared on mixed diet in July and Aug., notwithstanding 100 gm. carbohydrate in the diet. Thereafter it tended to reappear, particularly with glycosuria. It seemingly was governed not so much by the carbohydrate intake as by the fat in the diet and the specific diabetic condition.

Blood Sugar.—The hyperglycemia found on the morning of Sept. 12 was promptly reduced to normal by the single fast-day. It was again unduly high with feeding, but showed a downward tendency. The excessive figure of 0.4 per cent in whole blood and 0.445 per cent in plasma at the close of the carbohydrate test on Oct. 29, with only slight glycosuria, probably indicates renal impermeability, perhaps associated with the old nephritis. At the same time it must be borne in mind that the urine reactions are shown for the 24 hours, whereas the blood sugar was for the hyperglycemia during carbohydrate digestion. On the morning of Nov. 1, it was found that a single fast-day had again brought the blood sugar fully to normal. On Nov. 13, it was 0.125 per cent in whole blood and plasma, and was barely below 0.15 per cent on Dec. 19 in consequence of the recent violation of diet.

Exercise.—As soon as adequate mixed diet was begun in Aug., vigorous exercise was inaugurated, including daily walks of 8 miles. The strength and general appearance thereby improved. Glycosuria was present on Sept. 11, just before the routine fast-day. Exercise was then omitted, and it appeared earlier in the following week; namely, on Sept. 14 and 15. Without change in diet, an increase of exercise was ordered, and glycosuria immediately ceased and remained entirely absent in the subsequent weeks up to Oct. 9. Other observations concerning exercise, particularly the blood sugar, are given elsewhere (Chapter V).

Emotion.—The glycosuria of Aug. 10 and 11 was apparently associated with crying spells.

Weight and Nutrition.—The weight at admission was 44 kg. Some of the fluctuations in the curve, notably the rise during the carbohydrate test in July, were due to edema. It is noteworthy that the tolerance in Oct., after recovery of the original weight, was far different than at admission, but yet was lower than in July. It seems clear that the high diets from July to Oct. had been injurious, notwithstanding the use of exercise. At discharge the weight was 41.6 kg.; i.e., a loss of 2.4 kg. This was 12 kg. below her normal weight, and she had always been rather slight in figure. The above mentioned diet, prescribed at

patient never was guilty of any large violation of diet, but indulged herself in little things beyond permission. Glycosuria occasionally returned, and finally became continuous. When she began to feel rapidly worse, she returned for readmission on Dec. 2, 1916.

Third Admission.—The weight was 39 kg., partly edema. No acute symptoms were present, but there had been a perceptible loss in strength. With 3 days of fasting, sugar and ferric chloride reactions became negative. The diet was then built up in the usual manner, and the tolerance was found very low. The limit was approximately 1000 to 1100 calories with 50 gm. protein and no carbohydrate, and with the usual weekly fast-days. A considerable part of this long period in hospital was occupied with tests with fat feeding, some of which are described elsewhere (Chapter VI). On the very low diet the weight has fallen to about 33 kg. The strength also is diminished, so that the patient is now a confirmed invalid, able to be up and about, but not fit for work or for an independent existence. She has remained in the hospital up to the present.

Remarks.—The record of this patient during and following the first hospital period confirms the fact that exercise cannot atone for an unduly high diet. The essential reasons for her downward progress have been the almost perpetual, slight overstepping of diet, and the frequent colds and grippe. She has reached the point where nothing but a hard struggle for the bare maintenance of life is possible. With continuous hyperglycemia not tending to diminish, a slight continuous overstrain of the pancreatic function may be assumed, and downward progress may be expected under such conditions even in the absence of indiscretions or complications. The only hope lies in treatment radical enough to relieve the overstrain if possible. The later results will show whether downward progress can thus be checked at such an extreme stage.

CASE NO. 44.

Male, married, age 33 yrs. American; electrician. Admitted July 3, 1915.

Family History.—Parents lived to old age. Wife and three children of patient are well. One aunt died of cancer of the nose. History otherwise negative.

Past History.—Diphtheria at 4. Frequent colds in head but no cough or sore throat. Gonorrhoea 11 years ago. Syphilis denied. Has worked in electrical power house for past 15 years, for past 3 years as switchboard attendant. Moderately nervous and excitable. No alcohol except occasional glass of beer. Smokes considerably. Four or five cups of tea or coffee daily. Not a heavy eater in general, but a lover of sweets. Highest weight 170 pounds, average 165 pounds clothed.

Present Illness.—Headaches and lassitude began about a year ago. 5 months ago pleurisy with chills, cough, and bloody expectoration confined him to bed for 10 days. Weight has been steadily lost, and there have been night sweats for week preceding admission. Polydipsia and polyuria began shortly after the

pleurisy. A physician then diagnosed diabetes. In addition to medicines, he was given a diet restricted to protein-fat foods with gluten bread and such vegetables as grow above the ground. He continued to lose steadily; impaired hearing, numbness of hands and feet, cramps in legs at night, nervousness, and irritability have been present.

Physical Examination.—Height 175 cm. A fairly developed, moderately emaciated man without acute symptoms. Slight pyorrhea. Many teeth missing. Tonsils not enlarged. Slight lymph node enlargements. Reflexes normal. Blood pressure 90 systolic, 62 diastolic. Wassermann negative. Examination otherwise negative.

Treatment.—During the first few days in hospital, glycosuria and ketonuria were heavy on a diet of 2100 to 2400 calories with 5 gm. carbohydrate. The increase of carbohydrate to 40 gm. on July 7 made little difference. On July 8, only breakfast was given, and glycosuria cleared up during the day. 3 fast-days were then imposed nevertheless, followed by a carbohydrate period. An intake of 340 gm. carbohydrate in the form of green vegetables was reached without glycosuria. The ferric chloride reaction meanwhile became negative. After a fast-day on Aug. 1, the diet for 3 days was limited to potato, and 200 gm. carbohydrate were taken in this form without glycosuria. A mixed diet was then given, consisting of 100 gm. protein, 100 gm. carbohydrate, and 2600 calories. Ferric chloride reactions promptly appeared, and persisted notwithstanding increase of carbohydrate to 285 gm. on Aug. 21. The diet on this day also contained 130 gm. protein and 3100 calories. Of this carbohydrate, 40 gm. were in the form of bread and 100 gm. in the form of potatoes. The patient was discharged on Aug. 23, weighing 58.6 kg., on a prescribed diet of 115 gm. protein, 160 gm. carbohydrate, and 2700 calories (almost 2 gm. protein and 50 calories per kg., reduced one-seventh by weekly fast-days).

Acidosis.—The CO_2 capacity of the plasma was slightly below normal, and rose steadily under treatment without the aid of alkali. The most interesting feature from the standpoint of acidosis pertained to the ferric chloride reaction, for although this became negative on a solely vegetable diet, it reappeared on a liberal mixed diet, notwithstanding an ingestion of carbohydrate theoretically abundant to prevent all acidosis.

Subsequent History.—The patient resumed his regular work, and maintained health and normal urine. On Oct. 5, both sugar and ferric chloride reactions were absent from the urine, and the sugar in whole blood was 0.102 per cent, in plasma 0.110 per cent, weight 61 kg. In addition to his regular work of 8 hours a day he was making extra money and at the same time obtaining exercise by canvassing several hours daily. On Dec. 27, the patient reported at the Institute with temperature of 99.2° F., after having had gripe and precordial pain for 10 days. Acidosis remained absent and he had continued his regular work. The excessive diet was reduced to 97 gm. protein and 2170 calories. The gripe cleared up promptly, and later examinations showed lungs and urine normal.

Second Admission.—On Apr. 26, 1917, the patient was readmitted on account of lobar pneumonia (*Pneumococcus* Type IV). Physical signs and radiograms indicated consolidation of right middle lobe. The temperature on admission was 101°F., rose the next day to 104°, on Apr. 28 reached the maximum of 105.6°, was still as high as 105.2° on Apr. 29, and fell by crisis to normal the next day. Liquid diet was given, largely milk, containing as high as 40 gm. carbohydrate.

The course of the pneumonia was uneventful, and neither glycosuria nor acidosis appeared. The patient was transferred from the pneumonia to the diabetic service on May 5. He convalesced uneventfully, and was discharged May 28 on a diet of 100 gm. protein, 80 gm. carbohydrate, and 2250 calories. Weight 59.2 kg.

Subsequent History.—On June 19, the patient caught cold and also lost his temper in a dispute. Rather heavy glycosuria appeared promptly, but disappeared on omitting four meals. On resuming full diet glycosuria returned, and ceased with another fast-day. The patient then reduced his diet and reported on July 2, having been sugar-free since the attack. The diet was ordered diminished to 80 gm. protein, 60 gm. carbohydrate, and 2000 calories. On this he has since remained slightly hungry but free from symptoms and feeling strong and well. In July, 1917, the weight was 61.9 kg., the blood sugar during digestion 0.112 per cent, CO₂ capacity 60.2 per cent.

Remarks.—The diabetes was essentially mild, and it is hoped that it may be kept so. The most noteworthy feature is the wholly uneventful manner in which the patient passed through an attack of pneumonia of moderate severity. The absence of diabetic symptoms during this time may be attributed chiefly to the very low diet given during the period of active infection. Permanent injury of the tolerance was thus apparently prevented. Notwithstanding the excellent condition and the normal blood sugar, the outbreak in June shows that the latent diabetes must still be guarded against, doubtless throughout the patient's life, though improvement may perhaps continue with advancing years. On the other hand, the age is such as to threaten serious consequences if the condition is not held in check. The patient is now on a well balanced diet, which may be expected at least to delay any downward progress if it does not prevent it altogether.

CASE NO. 45.

Male, age 6 yrs. American Jew. Admitted Sept. 1, 1915.

Family History.—Parents and two brothers of patient (aged 9 and 11) are entirely well and free from glycosuria, though slightly obese. No diabetes in mother's family, but her mother died of cancer at 53. The father's family history is negative on his mother's side, but diabetic on his father's side; *i.e.*, a great grandmother died at 76 of diabetes, and the father and an uncle of the present patient's father are living and have diabetes. No tuberculosis, syphilis, Bright's disease, goiter, etc., known.

Past History.—Normal delivery. No childhood diseases; never sick a day. Always big and plump, but not obese. Never nervous. Has never gone to school but received a little instruction from a governess. He has been bright and quick to learn, and has spent nearly all his time playing, automobiling, or in other active recreations. Appetite always large, and he has eaten much cake, candy, ice cream, and other sweets.

Present Illness.—About Nov. 20, 1914, polyuria and loss of weight were noticed. A physician prescribed medicine without examining the urine. Another physician a few days later discovered glycosuria, and two eminent consultants were called. A repetition of oatmeal and green days was employed according to the von Noorden plan, and the patient with difficulty was made free from glycosuria, but acetonuria persisted. Last Mar. there was an attack of grippe, with otitis media requiring paracentesis, which was performed without anesthesia. The patient is said to have become completely comatose; he was treated with fasting and rectal drip, recovered from this attack, and became sugar-free on a diet of Whiting's milk and thrice cooked vegetables. A little carbohydrate was later added, but traces of acetone continued. During the past summer, at the parents' summer home, the control was too lax to prevent violations of diet, with the result that on July 10 the patient suddenly fell out of his chair at table. He was then brought to New York and placed under the care of one of the advocates of treatment with lactic acid bacilli. A full caloric diet was given with restricted carbohydrate during this treatment, and also sodium bicarbonate, from one to six heaping teaspoonfuls daily. There was steady loss of weight and strength. For 7 weeks past the patient has been confined to bed or chair, unable to stand because of weakness; for past several days he has been too weak to sit up. During this time apathy and stupor have been increasing, but he is not quite in coma. Greater edema than that now present is said to have occurred from bicarbonate in the past. The weight before onset of diabetes was 47 pounds; before the present bicarbonate edema, it was 36 pounds. Meantime a long series of urinalysis reports from a commercial laboratory, exhibited by the father, showed steady improvement under the lactic acid treatment, the glycosuria being diminished from heavy to slight and the acidosis having disappeared. The practitioner in charge blamed the laboratory for the mistake, but had been administering sodium bicarbonate in maximum doses rectally as well as orally. An inconsistency on the part of the laboratory was that their reports showed acid reactions of the urine with alleged negative ferric chloride reactions under this treatment.

Physical Examination.—Patient still shows signs of having been a splendidly developed, handsome child. He is now stuporous, and questions must be repeated several times before a response is obtained. Complexion pasty. High degree of general anasarca; deep pitting of extremities on pressure, and fingers or bed clothing leave marks all over the body. Eyelids are swelled nearly shut. Intraocular pressure very low. Mucous membranes very red; tongue coated;

gums swollen and spongy and bleed easily. Throat not examined because of mental condition and edema. No gland enlargements made out. Left chest hyperresonant. Right side shows everywhere flatness and other signs of a large pleural effusion. Systolic blood pressure approximately 62. Marked tympanites in abdomen, and movable dullness in flanks. Both testicles in scrotum, partly obscured by fluid which swells scrotum to about the size of a large apple. Knee and Achilles jerks not obtainable. Over the sacrum an area of dusky redness, as large as a man's hand, seems almost ready to slough. Temperature 97.4; pulse 66; respiration 16, without dyspnea.

Treatment.—(No graphic chart.) The patient was too weak to move himself in bed, and the nurses were instructed to turn him at intervals with a view to avoiding pressure sores and hypostatic pneumonia. Fasting was begun with very small doses of whisky. Notwithstanding the huge bicarbonate edema, the previous reports of acid urine were confirmed, and in the presence of incipient coma, fear was entertained of stopping bicarbonate suddenly, or using any strong diuretic which might alter the water balance in unknown manner. Accordingly, on the 1st day 10 gm. sodium bicarbonate, 16 gm. calcium carbonate, and 4 gm. magnesium oxide were given, and on the next day 20 gm. each of sodium bicarbonate and calcium carbonate, also 1 cc. aromatic cascara. Satisfactory laxative action was obtained, and there was neither nausea nor diarrhea. The tympanites was relieved. The attempt was made to force fluids, and 3850 cc. water were given on Sept. 2, but the total urinary output was only 1425 cc. It was evident that the child was unable to dispose of his fluid, and this fact was further evidenced by the gain of 2.6 kg. weight, with evident increase of edema. Strength did not improve, as it frequently does on fasting. On the contrary, there was a perceptible increase of weakness, though the mental condition decidedly improved. Both glycosuria and ketonuria were rapidly diminishing. Beginning Sept. 3, no alkali was used, and water was supplied only for thirst. By Sept. 5 glycosuria was absent, and on the next day the ferric chloride reaction was entirely negative. The child was mentally bright, and seemed in no immediate danger in regard to strength. Green vegetables representing 3.3 gm. carbohydrate were eaten with relish, and it was planned to begin protein feeding the following day, with encouraging prospects. Edema was beginning to subside, as shown by the falling weight; but albuminuria, which had been absent on admission, seemed to develop as the urine turned alkaline; casts were not found. During the night of Sept. 6-7, the strength suddenly collapsed altogether. The resident physician, immediately called, gave a saline hypodermoclysis, which was absorbed but had no perceptible effect. When seen at 4:30 a.m., the child was cold in spite of being surrounded with hot water bottles; temperature down to 95.8°; pulse 60, barely perceptible; respiration 16 to 20; completely unconscious, without eye reflex; rectal sphincter completely relaxed. 10 gm. levulose in 100 cc. water were immediately given by stomach tube, and another 10 gm. in 100 cc. saline subcutaneously. The condition seemed to improve slightly, but con-

sciousness did not return. At 6:50 a.m. another hypodermoclysis was given of 250 cc. saline containing 20 gm. levulose. Half an hour after this, when asked if he was hungry, the child answered yes. He swallowed 50 cc. bouillon containing 2 gm. ereptone. During the day six eggs, 50 gm. butter, and 700 cc. soup were taken with relish, also 20 cc. whisky. A similar diet was given on Sept. 8. The child seemed to be rapidly gaining strength; but diarrhea was present, supposedly due to the levulose and ereptone, and bismuth was given for this. By Sept. 9, the stools had become frequent, badly digested, and very putrid in odor. Tympanites had returned. In place of the former subnormal temperature there was now fever of 101.8°. The blood pressure could now be definitely determined at 85 systolic and 68 diastolic. The patient now moved his arms and legs voluntarily, but had not become able to turn his body. On account of the apparent putrefactive intestinal condition, and the impossibility of employing fasting in view of the former collapse, it was decided to try oatmeal. Therefore, the former egg diet was stopped after breakfast. A dose of 10 cc. castor oil was given; 16 cc. whisky, 60 gm. oatmeal, and 200 cc. clear soup constituted the diet for this day. The tympanites and diarrhea were not relieved; stools became frothy as well as foul smelling. Heavy glycosuria appeared immediately, as shown in Table XII, and with it a moderate ferric chloride reaction. Stupor and Kussmaul dyspnea came on rapidly. As the oatmeal had failed so completely, it was ordered stopped at evening, and 10 cc. more castor oil were given. Between 9 and 10 p.m., a 250 cc. cylinder containing 25 cc. 3 per cent sodium citrate solution was filled with blood from the patient's father. A vein was exposed in the patient's arm, the operation eliciting no sign of consciousness, and the blood was allowed to flow in. It was hoped by means of the transfusion to contribute a little strength to tide over the fasting necessary as the only hope for clearing up the coma. No immediate change was perceptible except a slight improvement in pulse. On Sept. 10, the temperature had become normal and the patient could be roused. Toward evening he wakened spontaneously and began to cry for food. 75 cc. clear soup were given. Edema of both face and feet became more marked. On Sept. 11, the child became unconscious in a different manner, with weak pulse and feeble Cheyne-Stokes breathing. Another transfusion of 150 cc. citrated blood from the father was given; a hypodermoclysis of 200 cc. saline containing 10 gm. levulose; and by stomach tube 6 cc. whisky, 10 gm. levulose, and 140 cc. Whiting's milk, from which the cream had been removed by centrifugation. The temperature was normal, and the picture was one of intoxication, different from the previous hunger collapse or diabetic coma. Eggs and whisky were given by stomach tube during the day, making a total diet of 40 gm. protein and 500 calories. The putrid smelling diarrhea returned, and death occurred with weakness, unconsciousness, and Cheyne-Stokes breathing at 5:30 p.m.

Acidosis.—The excessive use of bicarbonate, guided only by the urinary reactions, had produced not only extreme anasarca but a decided alkalosis. Prob-

ably this and the renal impermeability formed a vicious circle, each making the other worse. The lack of parallelism between urine and blood is illustrated by the acid urine of Sept. 9, with the highest plasma alkalinity of the series. The value of the direct determination of the plasma bicarbonate is thus illustrated. The only other indication that no more alkali was needed was given by the low ammonia values. These are of interest as evidence that the ammonia formation of diabetic acidosis is due entirely to acid and not to any toxic perversion of protein metabolism. On the other hand, the strict independence of coma and acid intoxication is shown by the beginning of diabetic coma, typical in everything except hyperpnea, observed on two occasions (at admission and Sept. 9) even with abnormally high plasma alkalinity. The effect of oatmeal on Sept. 9 is also remarkable, for it increased the ketonuria, raised the plasma bicarbonate from 67.8 to 84.9 vol. per cent, and brought on prompt coma. Clinically, therefore, it aggravated both the diabetes and the intoxication, irrespective of chemical findings. It is interesting that such administration of carbohydrate with reduction of fat should have had this effect, illustrating the fact that coma is generally treated more safely and effectively with fasting than with carbohydrate. The acidosis caused by oatmeal cleared up on fasting, and the urine at death was free from both sugar and ferric chloride reactions. The relatively low output of acetone bodies may be explained by the renal impermeability, which doubtless favored retention. Neither qualitative nor quantitative tests for acetone bodies in the blood were made, but the clinical picture indicated that death was not due to acidosis.

Lipemia.—The blood at admission showed one of the most intense grades of lipemia observed in this series. Analyses were not possible, and judgment is based on the thick, creamy appearance of the plasma. The lipemia showed no perceptible diminution up to Sept. 9, but on Sept. 11, after transfusion on Sept. 10, the plasma was perfectly clear. It was unfortunate that the effect of the transfusion was not observed in this connection.

Levulose.—The patient had tolerated 3.3 gm. carbohydrate on Sept. 4. The glucose tolerance in such a case must necessarily be close to zero. Nevertheless, 40 gm. levulose on Sept. 7 were assimilated without a trace of glycosuria. The most remarkable feature was the clinical transformation wrought by the levulose—a patient apparently dying restored in strength and consciousness within a few hours. As saline hypodermoclysis had previously failed, this effect must be attributed to the levulose and not to the fluid given with it. It is of interest that the quantity of carbohydrate in the form of levulose was almost identical with that given in oatmeal on Sept. 9. The contrast between the excellent assimilation of levulose and the prompt glycosuria and ketonuria from oatmeal is striking.

Transfusion.—This was performed for the purpose of improving strength, and not with the idea of conveying any special substances curative of either the diabetes or the acidosis. The facts pertaining to this, as also other special features of the case are given in Table XIII.

The analyses of the father's blood immediately preceding the two transfusions were as follows:

On Sept. 9, blood sugar 0.1 per cent, plasma sugar 0.091 per cent, corpuscle sugar analyzed 0.125 per cent, calculated 0.114 per cent. Hemoglobin (Fleischl-Miescher) 104 per cent. Corpuscles (hematocrit) 42 per cent. CO₂ capacity of plasma 56.4 per cent.

On Sept. 11, blood sugar 0.115 per cent, plasma sugar 0.137 per cent, corpuscle sugar analyzed 0.097 per cent, calculated 0.083 per cent. Hemoglobin 95 per cent. Corpuscles (hematocrit) 40 per cent. CO₂ capacity of plasma 52.8 per cent. The high sugar and low CO₂ are explainable by the anxiety and haste of the father when called to the hospital.

The purpose of improving strength was accomplished. No specific benefit to the diabetic condition was perceptible from the transfusion, also there was no indication of harm.

Sugar Permeability of Corpuscles.—As the abnormalities were so marked in several respects, observations upon the sugar content of the corpuscles were made in the same manner as with the exercise experiments in Chapter V; *viz.*, by direct analysis of the corpuscles after hard centrifugation, and by calculation from the values for whole blood and plasma. The agreement between the two results is generally as good here as can be expected. Deficient centrifugation, leaving some plasma with the corpuscles, is probably responsible for the unduly high figure from direct analysis on Sept. 1. No special abnormality in the permeability of the corpuscles to sugar was shown under the conditions in question.

Remarks.—Obviously there was little real hope for such a patient under any circumstances, and the relatives were surprised that life was continued for 10 days and that improvement seemed to be evident at certain periods.

CASE NO. 46.

Male, married, age 48 yrs. Russian Jew; dry goods storekeeper. Admitted Sept. 1, 1915.

Family History.—Mother died at 65 of supposed cardiac trouble. Father well at age of 72. Only brother is well. Patient's wife and five children well, but one daughter died of diabetes at age of 16, 9 years ago. No other heritable disease known in family.

Past History.—Healthy, rather sedentary life without special strain or worry. Pneumonia at 10 years the only infection remembered. Diet has been the concentrated, monotonous type characteristic of his class. No special excesses.

Present Illness.—Patient distinctly remembers a day in Oct., 1914, when he became acutely thirsty and drank much water. He immediately consulted a physician, who reported 5.5 per cent sugar in the urine. On a diet of protein, fat, and vegetables, glycosuria ceased in 2 days, and remained absent until Mar., 1915, when rapid loss of weight also came on. From the normal 150 pounds he

was now down to 130 pounds. He entered a hospital on May 5, 1915, where the sugar and diacetic acid cleared up on fasting with brandy. These returned within 2 days of his discharge from the hospital on May 17. His private physician, on account of fear of the diacetic acid present, then kept him on a liberal carbohydrate diet. In July the condition was again cleared up in the hospital. It returned promptly and was again treated with carbohydrate by the same physician. Loss of weight and strength has proceeded rapidly. There is chronic pain in back and legs.

Physical Examination.—Medium sized, thin, very exhausted appearing patient. Skin dry. Eczema in axillæ. Teeth in bad condition. Pharynx reddened; tonsils not enlarged. Scattered lymph nodes palpable. Heart slightly enlarged; systolic murmur heard all over precordia, loudest at apex. Slight arteriosclerosis. Double inguinal hernia retained by truss. Knee jerks not obtainable, even with reinforcement. Examination otherwise negative.

Treatment.—Fasting with whisky and 30 gm. sodium bicarbonate and 30 gm. calcium carbonate daily was begun immediately. After Sept. 5, both glycosuria and ketonuria ceased. Alkali was stopped and whisky continued. Green vegetables were then begun, and increased until glycosuria appeared with 140 gm. carbohydrate on Sept. 12. After a few days of low mixed ration, on Sept. 19 a diet was started containing 100 gm. protein and 50 gm. carbohydrate. Keeping this constant, the total calories were rapidly increased by addition of fat, with the result that sugar and ferric chloride reactions returned in the period Sept. 21 to 25. Exercise experiments were performed during this time as described elsewhere (Chapter V). Exercise was then continued in the period Sept. 27 to Oct. 9. The result showed that the discontinuance of alcohol, combined with muscular work to the point of exhaustion, did not cause acidosis as evidenced by either ferric chloride reactions or lowered plasma bicarbonate. Also, though the total caloric ration was much higher than that which had brought glycosuria on Sept. 21, sugar now remained absent until Oct. 6. A carbohydrate tolerance test was next instituted in the usual manner. Glycosuria appeared with an intake of 230 gm. on Oct. 30, but was not quite continuous when the intake was raised to 240 gm., or even to 300 gm. on Nov. 6. The heavy exercise probably contributed somewhat to this tolerance. The patient was discharged on Nov. 16 and resumed business, feeling well.

Acidosis.—Moderate acidosis was indicated by the heavy ferric chloride reaction, 1.1 gm. ammonia nitrogen, and plasma bicarbonate of 41.9 vol. per cent at admission. Under fasting and alkali the ammonia quickly fell to normal, and the CO₂ capacity rose to the high level of 73 per cent. The ferric chloride reaction diminished even during alkali administration, and became negative the day after alkali was stopped. But within 2 days thereafter (Sept. 7), the CO₂ capacity had fallen to 50.4 per cent. The lower figure of 39 per cent on Sept. 8 was obtained after hard exercise. Other tests in exercise experiments are omitted from the graphic chart. The last determination, on Oct. 27, during the carbo-

hydrate period, showed a low normal figure of 55.8 per cent. The ferric chloride reactions behaved as frequently noted, coming and going about the same time with small traces of glycosuria.

Blood Sugar.—On the first day in hospital the sugar in whole blood was 0.555 per cent, in plasma 0.606 per cent. Fasting brought a very quick fall, but not to normal, and marked hyperglycemia returned on feeding. The renal threshold was probably high. On Sept. 25, the percentage in plasma was 0.371 per cent as against 0.244 per cent in whole blood, indicating a very low sugar content in the corpuscles. The low plasma sugar of 0.123 per cent on Sept. 29 was obtained immediately upon finishing noon lunch, the patient having spent the morning at heavy exercise. The tendency of the blood sugar was continuously downward, the last analyses, on the morning of Nov. 13, showing 0.113 per cent in whole blood and 0.145 per cent in plasma.

Weight and Nutrition.—Weight at admission 51 kg.; at discharge 47.4 kg., a reduction of 3.6 kg. The patient had been pale and badly exhausted at admission. He was accepted because he appeared to represent a very pronounced degree of lowered resistance and susceptibility to infectious and other accidents. On undernutrition treatment he gained strength decidedly with the combination of loss of weight and heavy exercise, and though thin, pronounced himself feeling well. The diet prescribed at discharge was 100 gm. protein, 50 gm. carbohydrate, and 2000 calories (about 2.1 gm. protein and 42 calories per kg., reduced by the weekly fast-days to 1.8 gm. protein and 36 calories per kg.). Three factors were considered here: first, the low weight upon which this reckoning is based (47.4 kg. as against 65 kg. normal); second, the hard exercise prescribed; and third, the steady improvement, justifying some slight liberality of diet, which also seemed desirable for the purpose of building up weight and strength.

Lipemia.—The plasma at admission was heavily lipemic. This lipemia was present in marked degree up to Sept. 3, then ceased rather abruptly, for the plasma on Sept. 4 was clear. No analyses were done.

Subsequent History.—The condition remained favorable, and glycosuria was absent except for a trace on Feb. 1. About Feb. 20, he contracted a severe cold, and shortly thereafter began to raise large amounts of foul smelling sputum. When seen on Mar. 4 he was a very sick man. Necrotic tissue but no tubercle bacilli were found in the sputum. Glycosuria and acidosis had returned with this infection. The patient was referred to another hospital, and died of pulmonary gangrene on Mar. 15, 1916.

Remarks.—The low resistance suspected at admission was confirmed by the outcome. Diabetes probably contributed to increase susceptibility, but it is believed that the treatment, by improving strength and permitting outdoor exercise, tended to raise rather than lower resistance in such a case.

CASE NO. 47.

Female, married, age 31 yrs. American; houseworker and canvasser. Admitted Oct. 6, 1915.

Family History.—Parents alive; Bright's disease suspected in father. Two sisters are well. Maternal grandmother died of tuberculosis. Husband healthy. Patient pregnant only once; the child is well, aged 8. History otherwise negative.

Past History.—Life was spent in Wisconsin until 11 years ago, then in Porto Rico until 1 year ago, since then she has lived near New York. Always strong and healthy. Has had only some mild childhood diseases. Never nervous. Habits and diet normal.

Present Illness.—This began 4 years ago with pruritus vulvæ, not relieved by local treatments, but increasing during a year. By the end of the year polyphagia, polydipsia, and polyuria were present, and the normal weight of 185 pounds had fallen to 145. A physician then diagnosed diabetes and merely forbade sugar and starch. The pruritus has remained continuously present, and glycosuria was never reduced below 2 per cent. The patient applied to the Institute because she had been informed that she could not live more than 3 months.

Physical Examination.—Height 170.1 cm. A tall, large boned woman without marked emaciation but with flabby skin and muscles. She appears strong and plegmatic by nature, but worried and upset at present. Cheeks, high color; no dyspnea or other acute symptoms. Teeth in fair condition. Tonsils slightly enlarged. Lymph nodes palpable only in axillæ. Reflexes normal. Superficial genital infection from scratching. Blood pressure 90 systolic, 60 diastolic. Examination otherwise negative.

Treatment.—The patient was placed on an observation diet of 100 gm. protein, 100 gm. carbohydrate, and 3000 calories. Heavy glycosuria continued and acidosis increased. After 3 days of this diet a high ammonia and low plasma bicarbonate indicated danger. Accordingly 2 days of plain fasting were given (coffee and soup, each 300 cc.) followed by 4 days with alcohol up to 600 calories. Glycosuria was absent after Oct. 12, but the fasting was continued for 3 days longer, because it was acting favorably upon the acidosis and the patient was of a type requiring sharp undernutrition. With the cessation of glycosuria, the distressing vaginal pruritus of 4 years duration promptly cleared up. A carbohydrate test was then instituted. The ferric chloride reaction thus disappeared, and the limit of tolerance was found to be 240 gm. carbohydrate. After a fast-day on Nov. 14, the diet on Nov. 15 and 16 was 100 gm. protein and 2000 calories without carbohydrate. In order to test the effect of fat, this diet was built up by addition of fat. The first trace of ferric chloride reaction appeared with 2500 calories on Nov. 20. This reaction increased, the blood sugar rose, and glycosuria appeared on Nov. 27 with 4000 calories. It showed the characteristics of fat glycosuria in being slight and stubborn, not increased by the rise to 4500 calories on Nov. 29 and 30. Protein and fat were then stopped and nothing

but green vegetables given, increasing from 10 gm. carbohydrate on Dec. 1 to 70 gm. carbohydrate on Dec. 4. The ferric chloride reaction promptly cleared up, but traces of glycosuria persisted. After the fast-day of Dec. 5, a diet of 100 gm. protein and 2000 calories was begun, as on Nov. 15 and 16, but with the addition of first 10 and then 20 gm. carbohydrate. After Dec. 9 both glycosuria and ketonuria were absent on this diet, and on Dec. 18 it was possible to increase the carbohydrate to 70 gm. without glycosuria. The effect of the fat in lowering tolerance is thus evident. The patient was discharged Dec. 22 on a diet of 100 gm. protein, 50 gm. carbohydrate, and 2000 calories, (1.6 gm. protein and 31.8 calories per kg., reduced by the weekly fast-days to 1.4 gm. protein and 27.3 calories per kg.).

Acidosis.—The attending physician sent this patient to the Institute because confronted with the dilemma formerly feared; *i.e.*, continuous glycosuria notwithstanding restriction of carbohydrate, and acidosis present even with carbohydrate in the diet. The rise of ammonia nitrogen from 1.62 gm. on Oct. 7 to 3.63 gm. on Oct. 10 probably indicates that 10 gm. carbohydrate represented greater restriction than this patient had been accustomed to. The CO₂ capacity of the plasma, 41 per cent on Oct. 10, also gave evidence of well marked acidosis on this diet. There was the usual improvement on fasting, the CO₂ capacity rising promptly without the use of alkali, but not attaining the normal limit until near the close of the carbohydrate test on Nov. 12. Protein-fat diet thereafter brought a fall, and particularly with the increase in fat it is seen that well marked acidosis developed, the CO₂ capacity of 39 per cent on Nov. 27 being lower than recorded even in the first days after admission. Coma would almost certainly have resulted from continuance of such an experiment. The fast-day of Nov. 28 gave a prompt respite, so that the CO₂ capacity on the morning of Nov. 29 had risen steeply to almost 53 per cent. On the morning of Nov. 1, after 2 more days of higher fat intake, it showed a drop, but the small quantities of carbohydrate and omission of fat brought it up promptly within normal limits by Dec. 2. Thereafter, with reduced fat and introduction of a little carbohydrate, fully normal values of blood bicarbonate were obtained.

Ammonia determinations had been discontinued on Oct. 12, after it was evident that the course was downward. It may be assumed that the curve fell to normal during the carbohydrate test. Following the fat experiment it was up to 2.24 gm. N on Nov. 1. There was a prompt drop with carbohydrate, followed by a rise to 1.92 gm. N on the lower fat intake, and another fall after the fast-day of Dec. 12. The ferric chloride reaction roughly corresponded to the other evidences of acidosis.

Blood Sugar.—Though the restriction of carbohydrate caused acidosis, the high values of 0.38 per cent sugar in whole blood and 0.524 per cent in plasma on Oct. 9 indicated how far the diet still exceeded the tolerance. With fasting there was a prompt fall in blood sugar, but not to normal. Hyperglycemia gradually increased during the carbohydrate test, and persisted after it to Nov.

17. The abstinence from carbohydrate showed its effect in a fall on Nov. 20; but an increase of blood sugar due to an increase of fat in the diet was then clearly demonstrable, leading to glycosuria as mentioned. After the undernutrition period (Dec. 1 to 5), the first normal plasma sugar was obtained on Dec. 6. Thereafter the restriction of fat, though protein was kept the same and carbohydrate was added, resulted in a fall of blood sugar so that the patient was dismissed with a normal plasma sugar of 0.12 per cent.

Weight and Nutrition.—The weight at admission was 67.3 kg., at discharge 62.9 kg. The treatment thus represented undernutrition to the extent of 4.4 kg. At the same time vigorous exercise was employed. The patient was naturally strong, and after her immediate distress was relieved she was soon able to walk 4 miles, climb 40 flights of stairs, and practice roller skating and other exercises daily. Her weight at discharge was satisfactory for both strength and looks. Her muscles were firm, and she was in splendid health subjectively and objectively.

Subsequent History.—The patient reported on Jan. 4 free from glycosuria, but weighing 64.9 kg., a gain indicating that she had not been faithful to the prescribed exercise and quantity of diet. She was instructed to bring the weight down to that at discharge. Notwithstanding warnings, she gradually became more careless in regard to diet, and ceased weighing food. Glycosuria returned first in occasional traces which were cleared up, and then during Apr. continuously. On May 24, she was still looking perfectly well, but complained of weakness and weariness along with glycosuria. The sugar in both whole blood and plasma was 0.201 per cent, CO₂ capacity 52.1 per cent. When seen again on July 22, the findings were heavy glycosuria, moderate ferric chloride reaction, blood sugar 0.370 per cent, plasma sugar 0.385 per cent, CO₂ capacity 56 per cent, weight 68.3 kg. She was not seen again until June 7, 1917, when her weight was 70 kg., due in considerable part to edema. She was still looking and feeling fairly well, but the urine showed a heavy sugar and slight ferric chloride reaction. The carelessness in diet was continuous. Downward progress clinically, which seemed to be slow in appearing, was very rapid at the close, and reports in July, 1917 indicated that the patient was close to death from weakness and acidosis.

Remarks.—The case would have been a difficult one to manage under former treatment, but with the present methods showed itself as only moderately severe. The complete clearing up of the condition both chemically and clinically served to prolong comfort, strength, and life, even though diet was violated afterwards. The patient lacked the necessary will power to adhere to diet, and downward progress was therefore inevitable. She gained strength as she lost weight in hospital, and lost strength as she gained weight outside the hospital. At no time could it be said that she was stronger or better off on a diet in excess of the tolerance.

CASE NO. 48.

Male, unmarried, age 20 yrs. American; shipping clerk. Admitted Oct. 7, 1915.

Family History.—Partly unknown. Two uncles died of tuberculosis. Family said to be free of diabetes, cancer, syphilis, and nervous troubles.

Past History.—Healthy life in rather poor surroundings. Childhood diseases unknown. Occasional mild sore throats. Considerable trouble with teeth. No venereal disease. Reached graduating class in grammar school at 15, then began work as delivery boy, and 6 months ago was promoted to shipping clerk. No alcoholism. Cigarettes smoked to excess. Has had more than the average appetite for candy, pastry, and sweet things.

Present Illness.—Polyphagia, polydipsia, and polyuria began 1 year ago. Diagnosis was made within a month, and the physician forbade sugar and starch and ordered a teaspoonful of sodium bicarbonate three times a day. Patient did not adhere to the diet and became worse. Later he was treated by another physician and at a hospital clinic, and at the latter place was advised to come to this Institute.

Physical Examination.—A round shouldered, narrow chested, underdeveloped, undernourished boy. Teeth in fair repair; tonsils normal. General examination negative.

Treatment.—(No graphic chart.) The usual heavy glycosuria and ketonuria were present, but no signs of immediate danger. After 3 days of observation diet, a 5 day fast cleared up the glycosuria. Green vegetables were begun on Oct. 15, and 10 gm. carbohydrate added daily, until persistent traces of glycosuria appeared with 130 gm., Oct. 27 to 30. Meanwhile the ferric chloride reaction became negative. A mixed diet was then rather rapidly built up, but though this was adequate in amount, the patient proved himself entirely untrustworthy. He was kept in the hospital until July 28, 1916, but always showed the undependable character and degeneracy of the excessive cigarette smoker, and continually broke rules in regard to both diet and smoking. He insisted that he must have sugar on occasions, and 40 to 50 cigarettes daily. Under hospital management he had been kept free from glycosuria nearly the entire time. He was discharged with the certainty that he would go rapidly downhill.

CASE NO. 49.

Female, divorced, age 30 yrs. American; seamstress. Admitted Oct. 9, 1915.

Family History.—Father died of peritonitis, following gall stones. Mother living, aged 55, also has gall stones. Four brothers died in infancy; one brother and one sister are well. No diabetes or other heritable disease in family.

Past History.—Measles, mumps, chicken-pox, scarlet fever, before 10. Membranous croup at 6 years requiring intubation. Many sore throats, especially

tonsillitis previous winter. Married 8 years ago. Two children 13 months apart; both high forceps and died of weakness or convulsions within 6 months. Patient always nervous and overexcitable. 6 years ago nervous breakdown confined her to bed for 12 weeks. No excesses in diet or otherwise.

Present Illness.—Shortly before Christmas, 1914, began polyphagia, polydipsia, and polyuria. She found she had lost 25 pounds weight since the previous summer. She was given the usual diet but did not adhere closely to it. Last winter vision became blurred; glasses have helped somewhat, but at present she cannot read and has difficulty walking about because of blurring of sight. Has been tired and weak for 6 months past, and sleeps a couple of extra hours in the afternoon.

Physical Examination.—Patient fairly developed, only slightly emaciated. Mouth and throat normal. No lymph node enlargements. Reflexes normal. General examination negative.

Treatment.—The patient was admitted at 11 a.m., and up to 6 a.m. the next morning excreted 118 gm. glucose, with a heavy ferric chloride reaction and 2.93 gm. ammonia nitrogen. The first CO₂ determination on Oct. 9 was 34.4 per cent. The diet on Oct. 9 was 100 gm. protein, 100 gm. carbohydrate, and 2200 calories. The ammonia nitrogen rose to 3.36 gm., and the CO₂ capacity on the morning of Oct. 10 was down to 27.8 per cent. The patient was drowsy, with face flushed, and spent most of her time in seemingly normal sleep. There was no marked dyspnea, but the coryza present at admission persisted, with temperature up to 100.5° F. On Oct. 10 fasting was begun, with 120 cc. whisky and 60 gm. sodium bicarbonate. Whisky was continued, but no more alkali was given. The CO₂ capacity rose and the ammonia fell, and acidosis symptoms cleared up. Glycosuria ceased after 5 days of fasting. 10 gm. carbohydrate in green vegetables were added to the whisky on Oct. 15. Whisky was then discontinued and carbohydrate continued at 30 gm. daily. This caused glycosuria, which cleared up under exercise as noted below. It was then possible to make the usual increase of 10 gm. carbohydrate daily. A trace of glycosuria appeared with 150 gm. carbohydrate on Nov. 2, then disappeared, and reappeared with 170 gm. carbohydrate on Nov. 5. Meanwhile the ferric chloride reaction cleared up. A diet of 2000 calories with 75 gm. protein and 15 gm. carbohydrate was then begun with the usual weekly fast-days. The attempt to increase carbohydrate to 40 gm. on Nov. 23 resulted in glycosuria. The patient was dismissed on Dec. 3 feeling strong and well, having recovered her vision perfectly. An oculist found vision normal and considered that the blurring had been a functional weakness of accommodation.

Acidosis.—Even though the diet on Oct. 9 contained 100 gm. carbohydrate, restriction to this extent brought on symptoms of impending coma. There was the usual clearing up on fasting, and the recovery of a considerable carbohydrate tolerance. It is noteworthy that mixed diet tended to bring back the ferric chloride reaction. In the last analyses on Dec. 1, preceding discharge, the CO₂

capacity of the plasma was normal and the ferric chloride reaction negative, but a slight acidosis was indicated by the ammonia nitrogen of 1.24 gm. The sugar in both whole blood and plasma at admission was 0.333 per cent. On Oct. 15, after 2 days freedom from glycosuria, the sugar was still 0.217 per cent in whole blood and 0.244 per cent in plasma. Notwithstanding the high carbohydrate intake, the blood sugar on Nov. 4 was down to 0.169 per cent, plasma sugar 0.164 per cent, in consequence of continued undernutrition and exercise. After a rise to 0.204 per cent on Nov. 11 with mixed diet, the tendency of the blood sugar was downward, and on Dec. 1 it was 0.133 per cent in whole blood, 0.167 per cent in plasma.

Exercise.—Glycosuria had appeared with green vegetables representing 30 gm. carbohydrate on Oct. 17, and persisted with this intake on the following days. Beginning Oct. 19, exercise was ordered. The patient skipped rope for 15 minutes daily, and on Oct. 19 climbed 32 flights of stairs, on the 20th 48 flights, on the 21st 96 flights. On this day glycosuria ceased. Exercise to the point of exhaustion was continued as carbohydrate was increased on the following days. The effect in raising tolerance was demonstrated by the cessation of glycosuria as described, and the exercise doubtless contributed toward the high tolerance then displayed. Nevertheless simple continuance of undernutrition represented in the carbohydrate period must be given credit as the most beneficial factor.

Weight and Nutrition.—The weight at entrance was 52.4 kg., at discharge 49.8 kg., the treatment thus representing undernutrition to the extent of 2.4 kg. The diet at discharge was 75 gm. protein, 25 gm. carbohydrate, and 2000 calories, representing approximately 1.5 gm. protein and 40 calories, reduced by the weekly fast-days to an average of about 1.3 gm. protein and 34 calories per kg. This was considered a low diet in view of the amount of exercise which the patient was ordered to continue at home. She was some 36 pounds below her normal weight and was not expected to gain weight on this ration. Faith was largely reposed in exercise to bring down the blood sugar further and raise the tolerance. Later knowledge makes it evident that a lower diet with less strenuous exercise would have been better treatment, and reduction of the too large fat intake would have been the best means of bringing down both the ammonia and the blood sugar.

Subsequent History.—In Jan., 1916, the patient showed traces of glycosuria during a short attack of grippe. Thereafter she was free from sugar and ferric chloride reactions up to the last report in Feb. The next word received was notice of her death on May 19, 1916. Inquiry elicited the fact that she had broken diet about 1 month before death, and died with symptoms of diabetic coma.

Remarks.—The progress to a fatal end in 1 month indicates the severity of the case, and this result of breaking diet is in contrast to the excellent condition at the time of discharge.

CASE NO. 50.

Widow, age 54 yrs. American; teacher. Admitted Oct. 8, 1915.

Family History.—Negative for diabetes or other heritable disease.

Past History.—Very healthy life. No illnesses beyond those of childhood. Never pregnant. Regular habits. No excesses. Appetite, digestion, bowels, and menstruation normal until present illness; no menstruation since.

Present Illness.—In 1907, the patient entered a sanitarium on account of a "nervous breakdown." This had begun so gradually that the exact onset was unknown. She complained of general weakness and loss of energy, memory, and mental powers, also her teeth and hair were falling out, speech was slow, tongue thick, and face swollen. The diagnosis of myxedema was made, and thyroid extract restored apparently normal health. In 1912 she returned to the sanitarium, having taken thyroid extract throughout the interval. This time she had polyphagia, polydipsia, and polyuria. The diagnosis of diabetes was made, and thyroid extract was ordered discontinued for fear it might aggravate the diabetes. She has been unable to get along without thyroid, and has therefore continued to take it at intervals as the myxedema symptoms returned. Loss of weight has been only moderate, and the chief symptoms are a general breakdown, with weakness and nervousness, along with marked myxedema symptoms as above mentioned, coryza, headache, and complaint of pains all over the body.

Physical Examination.—Height 152.2 cm. A well developed, well nourished woman; hair turning gray, slightly coarse, abundant; broad puffy face; dry skin; pasty color; eyebrows and lashes scanty. A number of teeth missing; the others show some caries and pyorrhea. Throat normal. Lobes but not isthmus of thyroid palpable, apparently normal in size and consistency. Heart and lungs negative. Liver edge palpable 0.5 cm. below costal margin. Blood pressure 90 systolic, 75 diastolic. Fingers short, thick, not clubbed. Reflexes normal. The patient appeared as if intoxicated, and speech was difficult, almost incoherent. The diagnosis of myxedema was confirmed by several observers, and it was considered possible that intoxication of acidosis character was also present, notwithstanding the low ammonia and high CO_2 .

Treatment.—On Oct. 8 the diet contained 64 gm. protein, 28 gm. carbohydrate, and 1500 calories. The next day, with diminishing appetite, it was 35.5 gm. protein, 38 gm. carbohydrate, and 1375 calories. On this day there was nausea and one attack of vomiting. The symptoms at admission were still present. The highest temperature was 100.2° F. Fasting was begun on Oct. 10, with 300 cc. clear soup daily. 30 cc. castor oil and several high colon irrigations removed large quantities of feces. Glycosuria cleared up after 48 hours. On Oct. 10, 6 gm., and on Oct. 11, 22 gm. sodium bicarbonate were given. The urine remained acid or neutral, and the ferric chloride reaction, which had been slight, was increased to only moderate degree. On Oct. 13, 10 gm. carbohydrate in the form of green vegetables were given, and increased on subsequent days until on

Oct. 26, 110 gm. were taken without glycosuria, and a fast-day was necessary the next day because of indigestion due to the quantity of vegetables. The ferric chloride reaction had cleared up, and weakness and other symptoms had greatly improved. After the fast-day exercise was begun, particularly with a view to improving digestion, and by Nov. 1 the patient was on a regular program of walking 10 blocks and 24 flights of stairs daily. The bulk of vegetables was diminished by giving potato. On Nov. 2, the patient, feeling well and cheerful, experienced the sensation that the left foot was asleep. She stamped it and fell, fracturing the tip of the fibula. The leg was put up in plaster and exercise necessarily stopped. From Nov. 5 to 13, 200 gm. carbohydrate daily were tolerated without glycosuria and with diminishing blood sugar. Beginning Nov. 15, a mixed diet of 2000 calories and 65 gm. protein was begun with high carbohydrate, for purposes of a test with thyroid extract as described below. The subsequent glycosuria was cleared up by the fast-days of Dec. 19 and 20, after which a diet was built up of 75 gm. protein and 1500 calories, with carbohydrate gradually increasing up to 90 gm. on Jan. 14. The cast was removed from the fractured leg on Dec. 8, repair having been uneventful and perfect. She was discharged Jan. 14, 1916, with the feeling and appearance of complete health, to resume her duties as teacher.

Acidosis.—On the chemical side this never amounted to more than a slight ferric chloride reaction, but there was prompt and striking improvement in the intoxication symptoms under the usual treatment for acidosis. One subsequent feature is the steady rise of the CO₂ curve with increasing carbohydrate intake up to the very high value of 74.6 per cent on Dec. 17, then, with carbohydrate almost excluded, the steep fall to 53.8 per cent on Dec. 30. By Jan. 5, it had risen within low normal limits, without the aid of alkali, perhaps with the aid of the small quantity of carbohydrate.

Blood Sugar.—At admission, sugar was 0.375 per cent in whole blood and 0.371 per cent in plasma. By Oct. 16, it was found normal (0.113 per cent). With the subsequent high carbohydrate intake it tended to rise, but was brought promptly to normal on the morning after the single fast-day of Oct. 27. Values 0.3 to 0.32 per cent were obtained on Nov. 1 and 3 during digestion without glycosuria, but those taken mornings before breakfast tended to fall, so that toward the close of the period in hospital normal figures were the rule.

Weight and Nutrition.—The weight at entrance was 49.6 kg., at discharge 46.2 kg., the period of treatment thus representing undernutrition to the extent of 3.4 kg. The long period of relative protein abstinence is noteworthy, inasmuch as from Oct. 10 to Nov. 14 the patient received nothing but green vegetables, the protein of which is low in quantity and poorly assimilable. During this period there was a striking gain instead of loss of strength, and a fractured bone healed rapidly. The diet prescribed at discharge was 75 gm. protein, 50 gm. carbohydrate, and 1500 calories, representing, at her reduced weight, approximately 1.63 gm. protein and 32 calories per kg., diminished by the weekly fast-days to 1.4 gm. protein and 28 calories per kg. This was as much as her appetite desired.

Thyroid.—The history is remarkable in that diabetes accompanied not hyperthyroidism, but typical myxedema. Another surprising feature was that with the usual diabetic treatment of fasting followed by green vegetable diet, without thyroid or other medication, the myxedema symptoms rapidly improved, the mind and speech became clear, the face lost its puffy appearance, and the patient looked and felt almost well. It is not known whether this indicates that fasting may be beneficial for myxedema uncomplicated by diabetes. It might be supposed that the prolonged treatment with thyroid extract had brought on the diabetes. It was desirable to test this possibility, and also to establish the place of thyroid extract in the treatment of this patient. Accordingly on Nov. 15, a purposely high diet was begun, containing 65 gm. protein, 150 gm. carbohydrate, and 2000 calories. Glycosuria appeared on Nov. 17 but ceased the next day. On Nov. 19 the carbohydrate was increased to 250 gm. and at the same time 0.45 gm. desiccated thyroid was given, increased to 0.9 gm. the next day with the same diet. Glycosuria was heavy on the 19th, but cleared up completely on the 20th. After the routine fast-day on the 21st, the same diet was continued without thyroid. There was glycosuria on Nov. 23, a trace on the 26th, and continuous well marked reactions from Nov. 28 to Dec. 6. It thus appeared that the thyroid feeding had not injured the tolerance and perhaps had been slightly beneficial. Beginning Dec. 2 the carbohydrate was increased to 350 gm., with resulting continuous glycosuria. On Dec. 6, 0.032 gm. desiccated thyroid was given, the same on the 7th, 0.064 gm. on the 8th and 9th, 0.128 gm. on the 10th, and so on increasing up to 0.32 gm. on Dec. 18. Glycosuria stopped abruptly on the first day after beginning thyroid, and remained absent on the small doses for 3 days, while the blood sugar also fell to normal. Thereafter, with increasing thyroid dosage, glycosuria returned and became heavier, finally requiring 2 fast-days to stop it. Thyroid was omitted after Dec. 18, and by the first week in Jan. slight impairment of energy and mentality had returned. Therefore during the last week in hospital 0.05 gm. thyroid was given daily and was ordered continued after discharge. On this she was free from symptoms of thyroid deficiency. The tests, as far as judgment is possible, indicated that the carbohydrate tolerance was slightly improved by small doses of thyroid, although larger doses might injure it.

Subsequent History.—The patient continued well, and voluntarily diminished her diet because it was more than she desired. She twice experimented with herself, taking chocolate cake once and bread once, with immediate glycosuria which cleared up promptly. Otherwise she remained free from glycosuria and other symptoms. Apr. 15, sugar in whole blood was 0.142 per cent, in plasma 0.147 per cent. By July 11, the weight had fallen to 44.2 kg.; blood sugar was 0.137 per cent, plasma sugar 0.141 per cent, CO₂ capacity 52.3 per cent. The patient continued her duties as teacher and kept up thyroid medication as indicated by her own feelings. She began to take small quantities of bread without glycosuria. She was readmitted Oct. 2, 1916, at her own request to learn if these were safe.

Second Admission.—Oct. 2, 1916. Patient well nourished physically and mentally vigorous; no appearance of myxedema. General examination normal. Blood pressure 110 systolic, 78 diastolic. She was found to remain free from symptoms on the prescribed diet with 50 gm. carbohydrate taken in the form of bread and fruit. The blood sugar in daily determinations ranged from 0.102 to 0.118 per cent. As the patient was satisfied with the diet, it was decided to let it remain as stated. She was discharged Oct. 8, 1916, and has since continued her work in good health.

CASE NO. 51.

Male, age 7 yrs. Polish American; schoolboy. Admitted Oct. 10, 1915.

Family History.—Parents are Polish immigrants, well, except that mother is somewhat nervous. Only sister is well. No diabetes or other heritable disease known in family.

Past History.—Healthy life in small New York town. Whooping-cough the only illness known. Ordinary habits, diet, and development.

Present Illness.—1 year before admission patient was seen by a physician in his home town, with weakness and coma such that another physician had refused the case. The history was of polyuria and rapid loss of flesh and strength for only a week or two before that time. Intense glycosuria and acidosis were present. The patient recovered from the coma and has been kept almost continuously sugar-free by the local physician under fasting treatment. It became increasingly difficult to maintain freedom from glycosuria, and the patient was therefore referred to the Institute.

Physical Examination.—Height 121.1 cm. A well developed, pale boy with apparently moderate loss of weight. General examination normal. No acute symptoms.

Treatment. Only moderate sugar and ferric chloride reactions were present at admission. The former became negative on an observation diet of 40 gm. protein, 10 gm. carbohydrate, and 1000 calories. The latter was also negative after a single fast-day on Oct. 16. A carbohydrate test was then instituted in the usual manner, and glycosuria appeared with 100 gm. carbohydrate (Oct. 26 to 30). Mixed diet was then begun, with the usual weekly fast-days. Traces of glycosuria indicated that 50 gm. carbohydrate were too high. In general, a diet of 40 gm. protein, 25 gm. carbohydrate, and 1100 calories, with routine weekly fast-days, was tolerated with normal urine. He was discharged on this diet Jan. 19, 1916, with the appearance of very satisfactory health and strength.

Acidosis.—Although the ferric chloride reaction was never more than moderate, the first CO₂ determination on Oct. 16, following a protein-fat diet with 10 gm. or less of carbohydrate, showed the rather low value of 44.8 per cent. During the carbohydrate test this rose to 59 per cent by Oct. 29. The fast-day of Oct. 31 brought a remarkable drop in both the sugar and bicarbonate of the blood, the CO₂ capacity on the following morning being down to 33 per cent. On the

ensuing mixed diet it promptly rose, without the aid of alkali, and after a moderately subnormal period up to Nov. 18, thereafter held a normal level for a child. On Jan. 15, shortly before discharge, it was 57.2 per cent. The ammonia output in the few determinations made was normal.

Blood Sugar.—The first analysis on Oct 25, during the carbohydrate test, showed 0.35 per cent sugar in whole blood and 0.37 per cent in plasma without glycosuria, indicating a high renal threshold. With glycosuria present on Oct. 29, the sugar during carbohydrate digestion was at the high level of 0.46 per cent in whole blood and 0.511 per cent in plasma; but on the morning of Nov. 1, after the preceding fast-day, it was down to the normal level of 0.109 per cent. Hyperglycemia then ensued on mixed diet, but by Nov. 11 the percentage was below 0.1 in both whole blood and plasma. Thereafter the tendency of the curve was toward normal; but the rise to 0.164 per cent on Jan. 15, shortly before discharge, was an unfavorable indication, which should have called for more stringent treatment.

Weight and Nutrition.—The weight at admission was 18.3 kg.; at discharge 17 kg. Therefore, instead of growth, the undernutrition resulted in a loss of 1.3 kg. in a little over 3 months. The diet at discharge represented approximately 2.3 gm. protein and 65 calories per kg., diminished by the weekly fast-days to about 2 gm. protein and 56 calories per kg. The boy had been on nearly or quite such a diet throughout most of the hospital period, and it would seem that a normal child might have gained weight under these conditions. Part of the explanation is found in exercise, for he was kept busy with vigorous games and gymnastics all day long. The exercise was beneficial from the standpoint of enjoyment, freedom from nervousness, and development of strength and general health, but it is evident that the tolerance was not raised very high.

Subsequent History.—The patient attended school, played, and remained well, with no glycosuria except during a brief cold in Mar. In May, glycosuria began to appear frequently, and the explanation proved to be that the boy was taking extra food unknown to his parents. Because of inability to overcome this difficulty, the patient was readmitted June 27, 1916.

Second Admission.—The weight was 18 kg.; *i. e.*, a gain of 1 kg. since discharge. There was no detectable gain in height. Moderate sugar and ferric chloride reactions were present up to July 1, on observation diets of 40 gm. protein, 15 gm. carbohydrate, and 1000 calories daily, but diminishing during this time, indicating that the trouble had lain in violations of diet during the 2 months preceding. On July 2, the remaining sugar and diacetic reactions were cleared up by a single fast-day. 1 more fast-day was given, then green vegetables were begun in the usual manner, with addition of 10 gm. carbohydrate daily, and glycosuria appeared with 40 gm. carbohydrate on July 7 and 8, indicating a decided loss of tolerance as compared with the 100 gm. at the former admission. Mixed diet was then built up in the usual manner, and then kept at 30 to 35 gm. protein, 5 to 10 gm. carbohydrate, and 700 calories. The patient was discharged on this, Aug. 17, 1916. The weight had been approximately 17 kg. throughout this

time. The diet thus represented approximately 2 gm. protein and 41 calories per kg., diminished to about 1.7 gm. protein and 35 calories by the weekly fast-days. In correspondence with the other conditions, the patient was not so strong and well as before; he was still active, and comfortable except for the narrow diet, but perceptibly below normal in flesh, figure, and spirits.

Subsequent History.—The patient again deceived his parents in regard to diet and showed sugar more and more. Death occurred Oct. 11, 1916; details were not obtained.

Remarks.—The essential cause of trouble lay in the home conditions of an uneducated Polish laboring family. Aside from this, the following two features are noteworthy. First, there was the inability to grow normally, possibly characteristic of severe diabetes in some children even when the diet is adequate. Simple undernutrition should scarcely have prevented gain in stature. Second, no obvious recuperation or repair of the assimilative function was displayed by this child under these circumstances. In the absence of any marked tendency to gain tolerance, and under the policy of maintaining the highest possible strength and nutrition, which is now known to be a mistake, downward progress must inevitably have occurred later, even if the patient had been faithful to the prescribed diet.

CASE NO. 52.

Female, unmarried, age 27 yrs. American. Admitted Oct. 15, 1915.

Family History.—Negative for diabetes or other heritable disease.

Past History.—Healthy life under excellent hygienic conditions in a southern state. Measles and chicken-pox in childhood. Habits regular; no dietary excesses or overindulgence in sweets.

Present Illness.—Began with general lassitude in 1911. Medical examination showed nothing but a slight glycosuria. A physician prescribed a diet with carbohydrate limited to one slice of toast and one baked potato daily. There were no regular urine examinations for the next 2 years. Occasional tests showed sugar sometimes present, sometimes absent. During the past 2 years glycosuria has been continuous. The patient had no special thought of danger, and continued to lead her ordinary life and to feel fairly well. In May, 1915, she began to lose weight appreciably, and was treated by the same physician with fasting in hospital. Glycosuria ceased with 5 days of continuous fasting. She then tolerated a liberal diet without glycosuria, but a relapse occurred after her return home, and her physician advised coming to this Institute. Menstruation was absent 4 months prior to admission.

Physical Examination.—A well developed, well nourished, cheerful, and healthy looking young woman. Pasty complexion with some acne. On closer examination flabbiness of superficial tissues indicates loss of weight. Teeth normal. Tonsils barely visible. Thyroid a trifle prominent. Epitrochlear and axillary glands are the only ones palpable. Reflexes active. General examination negative.

Treatment.—Sugar and ferric chloride reactions continued very heavy with the observation diet of 100 gm. protein, 5 gm. carbohydrate, and 2000 calories on Oct. 16. They proved stubborn, and 9 days of fasting were necessary, glycosuria being absent during the last 36 hours. 300 cc. soup and 300 cc. coffee were allowed daily during fasting, but no alkali or alcohol was given. Fasting was borne without disturbance, and the patient went shopping and to matinées and remained strong and cheerful throughout. Green vegetables were begun in the usual manner on Oct. 26, with addition of 10 gm. carbohydrate daily, until glycosuria appeared with 90 gm. carbohydrate on Nov. 5. The protein-fat tolerance was low, for traces of both sugar and diacetic acid recurred with undue frequency on the subsequent carbohydrate-free diet of 66 gm. protein and 1250 calories. Colds, due to the winter weather, were responsible for part of the trouble. In particular an acute coryza was the occasion for the well marked sugar and ferric chloride reactions of Dec. 14 and 15. Treatment was not complete, but the climate evidently disagreed, and as the home conditions were good, the patient was discharged to return south on Dec. 17.

Acidosis.—No acute symptoms were present, but chronic acidosis was indicated by the intense ferric chloride reaction, the ammonia nitrogen of 0.8 to 1.4 gm., and the plasma bicarbonate of 44.7 per cent. All these signs improved with fasting, and by Oct. 28, early in the carbohydrate test, the ferric chloride reaction was negative and the ammonia and CO₂ normal. Thereafter on carbohydrate-free diet the CO₂ tended to remain on the lower, and the ammonia on the upper normal limits. The ferric chloride reaction showed the peculiarities characteristic for a diet barely at the edge of tolerance. Traces recurred from time to time, sometimes with glycosuria, sometimes alone. In no instance was there any loss of sugar from the body sufficient to account for these reactions, which apparently corresponded to slight fluctuations in the diabetic condition.

Blood Sugar.—On Oct. 16, the sugar in whole blood was 0.416 per cent, in plasma 0.434 per cent. Oct. 21, after 4 days of fasting, it was down to 0.384 per cent in the whole blood. The figure of 0.5 per cent in the plasma on that day is a discrepancy which would indicate a very low sugar content in the corpuscles. A similar, but less extreme discrepancy was also seen on Oct. 23. In the next few days marked fluctuations occurred, between 0.238 and 0.4 per cent, though all blood samples were taken in the morning fasting. On Nov. 1, the combination of 0.145 per cent in whole blood and 0.312 per cent in plasma is proof of a mistake, and the possibility must therefore be admitted that these analyses were not adequately checked. The poor protein-fat tolerance was indicated by the sharp rise in hyperglycemia, the highest figures of the series being reached with 0.426 per cent in whole blood and 0.464 per cent in plasma on Nov. 11. On the morning of Nov. 15, after a fast-day, the percentage was down to 0.185 in whole blood and 0.158 in plasma. Normal values were never attained, and the tendency was toward marked hyperglycemia, the analyses on Dec. 16, before discharge, still showing 0.185 per cent in whole blood and 0.222 per cent in plasma. The high blood sugars and recurrent traces of glycosuria indicated that the condition had not been brought adequately under control.

Weight and Nutrition.—The weight at admission was 48.4 kg., at discharge 42.3 kg., the treatment representing undernutrition to the extent of 5.2 kg. The patient was thus below average normal flesh, but the nutrition was still adequate and the strength and spirits, which were good at admission, were perceptibly improved. The diet prescribed at discharge contained 85 gm. protein and 1250 calories, with thrice cooked vegetables for bulk (nearly 2 gm. protein and 30 calories per kg., diminished by weekly fast-days to about 0.7 gm. protein and 26 calories average).

Subsequent History.—As usual with incomplete treatment, the condition became worse instead of better, and the patient was readmitted Jan. 5, 1916, after having shown glycosuria most of the time at home.

Second Admission.—Weight was almost the same as at discharge. Heavy glycosuria was present, but the ferric chloride reaction remained negative, and a slightly high ammonia was the only evidence of acidosis. Instead of an immediate fast, 3 days of carbohydrate-free diet of 620 calories were given; then a single fast-day stopped the glycosuria. Green vegetables being then begun, a trace of glycosuria appeared after 70 gm. carbohydrate. Protein-fat diet was then started, and freedom from glycosuria was maintained thereafter only by continued exclusion of carbohydrate and limitation of the diet to about 60 gm. protein and 1100 calories. The glycosuria on Apr. 11 to 12 and 15 to 16 was due to slight violations of diet. The patient was discharged Apr. 29, 1916, upon her own insistence on account of homesickness.

Acidosis.—In the general absence of indications on the part of the CO₂ capacity and the ferric chloride reaction, the only evidence was a slightly high ammonia. With the carbohydrate period in Jan. this fell to a fully normal level. Also on Feb. 7, following a fast-day, the output was rather low. The last recorded analyses showed 0.8 to 1.12 gm. daily.

Blood Sugar.—Hyperglycemia was continuous. The renal threshold was evidently high. Even without glycosuria, the blood sugar curve was such as to demonstrate inadequate control of the condition.

Weight and Nutrition.—The weight at this admission was 43.4 kg., at discharge 41 kg.; *i. e.*, a loss of 2.4 kg. in nearly 5 months in hospital. The strength and spirits were perceptibly impaired. The decline was no greater than might be expected from gradual deterioration during such a time in a case of only partially controlled diabetes. Probably better results as to strength, and certainly a very different influence upon the diabetic condition, would have resulted from sharp undernutrition to the degree necessary to bring the condition under control at the outset, followed by a diet of perhaps the same caloric value actually given, but which might then have been better tolerated. As usual, the attempt to keep up the highest possible nutrition brought only the necessity of diminishing nutrition continually further. The diet prescribed at discharge was carbohydrate-free, with 70 gm. protein and 1000 calories (1.7 gm. protein and 24.4 calories per kg., diminished to about 1.5 gm. protein and 21 calories average by the weekly fast-days, some of which were not quite absolute).

Subsequent History.—The patient remained nearly sugar-free for several months, but traces of glycosuria recurred rather frequently from trivial or unknown causes. In June, edema came on to a troublesome degree. After June 18, it became impossible to control the glycosuria except with fast-days, though it remained very small in amount. The patient was advised to return to the hospital, but seemed better in Sept., and therefore did not return until Oct. 14. At home her time was spent reading, sewing, driving, and preparing her meals. She was thin, but there was no discomfort, except worry and mental depression over her condition.

Third Admission.—The weight was 43.6 kg., but the apparent gain was due to edema, and there had obviously been some loss of flesh. The general condition was poorer than before. On a diet of 70 gm. protein and 600 to 800 calories, there was excretion of 15 to 19 gm. sugar and 4 or 5 gm. total ketones (as acetone), with 26.7 mg. total acetone per 100 cc. in the blood plasma, and CO₂ capacity 63.1 per cent. Instead of fasting, the diet for 4 days was limited to green vegetables, beginning with 25 gm. carbohydrate and diminishing to 2.8 gm., with the result that glycosuria stopped, and total acetone was diminished to 1.35 gm. in the urine and 15.7 mg. per 100 cc. in the plasma. The CO₂ capacity remained high. Protein-fat diet was then begun very gradually, at first with only 30 gm. protein and 300 calories. After about 2 weeks of such undernutrition, the total acetone remained consistently at 0.35 to 1.2 gm. in the urine and 8.3 to 17.3 mg. per 100 cc. in the plasma. Though glycosuria was absent the blood sugar on Oct. 16 to 21 was 0.244 to 0.20 per cent, plasma sugar 0.29 to 0.27 per cent. The weight by the 1st of Nov. was down to 35 kg., largely through loss of edema, salt-free diet being employed part of the time. Beginning early in Nov. the total calories were increased gradually as high as 700 to 800, of which usually 175 were in the form of brandy. The patient was discharged on Nov. 11, 1916, still weighing 35 kg. For continuance of undernutrition the diet prescribed was 35 gm. protein and 875 calories, of which 175 calories were alcohol (1 gm. protein and 25 calories per kg., reduced by the weekly fast-days to about 0.86 gm. protein and 21.5 calories average).

Subsequent History.—The patient remained sugar-free until about Christmas, then glycosuria began to recur frequently. She was also weaker and more depressed. She was readmitted to hospital Jan. 20, 1917.

Fourth Admission.—The weight was 36.6 kg., partly edema. Glycosuria and ketonuria were present, but as the condition was so far advanced, the staff member in charge chose not to clear it up. The diet was raised to 50 to 55 gm. protein and 1100 to 1380 calories, with slight subjective improvement. The stay in hospital continued until Feb. 21, 1917. No immediately threatening symptoms appeared, and the patient was about and outdoors part of each day as before. At discharge the weight remained approximately 35 kg.; weakness and discomfort were progressive.

Subsequent History.—The patient continued to be more uncomfortable than when sugar-free. It was impossible for her to take the more liberal diet which

had been granted, because eating practically anything made her nauseated. Under a local physician her diet on this account was less in quantity than before, but active diabetes continued. Death occurred Apr. 26, 1917, in coma.

Remarks.—The history is a typical one for many diabetic patients. There was first the long period of mild glycosuria, when the favorable opportunity for effectual treatment was allowed to slip by. The onset of a more severe stage seems to have been rather sudden. The physician in charge then employed radical measures, but these were not wholly adequate at this stage. As so frequently occurs, the patient was sent for a specialist's care when the condition was already too far advanced for any genuinely good result to be possible from dietetic measures. The severity was such that only the most rigorous program could have brought it under control, and there was the usual hesitation about taking a patient seemingly in fair condition and reducing weight and strength to the requisite degree. When more radical undernutrition was attempted in the third period in hospital, it was too late, and it is possible that the assimilative function was absolutely too low to support life. If the patient even at the first admission to hospital had been promptly reduced to the weight and diet to which the downward progress later brought her, the opinion may be ventured that she not only would have lived longer, but also this same period between Oct., 1915, and Apr., 1916, would have been characterized by a higher average of strength, comfort, and usefulness.

CASE NO. 53.

Female, age 9 yrs. American; schoolgirl. Admitted Oct. 15, 1915.

Family History.—Parents well, except that mother is nervous. One sister well. No diabetes or heritable disease known in family.

Past History.—Healthy life in good hygienic surroundings in a small town in the middle west. Measles, mumps, chicken-pox in early years. No tonsillitis for 2 years past; 4 or 5 attacks before that. Stiffness and pain in various joints at times, but no definite rheumatism. Child has made average record at school. Nervous disposition. Development normal; not obese.

Present Illness.—Polyphagia, polydipsia, and polyuria began 2 years ago. Under a specialist's care in a Chicago hospital, glycosuria was cleared up on restricted diet without fasting. Sugar-freedom was maintained until last Feb.; since then glycosuria has been continuous. Pruritus vulvæ for past 4 months.

Physical Examination.—Height 125.2 cm. A fairly developed but emaciated child, pale and weak. Mouth and throat negative. No notable lymph gland enlargement. Reflexes normal. General examination negative.

Treatment.—A 5 day fast was necessary to clear up glycosuria. On the usual green vegetable period, glycosuria appeared on Oct. 30 with 80 gm. carbohydrate. Thereafter a diet of 1000 calories with small quantities of carbohydrate was badly assimilated from the standpoint of hyperglycemia and occasional traces of glycosuria. Carbohydrate was omitted beginning Dec. 10, the usual diet being 40

gm. protein and 600 to 800 calories, with routine weekly fast-days. A second carbohydrate test beginning Jan. 24 showed increased tolerance; glycosuria appeared with 120 gm. carbohydrate on Feb. 5. By Feb. 21, the patient was able to assimilate a diet of 40 gm. protein, 15 to 20 gm. carbohydrate, and 750 calories. She was discharged Feb. 24 on this diet, except that only 10 gm. carbohydrate were permitted.

Acidosis.—No threatening symptoms were present at any time, but the heavy ferric chloride reaction and the CO₂ capacity of 37 per cent at admission were significant. Both these signs changed rapidly for the better on fasting, and on carbohydrate and mixed diet thereafter. With normal CO₂ and negative ferric chloride, the ammonia excretion still showed a slight acidosis in Dec. and Jan. This gradually diminished to a normal level by the time of discharge.

Blood Sugar.—There was evidently a far greater excess of plasma sugar over corpuscle sugar on Oct. 26 than at later periods. The salient feature is the steady decline of the blood sugar curve toward normal. The reason for the occurrence of hyperglycemia in the last analysis on Feb. 24 is not known.

Weight and Nutrition.—The weight was 20 kg. on admission, 16.9 kg. at discharge; *i. e.*, a loss of 3.1 kg. The child was emaciated at admission, and never showed improvement of appearance in consequence of treatment. Exercise was employed during most of the period in hospital. It afforded the child a more normal and enjoyable life, but did not build up tolerance appreciably or confer real strength. It may have been one factor along with the low diet in bringing down the blood sugar. There was one cold while in hospital; glycosuria did not result, and recovery under the low diet was normal. The diet prescribed at discharge represented about 2.4 gm. protein and 44 calories per kg., diminished to about 2.1 gm. protein and 38 calories average by the weekly fast-days. The diet therefore was absolutely low, but adequate as reckoned on the greatly reduced weight. The child was regularly up and about all day long, and amused herself with active play and other occupations, but always kept the appearance of a little invalid.

Subsequent History.—The patient remained free from glycosuria, except for rare traces due to accidents of diet and one attack of grippe. By Sept. 9, she had improved sufficiently to begin school, but weighed only 17.7 kg. Toward the end of Sept. she had a severe cold, and another in Oct. with temperature of 101.5°. Both caused glycosuria, and thereafter permanent sugar-freedom was difficult to maintain. She was advised to return to the hospital, but the parents delayed, and death occurred in coma on Jan. 25, 1917.

Remarks.—This was one of the worst cases among the children in this series, not only because of the low food tolerance, but also because of the frailness of the patient, whose whole appearance indicated exhaustion and low resistance. The diets were never excessively low, even those in the forepart of Jan. representing about 2.2 gm. protein and 36 calories per kg. for 18 kg. weight. The general result of treatment, by reason of the fasting and carbohydrate periods and exercise, was the above mentioned loss of 3.1 kg. during more than 4 months

in hospital. During 7 months thereafter at home, the weight showed a slight increase.

It is noteworthy that in a case of this very unpromising type a demonstrable increase of carbohydrate tolerance was produced in hospital, and also all symptoms, including hyperglycemia, were brought under control. No upward progress or actual recovery of assimilation was demonstrated; the improved tolerance was merely purchased at the price of diminished weight. But even with the necessarily unfavorable conditions, downward progress came only with an infection approximately 1 year from the time the patient was first received. The record is satisfactory to the extent that both life and comfort were evidently prolonged by treatment in an unpromising type of case.

CASE NO. 54.

Female, married, age 29 yrs. American; telephone operator. Admitted Oct. 16, 1915.

Family History.—Mother died with a "severe cold" in 1891. Father is well. One brother died of meningitis in childhood; eight brothers and sisters are well. Husband well. No diabetes or other heritable disease in family.

Past History.—Measles and whooping-cough in childhood. No other illnesses; no sore throats. Healthy life. No nervousness. Appetite, diet, and digestion normal. Menstruation normal. One miscarriage 3 years ago; no other pregnancy.

Present Illness.—June 1, 4½ months before admission, patient weighed 144 pounds and felt so well and free from strain that she went on with work instead of taking summer vacation at the usual time. Within 2 weeks from that time and with no illness or other disturbance of any kind, polydipsia and polyuria began, and there has since been progressive loss of strength and 30 pounds weight. Patient was first seen by a doctor and diabetes diagnosed on July 4. Under gradual withdrawal of carbohydrate she became free from glycosuria on Aug. 13 and remained so until Sept. 12, since when glycosuria has been present except on fast-days.

Physical Examination.—Height 169 cm. A well developed and fairly nourished woman, with no striking symptom except dyspnea and acetone odor. Mouth and throat normal. Abdomen slightly distended and tympanitic. Knee jerks sluggish. Blood pressure 110–80. General examination negative. Wassermann negative.

Treatment.—Impending coma was indicated by the dyspnea, heavy ferric chloride reaction, ammonia nitrogen of 2.52 gm., and CO₂ capacity of 29 per cent. A light observation diet was given, with 50 gm. sodium bicarbonate in the evening. The next day fasting was begun, with 300 cc. each of coffee and clear soup and 286 calories of alcohol daily. 30 gm. sodium bicarbonate were given on Oct. 17 and 19, 20 gm. on Oct. 20, and 15 gm. on Oct. 21. Glycosuria was absent after the 21st. On Oct. 22, 10 gm. carbohydrate were given in the form of lettuce, celery, and tomatoes; 20 gm. on the 2 succeeding days, and 14 gm. on Oct. 25. Glycosuria was continuous on this low intake, but was checked by the fast-day of

Oct. 26. On Oct. 27, 10 gm. carbohydrate were given, and increased by 10 gm. daily, glycosuria appearing with 40 gm. carbohydrate on Oct. 30, and continuing with diets of 50 to 30 gm. protein, 10 gm. carbohydrate, and 1000 to 800 calories on the following day. At first the patient had given the impression of a moderately severe diabetes with threatened coma, but now the case looked more serious when it appeared that the food tolerance was almost zero. Ketonuria, though diminished, persisted. Hyperglycemia was stubborn, and between Nov. 10 and 20 it was found that carbohydrate-free diets of 40 gm. protein and 800 calories sufficed to keep up almost continuous glycosuria. Nov. 21 was a fast-day with only 70 calories alcohol. On the following 3 days, 10 to 20 gm. carbohydrate in green vegetables were the only food. On Nov. 25 and 26, 40 gm. protein, 5 gm. carbohydrate, and 800 calories were given. Still glycosuria and ferric chloride reactions persisted. The former was stopped and the latter diminished by 3 fast-days, Nov. 28 to 30. Then, beginning with 5 gm. carbohydrate on Dec. 1, green vegetables were increased daily, until glycosuria appeared with 40 gm. carbohydrate on Dec. 5. On Dec. 8 to 11, carbohydrate-free diets of 60 to 25 gm. protein and 800 to 325 calories kept up marked glycosuria and ketonuria which did not cease even with 3 fast-days (Dec. 12 to 14). On Dec. 15 and 16, 30 to 50 gm. protein and 170 to 305 calories were given, with continued glycosuria and ketonuria. Dec. 17 and 18 were fast-days with coffee, soup, and 315 calories alcohol, and both sugar and ferric chloride reactions became negative. With continuance of the same liquids, one egg was allowed on Dec. 19 and two eggs the next day, and glycosuria and ketonuria remained absent on an increase up to five eggs on Dec. 25 (714 calories, 315 of which were alcohol). A precautionary fast-day with whisky was given on Dec. 26, then the diet again increased until continuous glycosuria appeared on 45 gm. protein and 1025 calories (315 alcohol, 710 food) following Dec. 30. The fast-day on Jan. 2 checked the glycosuria, but it reappeared on a diet of 45 gm. protein and 888 calories (alcohol 315, food 573). The menu for such a day, characteristic of the diets on which it was necessary to keep this patient, was as follows:

60 gm. bran.	6 eggs.
300 cc. coffee.	10 gm. olive oil.
300 " soup.	100 " thrice cooked asparagus.
90 " whisky.	100 " " " spinach.

Again relief from glycosuria was given by a fast-day on Jan. 9, and on the 11th glycosuria reappeared on four eggs, 300 cc. coffee, 450 cc. soup, and 90 cc. whisky (30 gm. protein and 634 calories)—no vegetables, bran, or any source of carbohydrate. On the following days, it became certain that the patient definitely could not tolerate the protein of four eggs. The fast-day of Jan. 16 failed to stop the glycosuria, therefore (Jan. 21 to 25) 5 successive days of fasting and alcohol were imposed. On Jan. 26 one egg was added, on Jan. 28 two eggs, on Feb. 3 three eggs, in addition to 200 gm. thrice boiled vegetables and 525 calories of alcohol. The chart shows the continuous slight glycosuria, not stopped by the fast-day of

Feb. 6. Reduction to one egg on Feb. 10 and fasting the next day stopped the glycosuria, but it returned when the eggs were increased to three on Feb. 15. The remainder of the long graphic record shows practically the same story of continuous inability to tolerate anything approaching a living diet. On some occasions, the limit of tolerance was only two eggs without other food, three eggs causing glycosuria. On this account alcohol was pushed to a maximum of about 500 calories, to keep up nutrition as well as possible. Beginning with a fast-day on June 13, another carbohydrate period was tried. By June 18, 25 gm. carbohydrate were taken without glycosuria, but the patient's strength had collapsed and a change to other food was imperative. Accordingly on June 19, the 8 month attempt to control the condition was abandoned. Glycosuria was present on the carbohydrate-free diet of 36 gm. protein and 1000 calories (490 alcohol, 590 food). It increased, and ferric chloride reactions promptly returned, when the diet was raised to 45 gm. protein and 1490 calories (490 alcohol, 1000 food). An alarming fall in the blood bicarbonate promptly followed, down to 28.7 per cent on June 29. To meet the combination of extreme weakness and impending coma, alcohol and protein were continued the same and the fat diminished to make a total ration of only 900 calories. The threatening symptoms passed off, and without the use of alkali the CO_2 capacity had risen to 61 per cent by July 6. The fat was increased to make the same 1490 calories as before. Meanwhile also carbohydrate had been introduced up to 17.5 gm. daily. With the increase in fat came another sharp fall of the CO_2 capacity, so that on July 12 it was 35.9 per cent. 40 gm. carbohydrate were given on that day without clinical benefit. Resort was had to fasting to avert the imminent coma. On July 13, the only food was 7 gm. carbohydrate and 70 cc. whisky; on the 14th only whisky was given; on the 15th, 15 gm. protein were added. By this time the CO_2 capacity was up to 62.5 per cent, again without the aid of alkali. July 16 was a fast-day, and on the 17th the diet was 30 gm. protein, 20 gm. fat, and 35 cc. whisky; 430 calories in all. On the 18th, the patient awoke clearly conscious, but weak. She went into collapse with loss of consciousness, and died from final exhaustion of strength at 2:40 p.m. Death occurred with insignificant ammonia, negative sugar and ferric chloride reactions, and normal plasma bicarbonate as far as can be judged by the last analysis on July 15. There were no symptoms suggesting diabetic coma, and the unconsciousness was merely such as precedes death from starvation.

Acidosis.—This patient always responded to fasting with a quick clearing up of acidosis. The ferric chloride reaction was stubborn for about 2 months, then remained almost continuously negative until the final period of overfeeding in June. The plasma bicarbonate maintained a normal level throughout most of the time. A more delicate index of the slight acidosis was frequently found in the slight elevation of the ammonia output. Aside from the bicarbonate dosage on the first few days as mentioned, no alkali was used. A sharp fall in the CO_2 capacity in Jan. (62 per cent on the 15th, 56 per cent on the 17th, 44.2 per cent on the 19th, 43.2 per cent on the 25th) occurred without known cause or disturbance. By Feb. 2, it had risen spontaneously to 56.6 per cent. The terminal record in

TABLE XIV.

Date.	Diet.					Weight. kg.	Urine.				Blood.		Average daily diet. gm.		
	Protein. gm.	Fat. gm.	Carbo- hydrate. gm.	Alcohol. cc.	Calories.		Volume. cc.	Sugar. gm.	Total nitrogen. gm.	D:N ratio.	NH ₄ -N gm.	FeCl ₃ reaction.		Plasma sugar. per cent.	Plasma CO ₂ . vol. per cent.
1916															
June 14	1.4	0.4	5.0	70	518	32.1	2178	0	—	—	0	0.14	60.7	Protein 5.8	
" 15	4.1	0.4	10.0	70	550	32.1	2650	0	—	—	0	—	—	Fat 0.7	
" 16	6.4	0.6	15.0	70	584	30.7	3082	0	—	—	0	—	—	Carbohy- drate 15.0	
" 17	8.1	0.8	20.0	70	616	30.0	3370	0	—	—	0	—	—	Alcohol 70.0	
" 18	9.3	1.4	25.0	70	643	29.2	3352	0	—	—	0	0.061	63.2	Calories 582	
" 19	35.7	39.0	1.3	70	1003	—	2315	0	—	—	0	—	—		
" 20	46.1	38.9	1.0	60	974	—	2850	0	—	—	0	—	—		
" 21	45.3	44.3	1.1	70	1090	—	2320	+	—	—	+	—	—	Protein 46.9	
" 22	45.3	44.3	1.1	70	1090	—	2400	+	—	—	+	—	—	Fat 58.7	
" 23	45.0	54.6	2.2	70	1189	—	2040	+	—	—	+	—	—	Carbohy- drate 1.9	
" 24	45.0	64.5	2.7	70	1284	—	2383	++	—	—	++	—	—	Alcohol 70.0	
" 25	45.0	84.1	2.7	70	1483	—	2885	++	—	—	++	—	—	Calories 1231	
" 26	50.0	84.3	2.7	70	1489	—	2140	17.35	—	—	++	—	—		
" 27	60.0	79.3	2.7	70	1484	—	2540	9.15	2.07	2.57	++	—	—		
" 28	52.5	54.3	1.8	70	1216	—	2750	23.95	11.02	3.57	++	0.23	29.7		
" 29	50.0	24.6	—	70	923	28.0	2295	15.84	8.10	2.47	++	—	—	Protein 50.8	
" 30	50.0	24.6	—	70	923	27.8	2172	18.85	12.43	3.27	++	—	—	Fat 33.1	
July 1	50.0	24.6	—	70	923	27.4	1855	24.70	—	1.48	++	—	—	Carbohy- drate 5.1	
" 2	50.0	24.6	—	70	923	28.2	2010	29.20	—	2.14	++	—	—	Alcohol 70.0	
" 3	52.3	44.4	11.9	70	1164	28.2	3355	25.80	9.47	2.00	++	—	—	Calories 1026	
" 4	52.3	44.4	11.9	70	1164	28.2	2795	32.80	11.30	1.85	++	—	—		
" 5	52.3	44.4	11.9	70	1164	28.8	2920	18.82	11.55	0.84	+	—	—		

July 6	55.0	61.9	11.9	70	1338	28.0	2654	23.00	11.20	0.98	1.59	++	0.15	61.0	Protein Fat Carbohy- drate Alcohol Calories	58.0 68.6 15.0 70.0 1420
" 7	55.0	61.9	11.9	70	1338	28.0	2540	20.30	—	—	1.63	++	—	—	—	—
" 8	60.0	73.3	17.2	70	1487	28.0	2039	34.50	11.27	1.73	1.97	++	—	—	—	—
" 9	60.0	73.3	17.2	70	1487	28.4	3090	37.70	9.84	2.08	2.56	++	—	—	—	—
" 10	60.0	73.3	17.2	65	1452	27.7	2505	18.70	—	—	2.46	++	—	—	—	—
" 11	2.9	2.1	—	35	275	26.7	2065	1.03	6.12	—	1.67	++	—	—	—	—
" 12	65.0	81.1	45.0	35	1454	25.8	2030	—	—	—	1.84	++	0.42	35.9	Protein Fat Carbohy- drate Alcohol Calories	16.1 16.1 10.0 32.0 475
" 13	—	—	7.0	35	274	25.4	1455	+	—	—	1.58	++	—	—	—	—
" 14	—	—	—	35	245	23.7	2360	+	—	—	1.11	0	—	—	—	—
" 15	15.0	10.2	—	35	402	24.4	2010	0	—	—	0.82	0	0.23	62.5	Carbohy- drate Alcohol Calories	10.0 32.0 475
" 16	—	—	—	35	245	24.0	1730	0	—	—	—	0	—	—	—	—
" 17	30.0	19.7	17.5	17.5	428	24.2	1700	0	—	—	0.61	0	—	—	—	—

June and July is of interest as showing how a low fat allowance brought on prompt severe acidosis, not prevented by alcohol, nor on the second occasion by carbohydrate, but yielding very easily to simple withdrawal of fat both times (Table XIV). The fat allowance bringing on the dangerous acidosis in each instance was rather high in proportion to the weight of the extremely emaciated patient, but in absolute quantity was very low. It is evident that the production of acidosis cannot be attributed to protein, because it developed on 35 to 60 gm. protein in the period June 14 to 28 and cleared up on 50 to 55 gm. protein in the period June 29 to July 6. Diets predominantly protein, as those of July 13 to 17, acted favorably in diminishing acidosis, but protein was not indispensable for the purpose, as fast-days always acted favorably in this patient. Carbohydrate was scarcely important in checking the acidosis, since the quantities in the period June 29 to July 6 were so small, and acidosis similarly was controlled on July 15 without carbohydrate. The influence of alcohol was not perceptible; acidosis was controlled as readily on 35 gm. alcohol as on 70 gm. It is clearly evident that the giving or withholding of fat was the sole determining factor in producing and abolishing acidosis, and the specially noteworthy point is the small absolute quantity of fat which was effective for this purpose.

Blood Sugar.—The marked and stubborn hyperglycemia, and the response of both blood sugar and glycosuria to slight changes in the diet, proved that actual severity of diabetes was the sole cause of difficulty, and not altered renal permeability. Normal blood sugar was attained on only a few occasions. On Dec. 2, there was a practically normal reading for the whole blood, but hyperglycemia in the plasma, as if the corpuscles were almost sugar-free. Both were normal on Apr. 5. The low normal figure before breakfast on June 18 doubtless represented extreme exhaustion rather than genuine improvement in the diabetes.

Weight and Nutrition.—This was the most extreme undernutrition in the entire series. The patient appeared well nourished at a weight of 49 kg. at admission, and died of inanition 9 months later at a weight of 24 kg.; *i. e.*, a loss of 25 kg. since admission, and 41 kg. since the onset of diabetes.

The nitrogen analyses show a fairly uniform excretion of about 8 gm. daily. The negative balance during this time was not so great as will appear from the comparison of intake and output, because the nitrogen of the soup was not included in the dietary record. As no fecal analyses were done, an exact reckoning of the balance is impossible. Concerning the total energy intake, the following calculation can be made.

	276 days.	Per day (average).	Per day per kg.
Alcohol calories.....	90,348	315.6	9.6
Food "	96,692	362.1	10.9
Total "	187,040	677.7	20.5
Protein in diet.....	7,305 gm.	26.4 gm.	0.80 gm.
Fat " "	6,881 "	24.8 "	0.75 "

On Mar. 31, this patient was studied in the respiration calorimeter by DuBois and collaborators, who determined the following.⁷ "I. Her total metabolism is the lowest recorded in the literature, being only 23.3 calories per square meter per hour, which is 37 per cent below the average basal normal in women. Since her original weight with clothes had been 66 kg., one may be permitted to assume a weight of 62 kg. without clothes. Had her metabolism been normal for this weight, it would have been 63.3 calories per hour instead of 29.4 calories, which were actually measured when her weight had fallen to 32.5 kg. The extreme emaciation which had resulted in a reduction of body weight to nearly half of what it was originally, reduced the metabolism so low that only 40 per cent of the original heat production was necessary for life. II. The nitrogen excretion in the urine (0.39 gm. per hour) is the quantity commonly found in normal people. The total metabolism, however, is so low that the percentage of calories from protein is quite high, 35 per cent (15 per cent being the average normal). III. The respiratory quotients average 0.82, a normal figure. From this, one may calculate that fat gives 39 per cent of the calories of metabolism and carbohydrate 26 per cent. This corresponds to the utilization of 44 gm. of carbohydrate daily, and since none was given in the food, these results are difficult to interpret."

The patient's total heat production at this time was 29.5 calories per hour, or 708 per day. Presumably it was somewhat higher in the preceding months, and probably by June 15 had fallen even lower. If this 708 calories be taken as an average for comparison with the average intake of 677.7 calories above calculated, it is seen that the diet is deficient notwithstanding the great lowering of metabolism, and even without allowance for any loss through the feces. The nitrogen excretion of 0.39 gm. per hour in the calorimeter experiment represents an actual catabolism of 58.5 gm. protein per day, with no allowance for any specific dynamic action of ingested protein. There is a serious discrepancy between this and the average protein intake of 26.4 gm. There was thus a continuous consumption of both body fat and body protein in the process of slow starvation.

Lipemia.—Heavy and continuous lipemia was present at admission, gradually clearing up during the fasting and carbohydrate period. Thereafter the plasma remained clear until the terminal period in June and July, when lipemia reappeared and persisted in its original intensity. A noteworthy feature is the very limited fat intake which sufficed to produce such a heavy lipemia under these circumstances. No analyses were made.

Dextrose Nitrogen Ratio.—This was the type of case which could almost certainly be counted upon to show "total" D:N ratios, if the active symptoms had been allowed to gain full headway. The condition was held under control sufficiently that this ratio was never observed, the ratios in the terminal period of glycosuria

⁷ Gephart, F. C., Aub, J. C., DuBois, E. F., and Lusk, G., Metabolism in Three Unusual Cases of Diabetes, *Arch. Int. Med.*, 1917, xix, 908-930.

being never higher than 2.36, as shown in Table XV. This calculation is also confused by the unknown quantity and character of the nitrogen in the soup.

Remarks.—This case at the time was regarded as a unique example of spontaneous downward progress, resulting from some special factor. Strong suspicions were entertained that this might be an infectious or malignant process, probably tuberculosis, but repeated examinations by members of the staff and outside consultants failed to reveal any evidence of such lesions. Necropsy was positively refused, so this important point could not be settled. Experience with similar or worse cases since the close of this series indicates that they merely represent diabetes of extreme severity, very susceptible to downward progress when the trivial tolerance is overtaxed by diets such as described or even lower.

TABLE XV.

Date.	Urinary sugar.	Total nitrogen.	D : N ratio.
<i>1916</i>	<i>gm.</i>	<i>gm.</i>	
June 27	21.60	9.15	2.36
" 28	23.95	11.02	2.17
" 29	15.84	8.10	1.96
" 30	18.85	12.43	1.52
July 1	24.67	—	—
" 2	29.15	—	—
" 3	25.80	9.47	1.33
" 4	32.86	11.30	1.74
" 5	—	11.55	—
" 6	23.00	11.21	0.87
" 7	20.50	—	—
" 8	34.48	11.27	1.37
" 9	37.70	9.84	1.89
" 10	18.70	—	—

They are controllable only by such remarkably severe undernutrition as will maintain continuously normal blood sugar, and even with the most rigid treatment the metabolic function may be found actually too low to support life.

CASE NO. 55.

Male, age 26 mos. American. Admitted Nov. 3, 1915.

Family History.—Father aged 32, mother 26; both healthy. Patient is the only child. A paternal great grandmother died of diabetes. No other heritable disease known in family.

Past History.—A normally delivered, healthy child with no infectious history whatever.

Present Illness.—After gradual increase of polyphagia, polydipsia, and polyuria for 3 weeks, the father, a physician, made a urine analysis Oct. 26 and found heavy glycosuria. Treatment has consisted in a diet of 2 to 5 pints of milk and one poached egg daily. For a few days before admission the child has been acting cross and unwell. No sleepiness or dyspnea until the past day or two.

Physical Examination.—A well developed, well nourished child. Decided drowsiness, but no dyspnea. Hectic flush of cheeks. Tonsils moderately hypertrophied. Reflexes normal. Epitrochlear glands palpable. Otherwise fully normal to examination. Wassermann reaction of patient and both parents negative.

Treatment.—The patient was admitted just before noon Nov. 3, and received that day an observation diet of 1400 cc. milk. As the urinary findings and low CO₂ capacity showed danger of coma, the diet on the following 2 days was only 13.5 gm. protein, 20 gm. carbohydrate, and 280 calories, mostly as milk, with 600 to 800 cc. clear soup additional for the sake of fluid and salts. Fasting was then imposed, Nov. 6 to 9. Green vegetables were then begun and increased in the usual manner, and on Nov. 13, 40 gm. carbohydrate were thus taken without glycosuria. This diet was stopped to avoid too long undernutrition of such a young child, and also because edema was causing worry to the mother. After a fast-day on Nov. 14, a mixed diet of 25 gm. protein, 20 gm. carbohydrate, and 675 calories (including 400 cc. milk) brought on glycosuria. After a fast-day on Nov. 21, a diet of 44 gm. protein, 10 gm. carbohydrate, and 550 calories was assimilated without glycosuria. But on Nov. 29 to 30 an increase to 47 gm. protein, 15 gm. carbohydrate, and 612 calories brought glycosuria on the 30th. The patient was discharged on Dec. 9 in apparently perfect health, with all chemical findings normal.

Acidosis.—Acidosis threatening coma cleared up promptly on fasting. As children are supposed to show fasting acidosis very readily, notice may be taken of the fact that on the last day of the 4 day fast (Nov. 9) the ferric chloride reaction was fully negative, and the plasma bicarbonate had risen to 50.4 per cent, approximately normal for a young child. Signs of acidosis remained entirely absent thereafter. No alkali was used. An experience near the beginning gave an interesting illustration of the effect of food. The low diet shown in the chart for Nov. 4 was only breakfast. Fasting was then begun because of threatening coma symptoms. By the next morning the clinical improvement was very evident, and the CO₂ capacity showed a rise from 30.4 to 40.3 per cent. During this day of Nov. 5 the child received by mistake a tray intended for a cardiac patient, representing 18 gm. carbohydrate and 15 gm. each of protein and fat. The record shows how not only was glycosuria increased, but the CO₂ capacity by the next day was depressed to 32.6 per cent, notwithstanding the large proportion of carbohydrate and protein in the food. Resumption of fasting promptly cleared up acidosis as described.

Blood Sugar.—The very high value of 0.57 per cent at admission was due to the high carbohydrate diet. The immediate fall on fasting was characteristic

both of hyperglycemia due to carbohydrate and of early diabetes. The analyses of Nov. 10 would indicate that the corpuscles retained sugar longer than the plasma. A prompt fall to normal was easily obtained, and the subsequent figures for blood sugar in the morning before breakfast were fully normal. Analyses during digestion would doubtless have shown hyperglycemia.

Weight and Nutrition.—In a little over 1 month in hospital the weight was reduced by 1 kg. The rise of weight shown in the fasting and carbohydrate period was due to well marked edema. The diet prescribed at discharge was 45 gm. protein, 15 gm. carbohydrate (10 in milk, 5 in vegetables), and 575 calories (about 4.1 gm. protein and 52 calories per kg., reduced by fortnightly fast-days to 3.8 gm. protein and 48 calories per kg.). As compared with standard diets for children, this one was deficient in carbohydrate, but sufficiently abundant in other respects to assure gradual aggravation of the diabetes.

Subsequent History.—The patient remained free from glycosuria, regained normal behavior and activity, and for exercise coasted with his sled, walked, and climbed as many as 20 flights of stairs daily. On Jan. 12, the sugar in whole blood was 0.119 per cent, in plasma 0.159 per cent. There had been a gain of 0.3 kg. weight and 0.3 cm. height. Later in Jan. an attack of grippe brought on glycosuria, which was cleared up by fasting 3 days. Thereafter it was absent on a diet containing only 5 gm. carbohydrate. On Feb. 5, heavy glycosuria appeared without apparent cause. Thereafter 1 fast-day was given every week. Mar. 9, glycosuria again returned, and thereafter was more persistent. The patient was readmitted on Apr. 15 because of the difficulty in maintaining sugar-freedom.

Second Admission.—The weight was 0.1 kg. greater than at discharge, the height 87.7 cm., a gain of 1.7 cm. since the first measurement (Nov. 15, 1915). The appearance and behavior were excellent, and there were no subjective symptoms. Notwithstanding the trace of glycosuria, the fasting blood sugar had fallen to normal (0.095 per cent in whole blood, 0.110 per cent in plasma, CO₂ capacity 52.5 per cent; on the next morning 0.069 per cent in whole blood, 0.070 per cent in plasma, CO₂ capacity 49.8 per cent). Green vegetables were begun after a day of fasting, adding 10 gm. carbohydrate daily, and glycosuria appeared on 90 gm. carbohydrate. The blood sugar, mornings before breakfast, continued normal, hyperglycemia evidently being brief following carbohydrate ingestion. The CO₂ capacity rose markedly to 60.6 per cent, perhaps partly because of the carbohydrate and partly because of the alkaline diet. After a fast-day on Apr. 27, a diet of 40 gm. protein, 15 gm. carbohydrate, and 575 calories was assimilated without glycosuria. Glycosuria occurred on May 3 and 4, after the carbohydrate had been increased to 20 gm. beginning Apr. 30. In the last analyses preceding discharge, the blood sugar continued normal, the CO₂ was slightly low and the ammonia slightly high. The weight had been reduced to 10.5 kg. The strength and spirits were excellent. The prescribed diet was the same as at the previous discharge.

Subsequent History.—The patient showed glycosuria within the first few days after leaving the hospital, and this recurred stubbornly from time to time notwithstanding reduction to carbohydrate-free diet. The patient gradually declined in weight and strength. Glycosuria was controlled by the parents by means of fast-days and reduced diet. During June and July, on a trip to the seashore, there was some gain in weight and strength. After Aug. the decline was continuous. After Oct. the parents abandoned the attempt to maintain sugar-freedom, but regulated the diet carefully. From that time onward it consisted of almost nothing but eggs. Feeding was carried on until threatening symptoms resulted; these were cleared up by fasting, and so on. Death occurred Jan. 3, 1917.

Remarks.—Severe diabetes in a child of this age must often be hopeless under any dietetic treatment. The result is satisfactory to the extent that the ordinary duration of life in a patient of this type, according to the experience of Dr. Emmett Holt, who referred the child here, was formerly not more than 3 months, whereas in this patient excellent physical condition was maintained for at least 5 months and the total duration of life from the time of admission was exactly 14 months. The metabolic strain of growth may be sufficient to account for downward progress; but a longer preservation of life and health with equal or better growth and strength would probably be attainable on a lower diet containing a larger proportion of carbohydrate.

CASE NO. 56.

Male, married, age 30 yrs. American; railway clerk. Admitted Nov. 3, 1915.

Family History.—Father died of an injury. Mother well at 73. One brother is well. Of six sisters, two are well; one has severe, and another slight rheumatoid arthritis; the other two are weakly and anemic. One maternal aunt was temporarily insane after worry, but recovered and enjoys good health at 75. No diabetes or other heritable disease known in family.

Past History.—Healthy life with good hygiene. Whooping-cough in childhood. Rather frequent gastrointestinal upsets with fever as a child. There were swollen glands below the angle of the jaw on both sides in childhood up to the age of 12 or 14; they became inflamed whenever patient had a cold. Enuresis up to 12 or 14. No other illnesses. Married 6 years. Wife and only child healthy. Patient has been almost a total abstainer from alcohol. Has smoked moderately, taken three cups of tea daily, and has been very fond of desserts and candy. Chronic constipation.

Present Illness.—Grippe in the fall of 1912 was followed by weakness and depression until Jan., 1913, when an examination showed glycosuria. Polyphagia, polydipsia, and polyuria were then also present. On restricted diet he has remained at work, but has continually lost weight and strength, until he is now incapacitated.

Physical Examination.—Height 183.8 cm. A tall, emaciated man without acute symptoms. Teeth show caries, but no pyorrhea. Throat and tonsils normal. Cervical lymph nodes not palpable. Small, hard epitrochlear, axillary, and inguinal nodes palpable. Blood pressure 100 systolic, 80 diastolic. Knee jerks diminished. Examination otherwise negative.

Treatment.—Patient had been on restricted diet, with the consequence that he showed only slight glycosuria but heavy ferric chloride reaction at admission. 2 fast-days on Nov. 6 and 7 sufficed to abolish glycosuria. In the subsequent test with green vegetables, glycosuria appeared with 90 gm. carbohydrate on Nov. 16. The carbohydrate period was prolonged to determine whether this was the true tolerance, and also for the sake of prolonging undernutrition and diminishing any latent tendency to acidosis. Mixed diet was then begun, and a trace of glycosuria appeared on Dec. 11, after 3 days of 100 gm. protein, 60 gm. carbohydrate, and 2000 calories. The patient was discharged on Dec. 20 with urine normal.

Acidosis.—The ferric chloride reaction was abolished early in the carbohydrate period. The plasma bicarbonate, which was down to 44 per cent on the morning of Nov. 8, after the 2 preceding fast-days, rose sharply within normal limits by Nov. 11, and remained there except for a slight drop following the fast-day of Nov. 23.

Blood Sugar.—There was the usual hyperglycemia at admission and fall on fasting. The low values found on Nov. 24, after the fast-day of Nov. 23, following the undernutrition of the carbohydrate period, proved that the blood sugar could be brought to normal. The subsequent treatment did not hold it down. On the contrary, the last analysis on Dec. 8 showed 0.2 per cent plasma sugar. This and the preceding analysis of 0.245 per cent (Nov. 10) without glycosuria indicated a high renal threshold, especially as the percentages must have been somewhat higher during the day than in the morning, and those in the plasma were slightly higher.

Weight and Nutrition.—Weight at admission 51 kg., at discharge 48.2 kg.; i.e., a reduction of 2.8 kg. The diet prescribed at discharge was 100 gm. protein, 50 gm. carbohydrate, and 1750 calories (about 2.1 gm. protein and 36 calories per kg., reduced by the weekly fast-days to 1.7 gm. protein and 31 calories average). The patient felt greatly strengthened and benefited, and hoped to resume regular work after a vacation in the south. The undernutrition, however, had not been stringent enough to bring the condition under control, as proved by the marked hyperglycemia. Letting a half treated patient go on a diet as liberal as this was a certain means of assuring a relapse. Considerable exercise was required of the patient, both inside and outside hospital, but this had obviously failed to bring the condition under real control.

Subsequent History.—The patient caught cold shortly after returning home and showed glycosuria, which he cleared up by fasting, but sugar returned when he tried to resume even a lower diet than before. After having shown sugar most of the time, he was readmitted Feb. 17, 1916.

Second Admission.—Repeated fasting for clearing up glycosuria had brought the weight down to 46.8 kg., a loss of 1.4 kg. since discharge. The plasma bicarbonate was approximately normal, the ferric chloride reaction negative, while the ammonia nitrogen of 0.87 gm. indicated a slight acidosis. Fasting was begun after breakfast on Feb. 19. Glycosuria promptly ceased, but reappeared on diets of 80 to 100 gm. protein and 1500 calories, even though all carbohydrate was excluded. Beginning Mar. 6, glycosuria was absent on 1200 calories with 70 gm. protein and no carbohydrate; and subsequently 75 gm. protein, 15 gm. carbohydrate, and 1700 calories were taken without glycosuria. The CO₂ capacity stood at low normal nearly all the time. Doubtless ammonia determinations would have shown slight acidosis. The blood sugar was never brought to a normal figure and was still 0.2 per cent when the patient was discharged on May 3.

The patient felt well on the prescribed diet last mentioned. There had been no undernutrition in consequence of either diet or exercise this time, since the weight was the same as at admission. Accordingly, the condition had again not been brought under any control, except for the transitory freedom from glycosuria.

Subsequent History.—Slight transitory glycosuria occurred with a cold in May. It then remained absent, except for rare traces up to Aug. 18, when the patient called to report. He was then planning to return to work. The next heard from him was on Dec. 4. He had tired too easily on attempting to work, and also glycosuria appeared. He tried to control his condition by modification of diet himself, but finally reached the point of continuous glycosuria and downward progress. He was readmitted to hospital Dec. 6, 1916.

Third Admission.—The weight was down to 43.4 kg.; *i.e.*, a loss of 7.6 kg. since the first admission and 3.6 kg. since the last discharge. Some edema was present. Fasting was begun immediately on admission. On the first day there was glycosuria of 10 gm. with excretion of 2.62 gm. total acetone. The plasma showed sugar of 0.358 per cent, total acetone 14 mg. per 100 cc., CO₂ capacity 64 per cent. Glycosuria ceased on the 2nd fast-day. Instead of a carbohydrate period, a diet of meat, eggs, and thrice cooked vegetables was begun, at first with only 20 gm. protein and 200 calories, but increasing to 40 gm. protein and 400 calories on Dec. 11. Fat was then added very gradually up to a maximum of 1450 calories on Feb. 6. The diet was then kept mostly at 1000 to 1350 calories, but in Mar. by means of alcohol it was raised as high as 1650 calories. The continuous hyperglycemia and frequent glycosuria are shown by the graphic chart. The patient was discharged Apr. 5, 1917, on a carbohydrate-free diet of 40 gm. protein and 1000 calories, of which 350 were alcohol. The weight was 44 kg. Edema being present, former weights of 41 to 42 kg. were probably more nearly correct. The diet thus represented about 0.95 gm. protein and 24 calories per kg., reduced by weekly fast-days to 0.82 gm. protein and 21 calories average. The condition had been kept under partial control but the patient was not benefited, for he was emaciated, weak, and neurasthenic, though still up and

about. He had also become discouraged. He continued treatment along the above lines for several months at home, then gradually gave up the attempt to remain sugar-free. He continued, however, to follow a low regulated diet, with occasional fast-days to check progressive symptoms. Reports in the fall of 1917 indicated heavy glycosuria and acidosis and the certainty of early death.⁸

Remarks.—One fact stands beyond question; in a case of this type the functional overstrain represented by continuous hyperglycemia and tendency to recurrent glycosuria is of itself sufficient to bring about relapse and downward progress. Life was very much longer than in patients of similar type who abandon dietary restriction altogether. Whether any other cause of downward progress was present in this case is not known.

CASE NO. 57.

Male, married, age 37 yrs. American Jew; physician. Admitted Nov. 15, 1915.

Family History.—Grandparents all lived to healthy old age. No family disease known up to this point. Patient's father and mother were first cousins. Father still enjoys excellent health at age of 69. No taint on his side of family, except death of a sister from carcinoma of stomach. Patient's mother died at age of 27 of diabetes. She was one of four children. One brother is well, another brother has diabetes, a sister died a year ago of diabetes. The present patient was the third of four children. The first died of unknown cause 1 year after birth, the second is alive but highly neurotic, the fourth child is a sister still living but with severe diabetes. The entire family are moderately but not extremely obese.

Past History.—Patient always strong, though somewhat obese. Measles at 8. No sore throats or other childhood infections, but a few attacks of tonsillitis since diabetes began. Even in childhood he had huge appetite and has always eaten excessive quantities of sweets and desserts. No tobacco. No alcohol beyond one glass of beer daily. Eight cups of strong coffee every day. Has taken relatively little exercise. Has slept well, but is of fairly nervous disposition. In the 2nd year of medical school in 1899, he tested his urine in chemistry class, and it contained sugar at that time. During his interne year he was yellow with catarrhal jaundice for about 8 weeks, but there was no fever or confinement to bed and no sign of any such trouble since. Always had tendency to profuse sweating, but very marked hyperidrosis began that year, and he has since been compelled to use $\frac{1}{16}$ to $\frac{1}{8}$ grain atropine occasionally to control sweating; has sometimes taken it every day or two in summer. His weight before diabetes was 250 pounds, girth of waist 54 inches. He has been married 9 years; wife healthy, but they have avoided pregnancy because of diabetes.

⁸ Coma death occurred in Jan., 1918.

Present Illness.—No attention was paid to the glycosuria found in 1899, and it presumably continued. In 1907, losses during financial panic caused worry. An attack of general furunculosis came on 2 weeks later, and glycosuria of 5.4 per cent was then found. The diet was only moderately restricted; in particular much oatmeal was allowed. Since that time he has almost never been free from superficial infections, chiefly as boils on the neck; but any scratch or even a chapped finger always takes a very long time to heal. In 1908, he received treatment with oatmeal, codeine, and arsenic. Another physician subsequently applied the oatmeal treatment. Such treatment was also supervised by von Noorden on one of his visits to this country. In 1913, 10 months of lactic acid bacillus treatment was tried under two of the chief advocates of this plan. Glycosuria remained heavy through these years. There was no acidosis or loss of weight, and the patient merely felt continually weak and run-down. In 1914, stricter treatment was undertaken by still another diabetic specialist, who ordered a measured diet, with 2 slices of toast as the only carbohydrate daily, and green days twice a week. Later the toast was replaced by casoid biscuit. Even with strict following of diet, heavy glycosuria persisted; but at times the patient found the restrictions intolerable and consumed huge quantities of hot cakes and maple syrup at restaurants. Last June there was another attack of general furunculosis; four of the boils had to be incised. The patient was in bed 3 weeks, and healing of the wounds required 3 months. His gums have been receding and his teeth breaking. The very troublesome hyperidrosis and unbearable sensations of heat in a warm atmosphere are one permanent complaint.

Physical Examination.—Height 170 cm. A healthy, comfortable looking, florid faced, moderately obese man with sweaty skin. Numerous scars of healed or nearly healed furuncles scattered over body. Teeth as described. Tonsils so large that they block throat, crowding uvula up and leaving only a narrow slit between them, yet patient says that one slight attack of tonsillitis per year is all the trouble they ever make. Several glands beneath jaw are enlarged to hazel nut size. Blood pressure 120 systolic, 85 diastolic. Knee jerks present but diminished. Physical examination otherwise negative.

Treatment.—During 4 full days in hospital the patient was allowed to follow his appetite, with carbohydrate limited to green vegetables. Thus, on Nov. 17 to 19, he ate 166 gm. protein, 30 to 40 gm. carbohydrate, and 4000 calories daily, and excreted 16.7, 31.6, and 14.5 gm. sugar, with only slight ferric chloride reactions and low normal plasma bicarbonate. 4 days of fasting were then imposed, a trace of glycosuria remaining in the early hours of the last day. Without waiting for full 24 hours of sugar-freedom, feeding with green vegetables was begun on Nov. 24 and increased to 100 gm. carbohydrate on Nov. 26, when a trace of glycosuria appeared. After a fast-day on Nov. 28, carbohydrate was begun in the form of oatmeal, for comparison with the green vegetables. Glycosuria appeared with 250 gm. carbohydrate on Dec. 5, and remained no more than a trace with increase to 300 gm. carbohydrate on Dec. 6. The oatmeal being eaten plain after 3 hours boiling, with no flavoring but salt, and nothing else being

permitted but 300 cc. coffee and 300 cc. clear soup, the caloric intake was thus kept down to undernutrition level. After a fast-day on Dec. 7, another test was begun with potato under the same conditions. 500 gm. carbohydrate were tolerated in this form, causing only a trace of glycosuria on Dec. 15, which cleared up with the same intake on Dec. 16. The patient had been longing for potatoes for many years, but the test was stopped because he could not eat a larger quantity.

After a fast-day on Dec. 17, an attempt was made to compare the different proteins in their effect upon the carbohydrate tolerance, potatoes being used because the patient enjoyed them so much. On Dec. 18, glidine was given with potato, but the test had to be broken off because the taste of glidine caused nausea. Beginning Dec. 19 the protein used was in the form of meat (beef, veal, pork, every day). A trace of glycosuria thus appeared on Dec. 19 with 136 gm. meat-protein and 300 gm. potato-carbohydrate, and increased only slightly with the increased intake of 150 gm. protein and 400 gm. carbohydrate on Dec. 20 and 21. Instead of a fast-day on Dec. 22, 927 calories of fat were given in the form of butter. The glycosuria cleared up in practically the same manner as on plain fasting, a trace being present only in the early hours. The ferric chloride reaction remained negative, notwithstanding the fears once entertained concerning lower fatty acids in butter. On Dec. 23, this same quantity of butter fat was given with 100 gm. potato-carbohydrate, and glycosuria resulted, in contrast to the far higher tolerance shown for potato without fat. On Dec. 24, three eggs were added and the carbohydrate simultaneously increased to 200 gm. On Dec. 25, 300 gm. potato-carbohydrate with 100 gm. butter fat without eggs resulted in still heavier glycosuria. Protein starvation was continued on Dec. 26 and 27, 400 gm. potato-carbohydrate being given daily with 100 gm. butter fat. Moderately heavy glycosuria was continuous, showing a well marked reduction of tolerance by fat as compared with the former period of potato alone. A fast-day on Dec. 28 stopped the glycosuria.

Beginning Dec. 29, the desired test with vegetable protein was made by the use of Barker's gluten flour. Glycosuria appeared on the first day with 124 gm. protein and 204 gm. potato-carbohydrate. It became constantly heavier as the intake was raised to 148 gm. protein and 404 gm. carbohydrate. No appreciable advantage of vegetable protein, therefore, was perceptible in comparison with the previous period of potato and meat. After stopping the glycosuria by the fast-day of Jan. 2, green vegetables were resumed. On account of the quantities of carbohydrate, it was necessary to include the higher classes up to green peas, green lima beans, beets, turnips, etc. Faint or doubtful traces of glycosuria were present on each day, but did not increase as the intake was increased from 200 to 400 gm. carbohydrate in this form. Therefore, no special superiority of the form or kind of carbohydrate was definitely demonstrable between oatmeal, potatoes, and green vegetables, variations of the patient's tolerance being sufficient to account for the facts observed.

This patient was one of several diabetics discharged rather hastily because of an epidemic of grippe in the hospital. Jan. 8 to 10 his diet was rapidly built up to 150 gm. protein, 50 gm. carbohydrate, and 3000 calories. The reduction of copper shown amounted to only doubtful traces in a single voiding each day, and was judged to be due to a concentrated urine, not true glycosuria. The patient had recovered complete health, such as he had never enjoyed during the time of his diabetes, and left to undertake active medical work. Hyperidrosis had ceased, along with the other symptoms.

Acidosis.—The slight degree of acidosis after so many years of heavy glycosuria was one of the indications that this was essentially a mild case, though the patient and all who had treated him regarded it as severe and intractable. The specific difference as respects acidosis seems to be illustrated by comparison of this patient with others in the series. Not only was this patient rather obese, but also on Nov. 18, for example, he ingested only 37.7 gm. carbohydrate in the form of green vegetables (presumably not all absorbed) and excreted 31.6 gm. sugar. The rest of the diet consisted of 166 gm. protein and 344 gm. fat. Yet this large quantity of fat was disposed of with such slight traces of ketonuria that quantitative estimation was considered not worth while. The plasma bicarbonate likewise remained within normal limits. There was a slight fall in CO₂ capacity in the initial fast, but no serious acidosis was shown either by this or the clinical symptoms, though the ferric chloride test became heavy. It is noteworthy that distinct ketonuria continued during the period up to Dec. 7, when the patient was receiving absolutely no food but oatmeal, in quantities increasing from 25 up to 300 gm. carbohydrate. Even large quantities of assimilated carbohydrate therefore did not necessarily clear up ketonuria promptly and completely.

Blood Sugar.—This gave another indication of the inherent mildness of the case. Hyperglycemia between 0.25 and 0.3 per cent, as shown at admission, had presumably been present for a number of years. It was remarkable that it should have fallen to normal so quickly. The marked hyperglycemia with slight glycosuria during the subsequent carbohydrate tests indicated a high renal threshold. Fast-days brought the sugar promptly to normal.

Carbohydrate "Cures."—The diabetes here was so stubborn that it had for years resisted oatmeal "cures," "green days," and restricted diet, under the care of consultants experienced in the management of diabetes. The case was a typical example of so called "protein sensitiveness," "fat sensitiveness," and "paradoxical tolerance." The first two terms have been used to denote susceptibility to glycosuria from the addition of protein or fat to a standard diet. The last is Naunyn's expression for cases with glycosuria continuously present, but showing little diminution of glycosuria on diminishing carbohydrate and little increase upon addition of even considerable quantities. These peculiarities were all illustrated in the above tests. The actual condition was a mild diabetes with obesity. Under the prevalent misconception that obesity in itself is a favorable feature, this patient had been restricted in carbohydrate, but continuously "built up" with protein and fat, and the intractable glycosuria was due to this

War Demonstration Hospital of this Institute on Jan. 21, 1918, for Carrel-Dakin treatment or amputation if necessary. Immediate fasting changed the condition so promptly that surgery was unnecessary, and rapid healing without deformity resulted. On Feb. 2, the patient was able to leave, free from hyperglycemia as well as glycosuria and acidosis, to finish convalescence at home. The lesson has been effective, and he has returned to the condition stated after his first discharge.

Remarks.—The record illustrates what can be hoped for in a large proportion of cases not of such maximal severity as those comprising the majority of this series; it further illustrates the dangers of excessive diet and weight even in patients of this type.

CASE NO. 58.

Female, married, age 72 yrs. American. Admitted Dec. 3, 1915.

Family History.—No heritable disease.

Past History.—Very healthy life under excellent hygienic conditions. Whooping-cough in childhood the only infection remembered. "Never sick a day." Never any throat or tonsil trouble. Eyes have always been weak. Teeth all removed within the past decade. Married 55 years. One still-birth; one child died in infancy; five children are well. Habits regular, appetite moderate. No excesses of any description.

Present Illness.—4½ years ago patient consulted an oculist for failing vision. Diabetic retinitis was diagnosed, and the oculist advised that efficient treatment of the diabetes was necessary in order to save her eyes. Physicians have employed half-hearted measures, and she has never been free from glycosuria. There has been polydipsia and polyuria, but no polyphagia. Vision has grown progressively worse, and the patient came to the Institute on this account.

Physical Examination.—Height 155 cm. Normal development, slight obesity. Skin very dry. Blood pressure 185 systolic, 120 diastolic. Teeth false. Slight emphysema. Liver edge palpable 4 cm. beneath costal margin. Examination by oculist showed double senile unripe cataract preventing retinal examination; amblyopia with inability to count fingers at 2 meters. Over internal malleolus of left foot is an encrusted, red and angry-looking, but painless sore about 2 cm. in diameter. Scabs showing less inflammation are present over the metatarsal joint of the great toe and on the dorsum of the third toe of the same foot. Examination otherwise negative.

Treatment.—The 1st full day in hospital, a diet was given of 99 gm. protein, 15 gm. carbohydrate, and 1900 calories. The urine showed 26.65 gm. sugar, and the ferric chloride reaction, which had been negative, became slight during this day. It then became apparent why physicians had failed to check the glycosuria, notwithstanding the ocular damage; for when carbohydrate was entirely withdrawn and the total diet reduced to 75 gm. protein and 1600 calories, glycosuria diminished slightly but remained rather heavy, and the ferric chloride reaction became moderately heavy. Accordingly, after a week of such diet, 2 days of fasting (Dec. 11 and 12) were given. Glycosuria ceased, but a moderate ferric

chloride reaction continued. The usual green vegetables were then begun with 10 gm. carbohydrate on Dec. 13 and increased rapidly, until glycosuria appeared with 100 gm. on Dec. 16. The ferric chloride reaction consequently became negative. The diet was then rapidly built up to 70 gm. protein and 1500 calories, the urine remaining normal. The patient was discharged Dec. 24. The dry skin, patches of threatened gangrene, and other minor conditions had cleared up, and the patient stated she felt better than for years past.

Acidosis.—There was never any clinical symptom of acidosis. The development of rather marked ferric chloride reactions in a mild case of diabetes when the diet is restricted, has frequently, as in this instance, frightened physicians so that they refrained from taking the measures imperatively demanded to control such a genuinely serious complication as diabetic retinitis. On the other hand, if this warning sign were entirely ignored and a high protein-fat ration kept up, it might readily bring on coma even in some patients with mild diabetes.

Blood Sugar.—On the day of discharge with normal urine, the sugar was still 0.147 per cent in whole blood and 0.175 per cent in plasma. In view of the patient's age, the mildness of the case, and the expectation of improvement with time, this hyperglycemia required no more rigorous measures for the immediate present.

Weight and Nutrition.—The weight at admission was 68 kg., at discharge 67.2 kg. The diet prescribed at discharge was 70 gm. protein, 15 gm. carbohydrate, and 1500 calories (a little over 1 gm. protein and 22 calories per kg.). Mild exercise suitable to her age was advised, and a continuance of slight undernutrition was desired, while the cataracts were ripening.

Subsequent History.—The patient remained sugar-free, aside from a few traces due to slight laxity in the care of an indulgent daughter. The diet was sufficiently bulky and entirely satisfied the patient, except that she still entertained some longing for the desserts of the past. She was readmitted to the hospital June 8, 1916 for cataract operation.

Second Admission.—The weight was now down to 62.6 kg., the urine normal, and the strength at its best. The prescribed diet was continued. On June 10, sugar was 0.145 per cent in both whole blood and plasma. By June 26 it had further diminished to 0.111 per cent in whole blood and 0.128 per cent in plasma, although the carbohydrate meanwhile had been increased to 30 gm. Tests showed that 50 gm. carbohydrate could be tolerated, but instead of maintaining this intake, 30 gm. carbohydrate were resumed and the protein increased to 90 gm. Cataract operation was performed on July 11 without glycosuria, acidosis, or any untoward incident. Diabetic retinitis was diagnosed thereafter. The patient was discharged July 28. The weight was now down to 59 kg., which was sufficient for her figure, and the health was still further improved.

Subsequent History.—After several months of sugar-freedom and favorable progress, she began to steal sweet and starchy foods, and reached a chronically weak condition with continuous glycosuria. Gangrene of the foot then necessitated fasting, which was conducted at home, and sugar-freedom has since been

maintained on restricted diet. At last report (1918) glycosuria was absent, but owing to two apoplectic strokes and an intestinal obstruction diagnosed as carcinomatous, death was expected within a few weeks or months.

Remarks.—Diabetes at such an age is usually easy to control. The very high proportion of senile patients who sooner or later lose comfort and even life by reason of gangrene or ocular or other complications indicates the error and danger of the widespread belief that glycosuria at this age is harmless enough to be neglected. Efficient treatment is indicated, for relief, if complications are present, and for prophylaxis if they are not present. The general health as a rule is improved, and it becomes evident that part of the trouble attributed to senility was due to diabetes. Surgical operations should then be performed if required.

CASE NO. 59.

Male, married, age 46 yrs. American; physician. Admitted Dec. 29, 1915.

Family History.—Father died supposedly of cancer of liver at 64 years, but there are indications that the condition may have been luetic. Mother is living, aged 83, and has rheumatism and gout. A maternal aunt died of diabetes. One brother of patient is well. One sister died after an acute illness of 3 days in some form of coma, apparently following tonsillitis; there was a history of increasing attacks of so called "acidosis" preceding, partially relieved each time by alkali; there was also the possibility of slight hyperthyroidism. Patient has been married 8 years; wife and one 6½ year child are well; another child died a year ago with lymphatic leucemia and *Streptococcus hæmolyticus* infection.

Past History.—Measles, whooping-cough, and probably scarlet fever before 10. Tendency to biliousness, nausea, and vomiting throughout childhood. One severe sunstroke in boyhood. Patient was always rather frail in physique, of nervous type, addicted to overwork. He blames overwork in college, financial worries, and subsequent professional strain for his condition. In 1899 he was refused life insurance because of albuminuria with casts. Subsequently, with some difficulty, he obtained a policy. Little alcohol; 10 to 15 cigarettes daily. No excesses in diet or carbohydrate. There was a period beginning in 1889 when diabetes may have been present unknown. There was persistent sciatica for the year 1889 to 1890. He has suffered for many years from true typical gout. There were numerous attacks in 1900, but the gout has diminished since 1907. In 1894, he underwent an operation for axillary abscess following a finger infection. In 1896, he had numerous boils and carbuncles, treated by incisions and vaccines.

Present Illness.—The diagnosis of diabetes was not made until 1910, when polyuria began. Treatment has been interfered with by professional duties, and owing to downward progress the patient visited a specialist 2 years ago. He was made sugar-free and his weight reduced from 137 pounds to 120½ pounds. Upon returning to New York he resumed his attempt to carry heavy professional work and keep his diabetes secret. This necessitated violations of diet when attending dinners in company, so that relapse resulted. He came to the Institute because he had finally lost power to continue his work.

Physical Examination.—Height 176 cm. Normal development, decided emaciation, marked weakness, but no acute symptoms. Slight diarrhea. Lymph glands generally palpable. Blood pressure 118 systolic, 88 diastolic. Knee jerks just obtainable with reinforcement. Wassermann negative. Examination otherwise negative.

Treatment.—For 3 days the patient was kept on an observation diet of 76 gm. protein, 10 gm. carbohydrate, and 2100 calories, about 200 calories being whisky. The glycosuria of 0.88 per cent on the first day diminished to a trace by the third day, and then ceased with 1 day of fasting. The ferric chloride reaction cleared up in parallel. A carbohydrate test in the usual form showed a tolerance of 90 gm. carbohydrate, glycosuria resulting from 100 gm. on Jan. 10 to 11. A mixed diet was then built up, containing 20 gm. carbohydrate and 1900 to 2400 calories. The patient contracted a mild but persistent grippe infection, which was largely responsible for the frequent traces of glycosuria. Beginning Feb. 18, the calories were diminished to 1900. The grippe passed off and the tolerance improved, so that at the end 90 gm. protein, 50 gm. carbohydrate, and 2245 calories were taken without glycosuria. He was discharged Mar. 16 feeling improved, but still below normal strength.

Acidosis.—The ferric chloride reaction promptly became negative. The CO₂ capacity was practically normal throughout. In the initial fast it fell from a high to a low normal, and it at first tended to be down after fast-days. The tendency to a slightly high ammonia excretion was the only evidence of acidosis.

Blood Sugar.—Marked hyperglycemia present at admission was rather promptly brought to normal. Subsequently the figures were generally normal after fast-days, but showed hyperglycemia on other days. Grippe was partly responsible, but the marked hyperglycemia, particularly at the close, was clear evidence that the diet was too high.

Weight and Nutrition.—The weight at admission was 52.6 kg., at discharge 50.4 kg.; *i.e.*, a loss of 2.2 kg. The above mentioned diet at discharge thus represented 1.78 gm. protein and 44.6 calories per kg., reduced by the weekly fast-days to about 1.5 gm. protein and 38 calories per kg. The body weight in this calculation was a very low one; nevertheless the condition was obviously not under good control, and therefore such a liberal diet was a mistake.

Subsequent History.—The patient went to the seashore to rest under favorable conditions. In the 2 weeks between discharge and Apr., he gained 4½ pounds and showed glycosuria 9 times, a slight cold being blamed for part of the trouble. The diet was then changed to 127 gm. protein, 35 gm. carbohydrate, and 1950 calories. On this, glycosuria was almost continuously absent. He tried to build himself up with exercise in the form of golf, but in the middle of Apr. developed a slight infection and herpes zoster. He then returned to New York, where his diet could be more closely supervised, and the ration was reduced to 75 gm. protein, 10 gm. carbohydrate, and 1900 calories. On this, glycosuria was almost continuously absent; but in June another cold occurred with sinus infection, so that traces of glycosuria were present almost continuously June 5 to 20. Twelve

blood analyses between Apr. 28 and June 12 showed continuous hyperglycemia and normal CO₂ capacity, the lowest plasma sugar being 0.135 per cent, the highest 0.218 per cent, and the average 0.177 per cent. Because of the unfavorable progress, the patient was readmitted June 20, 1916.

Second Admission.—The weight was 52.2 kg., as against 50.4 kg. at discharge and 52.6 kg. at the first admission. The strength and spirits were decidedly improved as compared with the first admission. On June 21, the glycosuria was 6.7 gm., the CO₂ capacity 56.1 per cent, the sugar in whole blood 0.228 per cent and in plasma 0.244 per cent. The diet was kept up to the maximum prescribed outside the hospital, and no fast-days were imposed. Traces of glycosuria were present frequently on 2100 to 2250 calories, but for 3 days at the close (July 10 to 12), 90 gm. protein, 15 gm. carbohydrate, and 2000 calories were taken without glycosuria. The patient's strength had improved so that he was able to go on with moderate professional work. The weight was unchanged during this period in hospital. The hyperglycemia also showed practically no change. The renal threshold for sugar was evidently high, but the urea index on June 28 was determined by Dr. Palmer as 200; also (the patient frequently worrying over his gouty history) the uric acid in the blood was 2.8 mg. per 100 cc.

Subsequent History.—The patient went to a country place and attempted to build up his physical condition by exercise and general care, but never succeeded in regaining strength or working capacity. He had trouble with nausea, edema, and mental irritability and depression, partly due to trouble with a tooth. Glycosuria was almost continuously absent.

Third Admission.—July 31 the patient was readmitted to undertake a somewhat more thorough treatment. His intense desire to go on with active professional work had been a hindrance to radical measures. With glycosuria and ketonuria absent, the sugar was 0.200 per cent in whole blood, 0.208 per cent in plasma, CO₂ capacity 52.8 per cent. The output of ammonia nitrogen was 0.76 gm.; of acid (Folin) 468 cc. 0.1 N. The weight was 52.5 kg.; *i.e.*, practically the same as at first admission. After 3 days on the prescribed diet, a fast-day was given on Aug. 4, followed by a carbohydrate tolerance test. A trace of glycosuria appeared Aug. 17 to 18 with 130 gm. carbohydrate. The tolerance of 120 gm. thus seems to indicate an increase of 25 per cent over the first test in Jan. He was then put back on a mixed diet of 90 gm. protein, 15 gm. carbohydrate, and 2000 calories, and was discharged on this Aug. 24. The weight had been reduced to 50 kg., and the blood sugar to 0.143–0.185 per cent. There had been another slight gain in general health and spirits.

Subsequent History.—The patient went to the Catskills for the summer and to California for the winter. On account of recurrence of glycosuria, his diet has had to be again reduced to 75 gm. protein, 10 gm. carbohydrate, and 1900 calories. He remains a fairly comfortable semi-invalid, stronger and better in all respects than at first admission, and hoping to return to work if he can improve a little more.

Remarks.—A number of these patients have been tried on what could be called a modified Naunyn treatment; that is, using more or less prolonged fasting and perhaps transitory reduction of weight to suppress glycosuria, and then giving the maximal diet possible in order to keep up a maximum of weight and strength. If the diabetes has any claim to be called severe, the results of such a method are uniformly and necessarily bad. In view of this patient's age, some power of recuperation may be expected. There is a possibility that slight improvement may occur, as indicated by the higher tolerance in the carbohydrate test in spite of the excessive diet, the case somewhat resembling the milder ones in older persons. It is more probable that a case of this severity will sooner or later show downward progress, which may be called "spontaneous," but is sufficiently accounted for by inadequate treatment. The persistent marked hyperglycemia not tending to improve, and the slight acidosis indicated by a slightly elevated ammonia output, are plain evidence that overstrain of the weakened function has been only diminished and not stopped, and unless there is an unexpectedly high spontaneous recuperative power, the downward progress will be merely slowed, not stopped. The high diets in this and other patients do not even serve the intended purpose of keeping up weight, strength, and resistance, for these poorly treated patients are the very ones who are most subject to infections and suffer most harm from them.

The patient's ambition of resuming active work has not been achieved. He would doubtless be far nearer to it, and in better condition in all respects, if he had at the outset been brought down to a suitably low level of diet and weight. A lower level of weight, efficiency, and comfort than required in such a plan will probably result here, as it has in other cases, from the gradual downward progress, and this loss of weight will be attended not by benefit but serious injury of the assimilative function. Thorough treatment should still offer much hope.

CASE NO. 60.

Female, married, age 43 yrs. American; housewife. Admitted Jan. 1, 1916
Family History.—Parents lived to old age. Two brothers and one sister well. Husband and one 6 year old child well. No other pregnancies. No diabetes or other heritable disease known in family.

Past History.—Very healthy life. Whooping-cough, measles, and chicken-pox in childhood. "Gastric fever" in 1896; in bed 3 or 4 weeks. Frequent attacks of tonsillitis up to 10 years ago, none since. No other illnesses. Appetite, digestion, bowels, menstruation, and sleep normal. Never nervous. No excesses of any kind.

Present Illness.—About 9 months before admission, patient noticed that she was losing weight and was unduly thirsty. After 2 months (June, 1915) a physician consulted for pruritus vulvæ diagnosed diabetes. The patient was fasted for a day or two, then placed on a diet of eggs and milk. She was said to be "practically sugar-free," but continued to lose weight and strength. In Aug.

1915, she came under the care of a specialist for 6 weeks, first in hospital and subsequently at home. She was made sugar-free by fasting, and then kept on a minimal diet. She lost 60 pounds weight, and was referred to the Institute as a case of extremely severe diabetes.

Physical Examination.—Height 153.8 cm. A very emaciated woman, with fair strength and no acute symptoms. Slight hyperpnea and drowsiness are present, but are probably accounted for largely by weakness and weariness after her railroad trip. Teeth in good condition. Tonsils hypertrophied. Breath has acetone odor. Knee jerks not obtainable even with reinforcement. Wassermann negative. Examination otherwise negative.

Treatment.—On Jan. 1, the day of admission, the patient received 54 gm. protein, 5 gm. carbohydrate, and 1247 calories, and excreted 20.4 gm. glucose, 1.6 gm. ammonia nitrogen, and 495 cc. 0.1 N acid, with an intense ferric chloride reaction. 3 days fasting was then imposed, with resulting glycosuria of 11 gm. on Jan. 2, 9.2 gm. on Jan. 3, 12.1 gm. on Jan. 4. As the weakness seemed to be of dangerous degree, the tempting experiment was tried of feeding a liberal diet in the hope of getting a fresh start for subsequent fasting. Accordingly, on Jan. 5, 2 eggs were given, with coffee and clear soup each 300 cc. as during fasting. The diet was rapidly built up (Jan. 6 to 11) as high as 75 gm. protein and 2150 calories on Jan. 10. Glycosuria increased only to 24.1 gm., but hyperpnea, drowsiness, and nausea developed. The plasma bicarbonate fell sharply to 24.6 per cent, while the ammonia nitrogen rose to 3.19 gm., with urinary acidity of 335 cc. 0.1 N. Fasting had to be resumed to ward off coma, with the patient worse instead of better than before. Under fasting without alkali, the above mentioned low CO₂ on the morning of Jan. 12 rose to 27.6 per cent by evening of the same day. Thereafter it climbed steadily, and the patient was out of danger within 24 hours. On Jan. 14, 2 and on Jan. 15, 3 eggs were allowed in addition to soup and coffee. After a plain fast-day on Jan. 16, 420 calories of whisky daily were begun, 1 egg also being allowed on Jan. 17. Glycosuria had been diminishing, and cleared up on Jan. 19. After about 40 hours of sugar-freedom, 10 gm. carbohydrate in the form of green vegetables were given on Jan. 21, and 20 gm. on Jan. 22. Slight glycosuria resulted, and persisted as the carbohydrate intake was increased as high as 35 gm. on the following days. After a fast-day with 150 cc. whisky, 400 gm. thrice boiled vegetables, and 60 gm. bran biscuit on Jan. 28, a very low carbohydrate-free diet was attempted. On Feb. 5, when this had been built up to 50 gm. protein, 850 calories (245 being alcohol), and 300 gm. thrice boiled vegetables, a trace of glycosuria appeared, requiring a fast-day on Feb. 6. With the same number of calories, and diminution of protein to 40 to 35 gm., glycosuria continued. It still persisted with 12.5 gm. protein and 450 calories (315 being alcohol) on Feb. 10, and a fast-day on Feb. 11 was necessary to abolish it. Beginning Feb. 12, the diet was again cautiously built up to 42 gm. protein and 650 calories (315 being alcohol). Glycosuria on Feb. 17 and 19 required a fast-day on Feb. 20. With the same calories and reduction of protein to 35 gm., glycosuria still recurred, requiring another fast-day on Feb. 27. A

in whole blood and 0.333 per cent in plasma on Jan. 15. A fall then began, and on Jan. 25, on alcohol and green vegetables, the sugar was down to 0.143 per cent in whole blood and 0.167 per cent in plasma. The values then began to approach normal, and from Mar. 7 to 29 it can be said that undernutrition had brought about normal blood sugar as judged by morning samples before breakfast. The subsequent higher diets brought back hyperglycemia, which was reduced by the lower diet beginning June 3. Increased diet again brought a rise on June 23, but on June 28, on the diet proposed for discharge, the blood sugar was below 0.15 per cent, which seemed rather satisfactory in such a case at this stage.

Weight and Nutrition.—For 5 months before admission the patient had been extremely undernourished, green vegetables up to or slightly past the limit of tolerance, and a few eggs, having been almost the only nourishment in this time. This had repressed the dangerous acidosis to the greatest possible degree, but both body fat and body protein had necessarily been sacrificed heavily in the process. The process had been persisted in, though the patient felt fairly well and strong at the outset in Aug., and on admission in Jan. was emaciated and seriously exhausted. Accordingly, the experiment was tried of feeding more liberally for a short time in the attempt to restore some strength, so as to get a fresh start for further fasting. Though the diets on Jan. 5 to 11 averaged only 33 calories per kg. of body weight, the attempt caused only harm instead of benefit, as always in genuinely severe cases. The question thereafter was whether the glycosuria could be controlled without starving the patient to death. The method used consisted in alcohol short of any perceptible symptoms, protein generally on feeding days above 1 gm. per kg. of weight, and close restriction of fat, so as to maintain almost continuous undernutrition. It would doubtless have been better if alcohol had been omitted and the fat had been excluded still further, and the condition thus controlled earlier and more radically. The weight at admission was 36.6 kg. The gain in weight about Feb. was due to edema, which was controlled by regulation of the salt intake, sodium chloride being given, weighed like the rest of the diet, first 10 gm. and later 8 gm. daily. The weight at discharge was 33 kg.; *i.e.*, a loss of 3.6 kg. The low level of metabolism caused by undernutrition is thus illustrated, for a patient starting well nourished at the outset would have lost much more weight on such a diet. The degree of undernutrition is shown in the following calculation.

	183 days.	Per day.	Per day per kg.
Alcohol calories.....	55,496	303	9
Food "	81,878	447	13
Total "	137,374	750	22
Protein.....	5,162.3 gm.	28.2 gm.	0.83 gm.
Fat.....	6,109.9 "	33.4 "	0.98 "

The diet prescribed at discharge was 50 gm. protein and 1000 calories, more than a third being in the form of alcohol as shown, (1.5 gm. protein and 33

calories per kg., reduced by partial fast-days to about 1.4 gm. protein and 31 calories per kg.).

Subsequent History.—The patient was discharged with the idea that she might be able by great care to remain 2 or 3 weeks at home. She was actually at home 4 months and 1 week, remaining free from glycosuria, except for traces on a very few days, on account of which the diet was ordered on Aug. 16 to be reduced to 40 gm. protein and 800 calories. She was readmitted for further treatment Nov. 8, 1916.

Second Admission.—Weight 29.9 kg.; *i.e.*, a loss of 3.1 kg. since discharge. In addition to glycosuria, a slight ferric chloride reaction was present. Instead of fasting immediately, the diet was limited to green vegetables representing 20 gm. carbohydrate, and diminishing to 5 gm. carbohydrate on Nov. 12. 2 fast-days, Nov. 13 and 14, left the urine normal. On Nov. 15, 5 gm. carbohydrate in the form of green vegetables were assimilated, but 10 gm. on Nov. 16 brought a trace of glycosuria. Carbohydrate-free diet was then built up, beginning with 1 egg and 360 calories on Nov. 17, and increasing to 6 eggs and 1200 calories on Nov. 22. Continuance of this diet brought glycosuria beginning Nov. 25, requiring a fast-day on Nov. 27. Thereafter similar diets (40 to 50 gm. protein and 1150 to 1300 calories) were continued, with routine weekly fast-days. The effect of these in checking acidosis is shown by the ammonia curve. No more than the faintest traces of glycosuria appeared, but these were unduly frequent. Though the food was thus pushed to the utmost limit of tolerance, it was not possible to prevent gradual loss of weight.

Lipemia was not noticed at the first admission. It was heavy at the second admission, and gradually disappeared during the first week of treatment. The difference may be attributed to the fact that the patient was eating little but green vegetables when first received, but preceding the second admission had been on protein-fat diet. No quantitative estimations were made.

The patient was dismissed Apr. 6, 1917, weighing 27.6 kg. The prescribed diet represented 1.45 gm. protein and 45 calories per kg., reduced by the weekly fast-days to 1.25 gm. protein and 39 calories average. The diet therefore was absolutely very low. It appeared relatively high on account of the emaciation, but either because of the relative increase in body surface, or the lack of carbohydrate, or a specific diabetic disorder, it did not produce gain in weight.

Subsequent History.—The patient has since remained at home on the same program as in hospital. She adheres rigidly to her diet and clears up traces of glycosuria promptly by fast-days. There is little perceptible change up to the present in weight, strength, or assimilative power.

Remarks.—By extreme undernutrition it has been possible to keep this patient alive over 2 years from her first fasting treatment. Though always hungry, excessively emaciated, and lacking strength for any real exertion, some of the noteworthy features are her constant cheerfulness, freedom from infection, and comfort in all other respects. She is able to be up and about, carries on light household duties, and—the point of most importance to her—attends to the

sponse to slight dietary restrictions indicates no special difficulty in bringing down the blood sugar. Nevertheless, the renal impairment served as a block to the ordinary glycosuria, and the finding of as much as 0.73 per cent blood sugar with only slight glycosuria shows the necessity of blood examinations in such circumstances. The treatment was not so rigid as would be advisable if the duration of life from other causes were less limited. On the other hand, to ignore the diabetes would probably lead to aggravation of the entire condition and materially shorten life.

CASE NO. 62.

Female, unmarried, age 19 yrs. American; houseworker. Admitted Feb. 19, 1916.

Family History.—Father, mother, one brother and two sisters are well. One brother died in infancy of "spinal meningitis." A maternal grandmother died of tuberculosis. No diabetes or other heritable disease known in family.

Past History.—Whooping-cough, measles, and chicken-pox in infancy. No throat trouble. Grippe once. There is a hazy description of what the doctors are said to have called diabetes at the age of 7. The symptoms are described as puffiness of the face in the mornings, whiteness of the skin, and urine which looked bloody and contained a heavy sediment. There was also skin eruption over the back and legs described as "poison water blisters," which were small, not hemorrhagic, and healed without scars. Treatment is said to have been by diet with prohibition of starches. This trouble passed off after about a year. The habits, appetite, digestion, bowels, and menstruation have been normal. No alcohol. Moderation in tea, coffee, and carbohydrates. Not neurotic. Always slept well and was under no strain.

Present Illness.—Polydipsia and polyuria began in the summer of 1911. Diabetes was promptly diagnosed, and the diet was limited to proteins and fats with vegetables. Glycosuria has been continuous since the beginning. Menstruation stopped 1 year after onset of diabetes, and bowels have become irregular. There have been no infections or distressing symptoms. The patient has felt reasonably comfortable while losing 30 pounds weight and corresponding strength. Recently she noticed slight edema of ankles and dyspnea on exertion. She applied for treatment merely on account of knowledge that her condition was serious, and not for any special urgent symptoms.

Physical Examination.—Height 157.5 cm. Medium development, rather marked emaciation. Skin dry. Cheeks flushed. Tongue red, teeth poorly kept, two carious. Examination by specialist showed nose and ears normal; no adenoids; tonsils slightly enlarged, showing a little thick yellow material on pressure. Very slight glandular enlargement. Reflexes normal. Moderate edema below knees. Examination otherwise negative. Wassermann negative.

Treatment.—On an observation diet of 75 gm. protein, 100 gm. carbohydrate, and 2000 calories, there was excretion of 145.5 to 131 gm. glucose and 5.3 to 4.5 gm. ammonia nitrogen with intense ferric chloride reaction. On Feb. 25 and 26

Weight and Nutrition.—Weight at admission 39.4 kg., at discharge 36 kg.; *i.e.*, a loss of 3.4 kg. The lowest weight was 34 kg. on Mar. 20, following the most extensive undernutrition. Some fluctuations in the weight curve were caused by slight edema. The diet prescribed at discharge represented nearly 1.4 gm. protein and 42 calories per kg., reduced by the weekly fast-days to 1.2 gm. protein and 36 calories average. Notwithstanding the loss of weight there had been improvement in strength and comfort, and the patient was now walking 3 miles daily and otherwise exercising without weariness.

Subsequent History.—On June 19, the plasma sugar was 0.161 per cent, CO₂ capacity 52 per cent. June 30, sugar 0.156 per cent in whole blood, 0.172 per cent in plasma, CO₂ capacity 63.6 per cent. The weight was still 36 kg. Strength had greatly increased, and the only complaint was of hunger. The urine had remained consistently normal. The diet was increased to 60 gm. protein and 1550 calories. Glycosuria remained absent until Nov., and the general condition was excellent. Readmission was necessary Dec. 8, 1916, because glycosuria was then persistent.

Second Admission.—Weight 37.2 kg., without perceptible edema. General condition good. Acidosis was shown only by the heavy ferric chloride reactions and the ammonia nitrogen of 1 gm. Instead of immediate fasting, Dr. Joslin's plan of a low fat-free diet was used. Thus, the diet on Dec. 9 consisted of lean meat and green vegetables, representing 40 gm. protein, 20 gm. carbohydrate, 10 gm. fat, and 336 calories. With gradual diminution of this diet to 20 gm. carbohydrate and 9 gm. protein on Dec. 16, the ferric chloride reaction became negative, the ammonia fell to 0.74 gm. N, and glycosuria diminished to traces. It is noteworthy also that the total nitrogen excretion at first was 13 gm. daily. This progressively diminished on the semifasting to the low figures of 4.71 gm. on Dec. 14, 4.76 gm. on Dec. 15, and 4.37 gm. on Dec. 16. A single fast-day on Dec. 17 cleared up the lingering traces of sugar. To protect body protein, 40 gm. protein daily were immediately given, without carbohydrate, and with fat so strictly limited that the total calories amounted to only 600. The patient was dismissed temporarily on this diet on Dec. 22, 1916, to be home for the Christmas holidays. Weight 34.4 kg.; strength and spirits good.

Third Admission.—Jan. 8, 1917. Patient returned according to arrangement, saying that she had enjoyed the holidays greatly. Weight 34.3 kg. Very slight edema of legs. The diet remained at 40 gm. protein and 600 calories.

On Jan. 11, sore throat was complained of, but temperature was normal. On Jan. 12, the temperature rose as high as 100.6°. On Jan. 13, it was not above 100°. On Jan. 14, the weight was 32.2 kg., and the temperature up to 103.4°. There were signs of typical pneumonia of right lower lobe; sputum showed Type IV pneumococcus; blood culture negative.

The conditions during this attack of typical lobar pneumonia in a severely diabetic patient are best shown in Table XVII. No alkali was employed.

Beginning Feb. 3, the protein was increased to 40 gm. daily. Thereafter the total calories were gradually increased to 900. Beginning Feb. 10, the protein

TABLE XVII.

Date.	Weight.	Temperature.	Diet.					Fluid intake.	Urine.				Blood plasma.	
			Protein.	Fat.	Carbo- hydrate.	Alcohol.	Total calories.		Volume.	Sugar.	FeCl ₃ reaction.	NH ₃ -N	Sugar.	CO ₂
	kg.	°F.	gm.	gm.	gm.	gm.	cc.	cc.				gm.	per cent	vol. per cent
1917 Jan. 13	32.6	94.4 100.0	4.3	—	10	—	61	2100	2547	0	0	0.80	—	—
" 14	32.2	102.0 103.4	8.6	0.9	20	—	125	3562	3017	+	0	0.57	—	—
" 15	32.3	104.2 103.5	18.3	10.9	8.2	—	209	3800	2265+	+	0	0.70	0.268	68
" 16	32.1	103.8 101.6	22.3	15.9	—	—	240	3025	3238	+	+	0.83	—	—
" 17	31.7	104.0 102.0	22.3	15.9	—	—	240	3700	2943	+	+	1.26	0.227	60
" 18	31.8	102.8 100.6	22.3	15.9	—	—	240	3900	2130	++	++	1.18	—	—
" 19	—	102.2 101.4	7.4	5.3	—	—	80	3100	3330	++	++	1.95	0.227	54
" 20	—	100.8 99.2	Fast-day.			—	—	3300	2420	+++	+++	2.02	0.256	—
" 21	—	100.8 99.2	"			—	—	3300	2225	++++	++++	2.16	—	—
" 22	—	99.4 99.0	"			—	—	3900	2780	+++	++	2.20	—	—
" 23	—	99.0 97.0	"			25	175	3525	3535	++	+	2.08	—	—
" 24	—	99.8 97.0	"			35	245	3900	3520	++	+	1.49	0.260	57
" 25	—	99.2 97.6	22.3	15.9	—	30	447	3200	2232	+	+	0.80	—	—

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			Protein.	Fat.	Carbo- hydrate.	Alcohol.	Total calories.		Volume.	Sugar.	FeCl ₃ reaction.	NH ₃ -N	Sugar.	CO ₂
1917	kg.	°F.	gm.	gm.	gm.	gm.	Total calories.	Fluid intake. cc.	Volume. cc.	Sugar.	FeCl ₃ reaction.	NH ₃ -N gm.	Sugar. per cent	CO ₂ vol. per cent
Jan. 13	32.6	94.4 100.0	4.3	—	10	—	61	2100	2547	0	0	0.80	—	—
" 14	32.2	102.0 103.4	8.6	0.9	20	—	125	3562	3017	+	0	0.57	—	—
" 15	32.3	104.2 103.5	18.3	10.9	8.2	—	209	3800	2265+	+	0	0.70	0.268	68
" 16	32.1	103.8 101.6	22.3	15.9	—	—	240	3025	3238	+	+	0.83	—	—
" 17	31.7	104.0 102.0	22.3	15.9	—	—	240	3700	2943	+	+	1.26	0.227	60
" 18	31.8	102.8 100.6	22.3	15.9	—	—	240	3900	2130	++	++	1.18	—	—
" 19	—	102.2 101.4	7.4	5.3	—	—	80	3100	3330	++	++	1.95	0.227	54
" 20	—	100.8 99.2	Fast-day.			—	—	3300	2420	+++	+++	2.02	0.256	—
" 21	—	100.8 99.2	"			—	—	3300	2225	++++	+++	2.16	—	—
" 22	—	99.4 99.0	"			—	—	3900	2780	+++	++	2.20	—	—
" 23	—	99.0 97.0	"			25	175	3525	3535	++	+	2.08	—	—
" 24	—	99.8 97.0	"			35	245	3900	3520	++	+	1.49	0.260	57
" 25	—	99.2 97.6	22.3	15.9	—	30	447	3200	2232	+	+	0.80	—	—

TABLE XVII—Continued.

Date.	Weight.	Temperature.	Diet.					Fluid intake.	Urine.				Blood plasma.	
			Protein.	Fat.	Carbo- hydrate.	Alcohol.	Total calories.		Volume.	Sugar.	FeCl ₃ reaction.	NH ₃ -N	Sugar.	CO ₂
	kg.	°F.	gm.	gm.	gm.	gm.		cc.	cc.			gm.	per cent	vol. per cent
1917 Jan. 26	—	98.6 97.8	30.0	40.5	—	10	569	3250	2526	+	0	0.88	—	—
“ 27	—	98.6 97.6	30.0	40.5	—	5	534	3550	3016	+	0	0.86	0.118	—
“ 28	—	98.4 97.4	30.0	40.2	—	20	637	3672	2913	+	0	0.72	—	—
“ 29	—	98.8 98.2	30.0	40.2	—	7	532	3405	2758	+	0	0.84	—	—
“ 30	—	98.6 97.0	30.0	40.6	—	10	605	3415	3278	0	0	0.68	—	—
“ 31	—	98.6 96.8	30.0	40.6	—	20	640	3470	3043	0	0	0.57	—	—

was raised to 50 gm., and Feb. 17 to 60 gm., and the total calories were gradually raised to 1300. Also 15 gm. carbohydrate daily were introduced with no glycosuria or ketonuria at any time. The ammonia nitrogen was 0.48 to 0.68 gm. The blood sugar was 0.12 per cent, the lowest yet attained in this patient. The plasma bicarbonate was 66 per cent. The patient was discharged on this diet Mar. 9, 1917, weighing 31 kg. The diet thus represented nearly 2 gm. protein and 42 calories per kg., diminished by weekly fast-days to an average of 1.7 gm. protein and 36 calories per kg. Absolutely, the diet was low. In view of the emaciation and the attendant lowered metabolism, it was relatively liberal.

Subsequent History.—The condition was excellent up to Apr. 11, then glycosuria began to recur and the patient lost control of it. She was readmitted May 23 on this account.

Fourth Admission.—Weight 32 kg. There was heavy glycosuria, with only faint traces of ferric chloride reaction. Blood sugar 0.326 per cent, CO₂ capacity 63.4 per cent. Fasting was begun immediately, with 300 cc. coffee, 300 cc. soup, and 3 gm. salt daily. The ferric chloride reaction immediately disappeared. Glycosuria fell to traces within 24 hours, and was negative in less than 48 hours. Nevertheless, fasting was continued until May 27, when a tolerance test with

green vegetables was begun, with 10 gm. carbohydrate and increasing 10 gm. daily, as usual. Glycosuria appeared only with 60 gm. carbohydrate, June 1 and 2. The tolerance of 50 gm. would thus indicate an increased assimilation to the extent of 20 gm. as compared with the earlier test in Mar., 1916. A mixed diet was then built up, until a trace of glycosuria appeared on June 7 with 60 gm. protein, 15 gm. carbohydrate, and 1300 calories. The ration was then fixed at 46 gm. protein, 10 gm. carbohydrate, and 1100 calories, and the patient discharged on this in good condition, June 15, 1917, weighing 31.1 kg. The diet thus represented almost 1.5 gm. protein and about 35 calories per kg., diminished by weekly fast-days to 1.3 gm. protein and 30 calories average. The CO₂ capacity of the plasma remained between 62.5 and 66.8 per cent throughout, the ammonia nitrogen between 0.37 and 0.77 gm. The blood sugar gave the only unfavorable indication, for with sugar-free urine it was found as high as 0.220 per cent and never below 0.166 per cent.

Subsequent History.—The patient has remained in good condition, free from symptoms.

Remarks.—The diabetes seemed to run a less rapid course in this patient than in most of her age, but without radical measures the end must have been fairly close when she was first received. The opportunity for restoring anything approximating normal condition was past, and the tolerance had been brought permanently and irretrievably low. The patient has been kept alive 1½ years since then, at a sacrifice of 8 kg. weight. It is to be emphasized that except for occasional periods of greatest rigor, she has been stronger and more comfortable and has actually looked better, according to her friends' judgment, than at the higher weight. She remains continually cheerful, fairly well satisfied, faithful to the diet, and strong enough for light labor and amusements, spending much of her time outdoors and evidently taking pleasure in life.

The usual recrudescence of diabetic symptoms with infection, and the smooth and uneventful recovery of a severely diabetic patient from typical lobar pneumonia on the undernutrition which was requisite to ward off acidosis, are also features of interest.

On the other hand, the gain of 20 gm. carbohydrate tolerance is too little return for the loss of 8 kg. weight. If by any means the weight could be built up by several kg., the tolerance would undoubtedly be less than at the first admission, and according to this standard there has been downward progress. Such progress is fully accounted for by the general policy of feeding too close to the limit of tolerance and thus keeping up slight overstrain of the assimilative function as shown by the persistent hyperglycemia. If in Apr. and May, 1916, the low blood sugar had been kept continuously normal, by fixing the body weight at 33 or 34 kg. and the diet at its present figure of about 1100 calories, with inclusion of a little carbohydrate, it is believed that the condition would today be more favorable as respects weight, strength, and laboratory findings. It is the old story of refraining from bringing the patient down to the necessary level of undernutrition for therapeutic benefit, and later being forced to accept a still lower

level of nutrition by reason of the downward progress resulting from the overstrain. The progress has been so slow even with the overstrain that it is hard to see how any "spontaneous" factor can be assumed. Notwithstanding the prolonged periods of comfortable existence and freedom from symptoms, it is probable that the slow aggravation will continue to ultimate death from coma or inanition unless the patient is radically taken in hand and undernourished far more rigorously than would have been necessary at the first admission. It is even doubtful if such an attempt can now atone for the lost opportunities of the past, or if the assimilative function may not have fallen too low to support life permanently at any feasible level of nutrition.

CASE NO. 63.

Male, age 13 yrs. Polish American; schoolboy. Admitted Feb. 22, 1916.

Family History.—Father and one brother are well. Mother dead, cause unknown. No diabetes or other heritable disease known in family.

Past History.—Measles, chicken-pox, scarlet fever. Otherwise healthy life. No sore throats or other minor infections. No abnormalities of diet. Never nervous or obese. Apparently a thoroughly healthy, active boy.

Present Illness.—Polydipsia and polyuria with loss of weight and strength began 1 year ago. He has spent most of the year in hospitals. On one occasion he had to be taken to a hospital because he "became sleepy" after eating a large quantity of cakes. About 6 weeks ago he was in an institution where he was given bread and other starches and made to take long walks "to build him up." He realized that the treatment was making him worse, and having heard of the Institute came here of his own accord on Feb. 21. The CO₂ capacity of the plasma was then 37.2 per cent, but dyspnea and other clinical symptoms were absent, so the patient was told to return in 3 days, when there would be room for him. On Feb. 21, he ate $\frac{1}{4}$ pound of pork, half a loaf of gluten bread, some fat, and some coffee and soup. That evening he is said to have appeared a little tired and cold. At 4 o'clock the next morning he woke up with extreme dyspnea. A physician pronounced him dying, and the father considered treatment scarcely worth attempting, and it was due to the patient's own request that he was brought to the hospital.

Physical Examination.—Height 142.4 cm. A well developed, moderately emaciated boy with intense air-hunger. Skin dry, cold, very white, and lips grayish-blue. He is nevertheless intelligent when roused. Tongue red, dry, brown-coated. Teeth and tonsils normal. No superficial glandular enlargement. Pulse rapid and thready. Abdomen much distended, but not rigid or tender. Knee jerks present but sluggish. Wassermann negative. Examination otherwise negative.

Treatment.—Death seemed imminent during the ambulance trip, and stimulants were used. On arrival at hospital the rectal temperature was too low to register on the ordinary clinical thermometer. Pulse 92; respiration 31, air-hunger type.

The CO₂ capacity of 12.3 per cent was the lowest witnessed in this series of cases. Sodium bicarbonate was immediately begun in 5 gm. doses by mouth, and hot water and soup were also given as freely as possible. The patient was surrounded with hot-water bottles, and rectal tube, turpentine stupes, and enemas were used to reduce meteorism. After 4 hours the rectal temperature was 94.2°, pulse 96, respiration 34. There was a gradual steady rise thereafter, until by 7 o'clock the next morning the temperature was 101°, the pulse 100, the respiration 44. Up to this time (12 hours) 45 gm. sodium bicarbonate and 4200 cc. fluids had been taken and 2180 cc. acid urine passed, with the usual intense ferric chloride reaction and 3.6 gm. ammonia nitrogen. By this time (Feb. 23) the CO₂ capacity of the plasma had risen to 26.8 per cent. Additional clinical details are shown in Table XVIII.

The parallel slowing of pulse and respiration with relief of acidosis is noteworthy; also the strikingly rapid loss of weight, notwithstanding fluid, salt, and alkali intake during the period of highest acidosis (Feb. 22 to 26).

On Mar. 2, when after 9 days of fasting the urine had been sugar-free for more than 24 hours, feeding was begun with 10 gm. carbohydrate in green vegetables. A trace of glycosuria immediately returned, but increased very little as the carbohydrate was raised to 35 gm. on Mar. 9. Meanwhile the ferric chloride reaction had become negative. After a fast-day on Mar. 11, another test showed a higher carbohydrate tolerance, glycosuria appearing only with 100 gm. carbohydrate on Mar. 23. After a fast-day on Mar. 26, mixed diet was begun, increasing up to 50 gm. protein, 15 gm. carbohydrate, and 1200 calories on Mar. 31 to Apr. 1, without glycosuria. Glycosuria appeared on the same caloric intake with 50 gm. protein and 20 to 30 gm. carbohydrate the following week. Also in the next week a diminution of protein to 40 gm. and carbohydrate to 5 gm., with increase of fat to make 1500 total calories, brought glycosuria on Apr. 15. In the following week with the same protein, without carbohydrate, glycosuria was absent with 1200 calories, but appeared when the fat was increased to make 1400 calories; it then continued with diminution to 1200 calories. As usual with the effects of fat, the hyperglycemia and glycosuria were stubborn, not ceasing with the fast-day on Apr. 23, a trace of glycosuria recurring on Apr. 24, and the sugar being still 0.232 per cent in whole blood and 0.250 per cent in plasma on Apr. 27. Nevertheless, the condition was conquered by restriction of fat. With the same 40 gm. protein, Apr. 27 to May 4, glycosuria remained absent with caloric intake up to 1000. An increase of protein to 60 gm. and of calories to 1200 brought a trace of glycosuria on May 6. By this time the general condition was good and considerable exercise was being taken. Perhaps on this account the diet of 40 gm. protein and 1200 calories, which caused glycosuria up to May 21, was subsequently tolerated; and in June the increase to 50 gm. and 1300 calories and finally (June 29 to 30) to 70 gm. protein and 1500 calories brought no glycosuria. In July the protein was diminished to 52 gm. and the calories to 1200, in order to permit the introduction of carbohydrate. This proved successful, so that by Aug., 30 gm. carbohydrate were tolerated with this diet. The course in hos-

TABLE XVIII.

Date.	Wghtl. kg.	Temperature. °F.	Pulse.	Respiration.	Diet.							Urine.					Blood plasma.	
					Sodium chloride. gm.	Sodium bicarbonate. gm.	Protein. gm.	Fat. gm.	Carbo- hydrate. gm.	Calories. cc.	Total fluids. cc.	Volume. cc.	Sugar. gm.	Total nitrogen. gm.	D:N ratio.	NH ₃ -N gm.	FeCl ₃ reac- tion.	Sugar. per cent
1916 Feb. 22	—	94.2 94.2	92 96	31 34	10 45	Fast-day with 450 cc. coffee, 600 cc. soup.				4200	2180	22.89	4.70	4.87	3.6	+++	0.345	12.3
" 23	27.8	101.1 99.4	100 80	44 18	50 10	500 cc. coffee, 600 cc. soup.			6750	6530	40.95	13.80	2.98	2.84	+++	0.400	26.8	
" 24	26.0	99.4 100.6	72 58	20 18	30 10	500 cc. coffee, 750 cc. soup.			5850	4915	24.08	9.10	2.65	2.21	+++	0.322	—	
" 25	25.4	98.4 100.2	50 60	16 20	30 10	500 cc. coffee, 750 cc. soup.			5870	4760	20.94	9.60	2.18	2.39	+++	0.294	—	
" 26	25.0	98.2 99.4	60 43	22 16	20 10	500 cc. coffee, 750 cc. soup.			3650	3115	12.15	7.70	1.58	2.09	+++	0.270	59.1	
" 27	25.2	98.6 99.8	74 44	18 18	15 10	500 cc. coffee, 750 cc. soup.			2600	2930	12.31	9.20	1.34	2.43	+++	—	—	
" 28	25.4	97.3 99.2	40 66	16 18	— 10	500 cc. coffee, 750 cc. soup.			3400	3670	5.87	8.10	0.72	2.48	+++	0.263	—	
" 29	25.2	97.3 98.6	42 50	16 20	10 —	500 cc. coffee, 750 cc. soup.			5600	3335	+			—	+++	—	—	

Mar. 1	25.2	97.1 98.8	42 48	16 20	10	—	500 cc. coffee, soup.	750 cc.	4150	4225	0	1.98	+++	0.244	—
"	25.0	97.3 98.0	58 44	18 16	10	—	3.9	0.4	61	3550	2410	+	+	—	—
"	25.6	97.4 96.4	64 42	18 16	10	—	8.6	1.1	127	2900	1635	+	+	0.256	—
"	26.6	97.9 97.0	88 42	16 24	10	—	8.6	1.1	127	4650	2565	+	0	—	—
"	28.0	97.8 98.0	48 44	16 20	10	—	10.0	1.0	152	3500	1790	+	+	—	—
"	30.0	97.4 98.4	86 44	20 20	10	—	10.0	1.0	152	3400	2330	+	0	0.232	—
"	31.4	98.4 97.2	100 48	18 16	10	—	10.0	1.0	152	2850	2790	+	0	—	—
"	31.8	98.3 97.0	48 52	16 20	10	—	11.5	1.3	182	3350	2965	+	0	0.278	—
"	31.8	97.0 97.6	78 52	17 20	10	—	13.0	1.4	209	3700	3755	+	0	—	—
"	31.6	97.8 97.4	76 42	20 16	10	—	3.3	0.4	52	1900	2820	+	0	0.263	—
"	30.4	98.0 97.0	42 44	18 16	10	—	Fast-day.			2200	1855	0	0	—	—

pital was uneventful, except that dental examination revealed three carious teeth, which were removed without ill effects. The patient was discharged Aug. 3.

Acidosis.—The acutely threatening condition at admission was described above. This patient was apparently the nearest to death of any of those who recovered in this series. Also there appeared to be a real acute need for alkali, and in this instance sodium bicarbonate seemed to be life-saving. It seems improbable that simple fasting and fluid would have proved sufficient to combat such an acute deficiency of alkali and high acid production. Thereafter the plasma bicarbonate ran a fully normal course without the aid of alkali, the ferric chloride reaction rapidly diminished with fasting and became negative after Mar. 6, probably more by reason of the continuous undernutrition than the small quantities of carbohydrate then given. It reappeared, as may be so often observed, on subsequent occasions about the same time with traces of glycosuria, even though the quantities of sugar lost were trivial and there were no significant differences in diet as compared with other times when the reaction was negative. The only evidence of continued acidosis was the ammonia nitrogen of 0.85 gm. on July 1, but with the aid of 20 to 30 gm. carbohydrate this had fallen to a normal level by the end of July.

Blood Sugar.—With blood sugars of 0.35 and 0.4 per cent at admission, it is conceivable that carbohydrate feeding would have been injurious from this standpoint, and possibly would have increased the acidosis by aggravating the diabetic condition. There was a fairly prompt fall in the blood sugar. The well marked rise, Mar. 2 to 10, indicated the genuine intolerance for even the small quantities of carbohydrate then allowed. The rapid change for the better with continued undernutrition was shown by the rapid fall to 0.123 per cent in whole blood and 0.141 per cent in plasma on Mar. 15. Notwithstanding the increased carbohydrate intake, the sugar on the morning of Mar. 21 was only 0.151 per cent in blood and plasma. On the morning of Mar. 29, it had reached the nearly normal level of 0.104 per cent in whole blood and 0.123 per cent in plasma. Instead of maintaining this advantage, with the added benefits of mixed diet, the fat intake was increased unduly, with the consequence of many traces of glycosuria and continuous hyperglycemia. With the improvement in tolerance the curve tended slightly downward, to 0.145 per cent in whole blood and 0.159 per cent in plasma on July 15. Then the simple increase of carbohydrate without change in total calories brought a further elevation to 0.179 per cent in whole blood and 0.182 per cent in plasma on July 29. As samples were taken before breakfast and hyperglycemia was presumably greater during digestion, it is evident that the renal threshold was high.

Weight and Nutrition.—Weight at entrance 27.8 kg., at discharge 25.4 kg.; *i.e.*, a loss of 2.4 kg. The strength rapidly returned, especially with the aid of exercise, and except for thinness and a persistent pallor (the latter perhaps natural) the boy appeared and acted normal. The diet prescribed at discharge was 52 gm. protein, 25 gm. carbohydrate, and 1200 calories, representing approxi-

mately 2 gm. protein and 48 calories per kg., reduced by weekly fast-days to 1.7 gm. protein and 41 calories per kg. The diet was absolutely low in view of the age and subnormal weight. The objection to it is that it was in excess of the assimilative power as demonstrated by the blood sugar.

Subsequent History.—The patient began school in Sept., and was able to do everything like other boys. He prepared, weighed, and cooked his own diet, and remained free from glycosuria. On Sept. 11, sugar in blood and plasma was 0.278 per cent (after 2 meals), CO₂ capacity 55.8 per cent; weight 27.4 kg. He had to be readmitted Nov. 20, 1916, because of difficulty with glycosuria, which began on catching cold and then became unmanageable.

Second Admission.—Weight 26 kg. Slight glycosuria, negative ferric chloride reaction. Patient still strong and comfortable, and normal to physical examination. Because of the stubbornness of the slight traces of glycosuria, a 4 day fast was imposed, reducing the weight to 24.2 kg. A diet of 30 gm. protein and 320 calories then brought back traces of glycosuria. The ferric chloride reaction remained negative; and the ammonia nitrogen, which was 1.2 gm. the first day, diminished to 0.5 gm. On Nov. 24 to 25, a diet of 30 gm. protein and 320 calories brought back traces of glycosuria, requiring a single fast-day on Nov. 26. This glycosuria was evidently due to the suddenness of beginning diet; therefore on Nov. 27, 7 gm. protein and 80 calories were permitted, with an increase of about the same quantity daily, until a trace of glycosuria reappeared with 45 gm. protein and 480 calories on Dec. 2. Dec. 4 to 16, a diet of 40 gm. protein and 600 calories caused almost daily traces of glycosuria, notwithstanding the usual weekly fast-days. These ceased on the simple withdrawal of 100 calories of fat beginning Dec. 18, protein continuing at 40 gm. Thereafter it became possible to increase the calories first to 600 and then to 700. Also, beginning Jan. 1, 2.5 gm. carbohydrate were introduced, and increased to 10 gm. by Jan. 4. The only evidence of acidosis was found in the ammonia nitrogen of 0.97 to 0.48 gm. This seemed to be perceptibly diminished by the carbohydrate, for after its introduction the range was 0.58 to 0.29 gm. The patient was dismissed on Jan. 10, weighing 25.2 kg., still in good condition although not so strong as before. The diet mentioned represented nearly 1.6 gm. protein and 28 calories per kg., diminished by weekly fast-days to 1.4 gm. protein and 24 calories average. This period of 2 months in hospital therefore represented extreme undernutrition, the aim being only to protect body nitrogen with as high a protein intake as permitted by the limit of tolerance. It is unfortunate that nitrogen balances were not carried out. During fasting, Nov. 21 to 23, the daily urinary nitrogen was 5.24, 4.74, and 4.41 gm. No analyses were made of the 450 cc. soup taken daily. Numerous analyses at other times indicate that the possible nitrogen content of this quantity might range from 0.6 to over 2.0 gm. Later, 4 widely separated days during the period of 40 gm. protein intake showed figures in close agreement, between 6.74 gm. and 7.48 gm. urinary nitrogen. With allowance for the above mentioned nitrogen taken in soup, this probably indicated nitrogenous equilibrium.

The body nitrogen was seemingly spared effectively, but no material was provided for growth. Also body fat must have been sacrificed continuously, and the relatively small loss of weight must have been due in part to water retention masking the actual loss of substance. The boy was discharged only temporarily on account of homesickness, and was instructed to report in 2 weeks.

Third Admission.—Nothing further was heard from the patient until he was readmitted in incipient coma on Feb. 12. It might seem that diabetic coma is not strictly a single or uniform condition, for at his first admission this boy showed chiefly dyspnea and extremely low blood alkalinity, with intelligence apparently as clear as the state of collapse permitted. This time the same boy, with CO₂ capacity of 26 per cent, showed moderate dyspnea and disproportionate stupor. The treatment this time was conducted without alkali. Owing to other work the laboratory study for this period is incomplete. No blood examinations were made, except the one at admission which showed CO₂ capacity 26 per cent and sugar 0.425 per cent. The case shows how treatment can be conducted essentially on the basis of clinical symptoms and qualitative reactions. The available data are shown in Table XIX.

The diet was built up in Mar. to 35 gm. protein and 600 calories, which caused occasional traces of glycosuria. Toward the close of Mar. this diet was tolerated, and was later increased to 45 gm. protein and 850 calories. The attempt to introduce 10 gm. carbohydrate in Apr. caused only temporary glycosuria, but was given up after Apr. 28 in order to increase protein to 55 gm. The patient was discharged May 5, 1917. Height 142.4 cm. Weight 25.9 kg. Diet 55 gm. protein and 750 calories (2.1 gm. protein and 29 calories per kg., diminished by the weekly fast-days to 1.8 gm. protein and 25 calories per kg.). He was definitely weaker and worse off than before, but even on this low diet was able to be about and was cheerful and courageous.

Subsequent History.—The patient was seen on June 8, weighing 24.8 kg., and feeling brighter and stronger than on leaving hospital. He had shown slight glycosuria in the first week at home, but thereafter had been sugar-free. He spent his time about the house and garden, raising vegetables and chickens, weighing and cooking his own diet, and keeping a complete record of diet and urine tests. The ferric chloride reaction was negative. Plasma sugar (during digestion) 0.264 per cent, CO₂ capacity 49.1 per cent.

Fourth Admission.—July 20, a telephone message was received from one of the family that the boy had broken diet by eating bread and fruit, that he had heavy glycosuria and seemed sleepy. Upon bringing him to the hospital, heavy sugar and ferric chloride reactions were found in the urine, but there were no clinical symptoms of acidosis. Weight 23.6 kg. The urinary conditions cleared up very easily and the boy was discharged Aug. 10, 1917, on the same diet as before. Hyperglycemia was persistent as before.

Subsequent History.—Another relapse occurred and the boy was taken to a public hospital, where he died Oct. 11, 1917.

TABLE XIX.

Date.	Weight.	Temperature.		Pulse.	Respiration.	Diet.					Urine.			
		kg.	°F.			Sodium chloride.	Protein.	Fat.	Carbo- hydrate.	Calories.	Total fluids.	Volume.	Sugar.	FeCl ₃ reaction.
1917	kg.	°F.				gm.	gm.	gm.	gm.	cc.	cc.			
Feb. 12	24.8	97.2 97.6	76 84	20 20	0	Fasting; 200 cc. soup.					1502	806	++++	++++
" 13	23.8	98.2 99.6	86 68	20 24	0	"	400	"	coffee.	5000	5090	++++	+++	
							600	"	soup.					
" 14	22.6	99.6 97.2	76 70	24 20	3	"	400	"	coffee.	5000	3611	+++	+	
							600	"	soup.					
" 15	23.1	95.6 97.6	46 70	60 16	3	"	400	"	coffee.	2500	2388	++	+	
							600	"	soup.					
" 16	23.0	96.4 98.2	60 40	16 16	3	"	400	"	coffee.	2500	1918	++	+	
							600	"	soup.					
" 17	22.8	97.4 98.1	80 50	16 22	3	22.3	15.9	—	240	2500	2366	+++	0	
" 18	23.0	97.4 99.4	48 76	17 20	3	22.3	15.9	—	240	2500	2126	++	0	
" 19	23.4	96.2 98.0	50 98	18 18	3	22.3	15.9	—	240	2500	2531	++	0	
" 20	23.7	96.4 97.6	68 52	18 16	3	22.3	15.9	—	240	2500	2346	++	0	
" 21	23.8	96.4 97.6	54 70	18 20	3	22.3	15.9	—	240	2500	2397	+	0	
" 22	24.0	96.4 96.0	44 60	16 18	3	22.3	15.9	—	240	2500	2468	+	0	
" 23	24.0	96.4 98.0	76 50	16 18	3	22.3	15.9	—	240	2500	2643	+	0	
" 24	24.0	96.0 98.0	68 50	20 15	3	22.3	15.9	—	240	2500	3413	0	0	
" 25	24.0	95.8 97.8	64 40	16 16	3	7.4	5.3	—	80	2500	2488	0	0	

Remarks.—The case is characterized by continuous downward progress, for which two causes are known. One is extreme youth. Though the boy did not gain in weight, nor to any significant extent in height, yet the growth impulse or general metabolic strain of youth may be held responsible for the unfortunate prognosis for diabetes of this grade of severity at this age. Nevertheless, it must be recognized that a definite improvement in the power of assimilating food is demonstrated by the record of the first period in hospital, so that the power to recuperate was not wholly lacking, even in this child. The second known factor is the excessive diet, which brought back hyperglycemia after the blood sugar had fallen to normal, and would have been responsible for downward progress even in an adult under the same conditions. The low diet was not used at first by choice, and therefore had to be used later by compulsion, after the real opportunity had been lost. Irrespective of the ultimate prognosis in such a case, the duration of life and comfort may vary as much as several years, according to the efficiency of treatment and the earliness with which it is begun. In this instance the boy was ready to die after 1 year of indifferent treatment, which had brought the tolerance almost to zero, and was thereafter kept alive a year and a half, most of the time in greater strength and comfort than during the earlier period under other treatment.

CASE NO. 64.

Male, age 12 yrs. American Jew; schoolboy. Admitted Feb. 24, 1916.

Family History.—Father, mother, and one sister are well. No diabetes or other heritable disease known in family.

Past History.—Fully healthy life except for measles and mumps. No sore throats, toothaches, or minor infections known. Appetite, digestion, bowels normal. Never nervous or under strain; always ranking well in school, and proficient in outdoor sports.

On Dec. 1, 1915, he fell down a flight of 10 stairs, landing on the front of his head. There was no cut in the skin, no unconsciousness, no bleeding from ear or nose, no paralysis or any perceptible symptoms beyond the slight bruise. The patient did not associate the accident at all with his present illness.

Present Illness.—About 3 weeks before admission there was acute onset of polydipsia and polyuria, but not polyphagia. There has since been very rapid loss of weight. Patient nevertheless continued at school until 1 week before admission. He then saw a physician, who diagnosed diabetes and prescribed only a moderate reduction of carbohydrate. During the present week the boy became increasingly sleepy, and has spent almost his entire time for several days past sleeping on a couch.

Physical Examination.—Height 142.5 cm. Normal development, moderate emaciation. Patient sleepy but easily roused. Moderate dyspnea of air-hunger type. Face is that of a mouth breather and suggests adenoids. Cheeks flushed. Skin dry and cracked. Mouth and lips dry; teeth poorly kept, several carious; some pyorrhea. Tongue and pharynx red and dry; tonsils do not protrude, but

show pus on pressure. Few small palpable lymph nodes in neck, axillæ, and groins. Knee jerks obtainable by reinforcement. Examination otherwise negative. Later examination by a rhinologist showed nose and ears normal, no adenoids, tonsils moderate in size, yielding considerable creamy pus on pressure.

Treatment.—On the day of admission the bowels were moved with calomel and magnesium sulfate. Fasting was begun immediately because of the imminent coma, 300 cc. clear soup and 3 to 5 liters total fluid being given daily. Within 24 hours, the CO₂ capacity of the plasma rose from 16.6 to 27.7 per cent. The D:N ratio had apparently been high, for on the first fast-day it was 2.65:1, and on the second day 1.43:1. On the second fast-day (Feb. 25) 25 gm. sodium bicarbonate were given. It was unnecessary, since the progress was favorable without it, but seemed to produce an effect quickly in making the patient brighter and less drowsy. Thereafter no alkali was given. Both glycosuria and acidosis rapidly diminished, and on Feb. 29, after more than 24 hours of sugar-freedom, 2.4 gm. carbohydrate were given. Green vegetables were increased progressively and it became necessary to add potatoes, green peas, and lima beans before the limit of tolerance was reached with 330 gm. carbohydrate on April 2 to 3. Mixed diet was then begun without difficulty, and the patient was soon taking 2 or 3 mile walks and other exercise daily. Four decayed teeth were extracted uneventfully and the mouth brought into good condition. The tonsils were not removed. The patient was discharged May 5, 1916, feeling and appearing perfectly well and strong.

Acidosis.—Even with the low CO₂ capacity of 16.6 per cent, it was evident that treatment could have been easily and safely conducted without alkali. The use of sodium bicarbonate on 1 day, however, seemed to hasten results. The ammonia nitrogen of 1.88 gm. on the day of admission covered 18½ hours. The ammonia on Feb. 25 (2.36 gm. N) showed little perceptible effect from the bicarbonate. On Feb. 26, it was 2.42 gm., on Feb. 27, 2.34 gm.; and only then, with the CO₂ capacity almost normal and the ferric chloride reaction down to traces, did the ammonia show a real fall. Seemingly it was the active neutralizing agent which permitted the spontaneous rise in blood alkalinity. Subsequently acidosis was entirely absent by all tests.

Blood Sugar.—The hyperglycemia of 0.25 per cent showed a prompt fall to normal, characteristic of an early case even though severe in symptoms. The thoroughly normal course of the blood sugar as estimated mornings before breakfast is one of the striking features of this case.

Weight and Nutrition.—The weight at admission was 25.2 kg., at discharge 25.6 kg.; *i.e.*, a gain of 0.4 kg. There was visible edema only with the sharp rise of weight up to Mar. 5, as so often happens on vegetable diet after fasting. It is to be supposed that there was loss of body substance during treatment, with retention of water due especially to the carbohydrate supply; in contrast to the dried tissues at admission. The evidence lies in the fact that on Apr. 3 the weight was 1.8 kg. more than at admission, though the fasting and vegetable period for 5 weeks had represented prolonged undernutrition, especially in pro-

tein. After Apr. 3 there was presumably some rebuilding of tissue, but the weight diminished by 1.4 kg. The diet at discharge was 65 gm. protein, 50 gm. carbohydrate, and 1750 calories. It thus represented about 2.5 gm. protein and 64 calories per kg., reduced by weekly fast-days to 2.25 gm. protein and 55 calories average. The diet was thus abundant for growth. Such a caloric burden would produce downward progress in almost any adult diabetic.

Subsequent History.—Progress seemed favorable until on Mar. 20, 1917, the boy had to be readmitted because of the development of persistent glycosuria.

Second Admission.—Height 142.4 cm. Weight 28 kg. Appearance like that of a normal boy. The very slight ferric chloride reactions were deceptive, for the true grade of the acidosis was shown by the high ammonia and low CO₂. The data for the early stage of treatment are shown in Table XX.

TABLE XX.

Date.	Diet.				Sodium bicarbonate.	Weight.	Urine.					Plasma.
	Protein.	Fat.	Carbo- hydrate.	Calories.			Volume.	Sugar.	FeCl ₃ reaction.	Total nitrogen.	NH ₃ -N	
1917	gm.	gm.	gm.		gm.	kg.	cc.			gm.	gm.	vol. per cent
Mar. 21	65.0	137.6	50	1750	—	28.0	1460	++++	++	10.16	2.13	38
" 22	65.0	137.6	50	1750	30	27.4	1530	++++	++	10.70	1.88	41
" 23	65.0	138.3	50	1757	30	28.4	1980	++++	+	11.25	1.23	60
" 24	65.0	47.3	50	910	30	28.7	1410	+++	+	6.56	0.94	56
" 25	65.0	39.1	50	834	—	28.5	1828	+++	+	8.56	1.33	50
" 26	65.0	31.7	50	766	30	28.5	1270	+++	+	7.70	0.73	—
" 27	65.0	31.7	50	766	24	28.8	2032	+++	+	8.84	0.67	70
" 28	31.4	13.9	50	462	—	29.0	2094	+++	+	6.01	0.34	67
" 29	18.5	2.9	50	307	—	29.0	1885	+++	+	4.82	0.38	—
" 30	18.5	2.9	50	307	—	28.8	1976	++	+	5.62	0.38	—
" 31	18.5	2.9	50	307	—	28.7	1855	++	+	4.49	0.28	—
Apr. 1		Fast-day.			—	28.6	840	0	+	3.13	0.26	

In this case it is seen that diminution first of fat and then of protein, without changing carbohydrate, reduced glycosuria so that it was abolished by a single fast-day instead of several. On the other hand the high ammonia, notwithstanding the large alkali dosage, indicates persistence of acidosis. There was no such rapid clearing of acidosis as is usually seen with fasting.

Apr. 2, a test with green vegetables was begun, with daily addition of 10 gm. carbohydrate in the usual manner. Faint glycosuria occurred with 100 gm. carbohydrate on Apr. 11. The test was not carried further to learn whether this was the true limit, but it seems strongly probable that a marked fall in tolerance had occurred since the previous admission. A mixed diet was then begun, of

60 gm. protein, 30 gm. carbohydrate, and 1000 calories, including 200 cc. milk. The blood sugar before breakfast on Apr. 13 was 0.110 per cent. Carbohydrate was gradually increased up to 55 gm. on Apr. 27, with no glycosuria. The patient was discharged again in apparently excellent health on May 2, 1917. The prescribed diet was 60 gm. protein, 50 gm. carbohydrate, and 1250 calories, representing, for the body weight of 26 kg., 2.3 gm. protein and 48 calories per kg., reduced by weekly fast-days to 2 gm. protein and 41 calories per kg.

Subsequent History.—The patient spent his time reading and playing at home. On June 2, 1917, he weighed 26.2 kg., but a trace of glycosuria was found. The diet was diminished to 45 gm. protein, 25 gm. carbohydrate, and 1000 calories. There was a suspicion that the trouble had been due to overstepping diet. On June 27, he reported again, weighing 25.8 kg., with normal urine, blood sugar 0.138 per cent, CO₂ capacity 55.2 per cent. The same condition has continued since. The patient is contented on his diet, attends school regularly, and expects to graduate from grammar school this year. He behaves and appears like a normal boy, except for being noticeably thin.

Remarks.—This was one of the most rapidly progressive cases of juvenile diabetes, coma being imminent within 3 weeks of the first known symptoms. In one respect such symptoms are advantageous, in that they call prompt attention to the condition and afford the opportunity for early treatment. As usual, a high carbohydrate tolerance was quickly recovered in this case. The blood sugar also became normal as tested mornings before breakfast, though the existence of abnormal digestive hyperglycemia must be assumed. As usual, a luxur diet resulted in downward progress. It then became necessary, as usual, to reduce the diet even lower than would have been required for proper treatment in the first place.

Measures may soon be taken to reduce the persisting hyperglycemia. Owing to the mistreatment during the most hopeful stage, the patient can never appear like a normal boy again, but with suitable care it may be possible to preserve the present condition of fair strength and comfort for a long, perhaps indefinite time.

CASE NO. 65.

Male, married, age 53 yrs. American; business man. Admitted Mar. 6, 1916.

Family History.—Father died in old age, with diabetes for some years previously, though it was not the direct cause of death. A brother died of Hodgkin's disease. History otherwise negative.

Past History.—Measles in childhood. Diphtheria at 14. Two attacks of "gravel" 14 and 16 years ago; no trouble since. 6 or 7 years ago began to notice cramp-like pains in calves of legs after long walking. On the whole, he has been a healthy, hard working, prosperous man of rather large business affairs, but without special strain. Appetite good, but not excessive. Acid stomach complained of for past 5 or 6 years. Slight constipation; little exercise. No special

indulgence in alcohol, tea, or coffee, but the smoking of 8 or 10 strong cigars daily is a fixed habit. Sleep normal. No nervousness.

Present Illness.—Onset not known. In 1914, life insurance was obtained, without abnormal urinary findings. Patient has continued to feel well and work efficiently. No polyphagia, polydipsia, or polyuria. Eyesight may have failed to undue extent. Occasional headaches. Persistent cough for 3 months before admission. No hemoptysis, fever, chills, or sweats. The one symptom noted has been gradual loss of about 15 pounds weight. On this account he consulted a physician, who found blood pressure 170–150, a trace of albuminuria, and 3 per cent glycosuria. The patient was badly frightened at the word diabetes. His physician slightly restricted starches and referred him to the Institute.

Physical Examination.—A well developed, well nourished man, slightly over weight. Râles without consolidation, especially in lower lobe, left lung. Blood pressure 160 systolic, 80 diastolic. Examination otherwise negative.

Treatment.—With only a trace of glycosuria, there was nevertheless hyperglycemia (fasting) of 0.212 per cent in whole blood and 0.244 per cent in plasma. Acidosis was absent by all signs. Glycosuria ceased quickly on a diet of 100 gm. protein, 50 to 75 gm. carbohydrate, and 1800 calories. A green vegetable period was begun with 25 gm. carbohydrate on Mar. 12 and 50 gm. on March 13. Glycosuria appeared only with 220 gm. carbohydrate on March 28 to 29. The patient was placed upon a diet of 90 gm. protein, 75 gm. carbohydrate, and 2200 calories, on which he was discharged Apr. 6. The weight had been reduced by 1 kg. The blood sugar had been brought to normal by the undernutrition of the carbohydrate period (Mar. 25) and had subsequently risen, especially on mixed diet, to 0.147 per cent in whole blood and 0.131 per cent in plasma. In view of the age and the mildness of the case, the hyperglycemia could be trusted to take care of itself if the patient followed diet and reduced his weight as instructed.

Remarks.—The question is often asked whether fasting is necessary for patients who readily become sugar-free without it and whose diabetes is mild. The general principle is undernutrition. This patient had no fast-days. A carbohydrate period is an agreeable means of undernutrition, and is furthermore useful as affording a standard of tolerance for comparison with some later time. By June the patient's weight was down to 59 kg., and by Aug. to 58 kg. He now estimates his diet instead of weighing it. There has been no return of symptoms. It is probably more important for such a patient to weigh himself than his food.

CASE NO. 66.

Female, age 15 yrs. American; schoolgirl. Admitted Mar. 6, 1916.

Family History.—Healthy, except that a paternal grandfather had diabetes at time of death.

Past History.—Adenoids and tonsils removed in infancy. No illnesses, except measles 4 years ago. Life and habits normal. Not neurotic. No excessive appetite or indulgence in sweets. Menstruation began at 12 years, was regular and normal up to Dec., 1915, when it stopped.

Present Illness.—5 months ago (Oct., 1915) patient had an attack of urticaria from unknown cause. She was instructed to drink much water, and when unusual thirst began thereafter she supposed it to be due to the habit of drinking. 1 month before admission she was seen by a physician, who did not examine the urine and pronounced her in good health. On account of the continuance of excessive thirst she was taken to another physician 1 week ago, who made the diagnosis from the urine.

Physical Examination.—Height 158.1 cm. A well developed and normally nourished girl with healthy color and no visible abnormality. Blood pressure 90 systolic, 60 diastolic. Examination normal throughout.

Treatment.—The patient had been on practically unrestricted diet except for abstinence from sugar. With the heavy glycosuria there was a trace of ferric chloride reaction. Instead of the usual fasting, limitation of the diet, especially in fat, was employed. On Mar. 7 the diet contained 51 gm. protein, 45 gm. carbohydrate, and only 17 gm. fat. Carbohydrate was then diminished while the calories were kept at approximately 800. Mar. 14 and 15 were almost fast-days, the latter being a green day with only 10 gm. carbohydrate. Glycosuria and ketonuria being absent, the usual test with green vegetables was instituted. Traces of glycosuria appeared on Mar. 22 to 23 with 80 gm. carbohydrate, but did not indicate the true limit of tolerance, which was only reached with 140 gm. carbohydrate on Mar. 29 to 30. Mixed diet was then begun, and allowances of 70 to 90 gm. protein, 25 to 65 gm. carbohydrate, and 1750 to 2200 calories were tolerated. Instead of fast-days, the patient took each week a day of six eggs, 450 cc. soup, and 60 gm. bran. Anemia was found to be present, with hemoglobin 75 per cent, and no cell changes to characterize the condition. Examination by rhinologist showed ears and nose normal, but cheesy deposits in crypts of the tonsillar remnants. The anemia was treated with fresh air, exercise, and iron. The only special event while in hospital was an attack of supposed appendicitis at the end of May. Without any other symptoms, a trace of glycosuria appeared on May 29 on a diet within the demonstrated former tolerance. It cleared up spontaneously, but on May 31 the patient woke up with abdominal pain and nausea without vomiting. There was some rigidity, slight tenderness, polymorphonuclear leukocytosis, and temperature of 99.8° and 100.8°. From the double standpoint of appendicitis and diabetes very little food was given from May 31 to June 2. With rest in bed the abdominal symptoms quickly subsided, and beginning June 3 the diet was cautiously built up to the former level. The patient was discharged June 29, feeling and appearing entirely well and exercising freely though not strenuously.

Acidosis.—Owing to the mixed diet, acidosis was absent at admission, aside from the trace of ferric chloride reaction. The CO₂ capacity was normal, and the ammonia nitrogen only 0.52 gm. Although, as stated, the diet on Mar. 7 was as nearly fat-free as convenient, the simple limitation of carbohydrate was followed by a moderate ferric chloride reaction, a rise of ammonia to 0.89 gm. N, and a fall in CO₂ capacity from 56 to 48 per cent. On Mar. 8, with a diet of 59

gm. protein, 69 gm. carbohydrate, and 36 gm. fat, the ammonia rose to 1.6 gm. N, and the CO₂ fell to 44 per cent. Carbohydrate was then diminished almost to zero, keeping protein the same, while fat was gradually increased to 53 gm. On this arrangement the ferric chloride reaction became negative, the ammonia fell to 0.85 gm. N, and the CO₂ capacity rose to normal without the use of alkali. The explanation of this effect of diminished carbohydrate and increased fat lies in the undernutrition, which amounted to a partial fast. Also the relief of the overtaxed metabolism, by stopping glycosuria, tends to stop acidosis, even though accomplished by diminishing carbohydrate. It must be added that this last sentence does not contradict the first in this paragraph. The tendency to acidosis accompanying diabetes can for some time be overcome by sufficient carbohydrate in the diet.

With the abdominal attack on June 2, a trace of ferric chloride reaction appeared. This and the slight irregularities in the CO₂ curve may have been due entirely to greatly reduced diet.

Blood Sugar.—The high percentage of 0.61 per cent in whole blood and 0.735 per cent in plasma at admission were merely the accompaniments of an acute case on carbohydrate-rich diet. With the simple restriction of diet stated, there was an abrupt fall within 24 hours to 0.277 per cent in whole blood and 0.294 per cent in plasma. Thereafter, with a more gradual decline, a fully normal value was reached on Mar. 16. Subsequently the fasting blood sugar was always found normal.

Weight and Nutrition.—Weight at admission 50 kg., at discharge 45 kg. The diet at discharge was 80 gm. protein, 40 gm. carbohydrate, and 1900 calories and included milk and a little bread. Three eggs were allowed on weekly fast-days. The diet thus represented about 1.8 gm. protein and 42 calories per kg., diminished by the partial fast-days to 1.6 gm. protein and 36 calories average. With the moderate exercise prescribed, this may be considered a fairly low diet for a girl of 15, though not so low as advisable under the circumstances.

Subsequent History.—The patient was next seen on Nov. 8 and reports of normal urine confirmed. The blood sugar was 0.110 per cent; total acetone in the blood less than 10 mg. per 100 cc. 2 kg. weight had been gained. The appearance was that of perfect health.

Second Admission.—Dec. 6 to 10 the patient was in the hospital solely for observation. The fasting blood sugar on 3 days was 0.13 per cent. Otherwise everything was normal, except for persistence of slight anemia. The diet was reduced to 1500 calories, with 80 gm. protein and 45 gm. carbohydrate.

Third Admission.—Apr. 4, 1917. The patient suddenly developed heavy glycosuria and was immediately brought to the hospital. On the regular prescribed diet the glycosuria immediately disappeared, and had apparently been due to error in diet. The weight was 50 kg., the fasting blood sugar 0.10 per cent. After 4 days of observation on this diet a test with green vegetables was begun, and only a trace of glycosuria appeared with 145 gm. carbohydrate on Apr. 18. The test was not continued to learn whether this was the actual limit of tol-

erance. It was demonstrated that the tolerance was at least as high as 1 year previously. The blood sugar on the morning of Apr. 19 was 0.1 per cent, the CO₂ capacity 74 per cent. The 1500 calory diet was continued, keeping the protein at 80 gm. and raising carbohydrate to 60 gm. by substitution for a little fat. Six eggs were allowed on fast-days. The weight at discharge on May 2 was 48.2 kg. The diet thus represented 1.66 gm. protein and 31 calories per kg., diminished by the partial fast-days to 1.55 gm. protein and 28 calories per kg.

Subsequent History.—On moving to the country for the summer the patient was allowed to substitute thick country cream for the poorer city cream, and when the mother reported traces of glycosuria the carbohydrate was diminished from 60 to 45 gm. The reports of marked increase of weight then aroused suspicion, and notwithstanding the record of vigorous health and continuous absence of glycosuria, the patient was ordered to return immediately to the hospital, where these facts were ascertained.

Fourth Admission.—Sept. 10, 1917. Weight 55.4 kg.; a gain of 7.2 kg. since last discharge, and 5.4 kg. more than at the first admission. The plasma sugar on the afternoon of Sept. 10 was 0.159 per cent; and though glycosuria was absent, a heavy reaction developed as soon as the regular diet with 60 gm. carbohydrate was given. The ferric chloride reaction was negative, but there was a strong nitroprusside reaction. A 2 day fast was necessary to abolish the glycosuria, and the acetone reaction became still heavier. A carbohydrate test was then carried out in the usual manner, and glycosuria appeared with 140 gm. carbohydrate. The tolerance was thus approximately the same as before. If anything there was improvement, because the weight was so much higher at the time of this test. The patient was discharged on Oct. 4 to resume her vacation in the country.

Acidosis.—The plasma bicarbonate was continuously at a high normal level (67.2 to 78.6 per cent) without the use of alkali. Though the ferric chloride test was always negative, the nitroprusside reaction was strongly positive all through the carbohydrate test and also on the diet at discharge. In other words, as much as 140 gm. carbohydrate without other food failed to abolish acetonuria at this time.

Blood Sugar.—This was not only dangerously high in consequence of the over-nutrition at admission, but was also stubborn, being 0.156 per cent on the first fast-day (Sept. 12) and 0.154 per cent on the second fast-day (Sept. 13). On Sept. 14, it was found to have fallen abruptly to 0.09 per cent. The subsequent values were normal when taken fasting. A sample taken after eating lunch on Oct. 2 showed plasma sugar of 0.123 per cent; *i.e.*, distinctly higher than a normal person would show after the same kind of a meal.

Weight and Nutrition.—The undernutrition in hospital brought the weight down to 52.7 kg. For the purpose of further reducing weight, an undernutrition diet was prescribed at discharge, representing 80 gm. protein, 50 gm. carbohydrate, and 1100 calories.

Subsequent History.—The patient continued to feel well and the urine remained negative for sugar. Nitroprusside reaction was negative after Oct. 18. She was slightly hungry on this diet. She returned by request for a brief observation in hospital.

Fifth Admission.—Oct. 23, 1917. Weight 51.7 kg. Blood and urine normal in all respects. The blood sugar before breakfast on Oct. 26 was 0.098 per cent. At various periods of digestion, Oct. 23 to 25, it ranged from 0.109 per cent to 0.119 per cent. The patient was discharged on the 3rd day (Oct. 26) on a diet of 70 gm. protein, 60 gm. carbohydrate, and 1275 calories, the plan being to reduce weight somewhat further while giving a balanced ration and protecting body protein.

Subsequent History.—The patient remains well and is pronounced by her mother the strongest and most energetic member of the family.

Remarks.—The diet prescribed at the first discharge was somewhat too high. The functional overstrain was detected from the slight hyperglycemia, and the diet accordingly reduced in fat and calories. The carbohydrate was actually increased by 5 gm. With this well advised change, normal blood sugar was again restored and the entire condition remained favorable. After the third admission, a more dangerous situation developed from the neglect regarding the fat intake, and this danger was masked by the reduction of carbohydrate. Serious damage would certainly have resulted had not suspicion been aroused by the increase in weight while the patient was seemingly in splendid condition. It is thus proved by two experiences that the appearance of "spontaneous downward progress" can quickly be produced in this patient by overnutrition. With rational regulation of the total diet, the subjective and objective appearance of perfect health has been maintained to date with no sign of downward progress. The only danger in sight at present lies in the patient's tendency to overstep her diet, particularly by taking fat. Though the ultimate outcome cannot be predicted, it is believed that if the mistakes committed in other cases are avoided, and early and efficient treatment be employed, the progress in the great majority of cases of juvenile diabetes can be at least as favorable as in this one.

CASE NO. 67.

Male, married, age 46 yrs. Spanish; lumber merchant. Admitted Apr. 20, 1916.

Family History.—A maternal aunt died of diabetes. A cousin on the father's side had diabetes. No other heritable disease known in family.

Past History.—Healthy life with considerable business strain, but also considerable recreation and outdoor exercise. No illnesses remembered except mild childhood infections. Luetic infection at age of 18 with secondary eruption. Has been treated with short courses of mercury for many years, but never continuously or with salvarsan. Tendency to nervousness and insomnia. Considerable but not excessive indulgence in brandy, wine, beer, and cigarettes. The appetite has also been rather large. Normal weight 85 kg.

Present Illness.—In Dec., 1913, patient consulted a physician for a sensation of heat like fever. Polyuria and other usual diabetic symptoms were absent. The temperature was found normal, and 4.1 per cent sugar was found in the urine. Patient states that he lived on "broths" for 15 days and glycosuria ceased, but a "blood test" still revealed diabetes. He soon afterward disregarded diet, and after 3 months, thirst and loss of weight were noticed and the glycosuria was found to be 7 per cent. Since then he has received treatment at a number of watering places and underspecialists on the European continent and in England. In Spain he once underwent the Guelpa treatment with benefit. Glycosuria has become more persistent with time, and acidosis, as evidenced by both ketonuria and lowering of the alveolar CO_2 , has been present at least since 1914. He has gradually lost 30 kg. weight.

Physical Examination.—A fairly developed, moderately emaciated man, with intellectual and rather nervous face. Teeth poorly kept, marked pyorrhea. Tonsils normal. No lymph node enlargement except a few palpable glands in groins. Arteries not perceptibly sclerotic. Knee jerks absent. Repeated Wassermann reactions strongly positive.

Treatment.—Fasting was begun immediately, and carbohydrate was used as liberally as possible with the idea of clearing up acidosis promptly. Notwithstanding the mild clinical character of the diabetes, the tolerance in a carbohydrate test was not above 150 gm. carbohydrate in the form of vegetables. Mixed diet was then begun and increased rapidly to 110 gm. protein, 30 gm. carbohydrate, and 2000 calories. A few slight sugar and ferric chloride reactions recurred, but on the whole this diet was apparently well tolerated, and the patient was greatly improved subjectively. He was discharged on the above diet on June 16, 1916.

Acidosis.—The slightly subnormal blood bicarbonate quickly rose, and the ammonia correspondingly fell to normal.

Blood Sugar.—This was 0.27 per cent on admission, but fell to normal with the rapidity characteristic of an early or mild case. The later values were normal or on the upper limit.

Weight and Nutrition.—Weight at admission 54.2 kg., at discharge 55.7 kg.; *i.e.*, a gain of 1.5 kg. Part of this was evidently water retention, for there was no appreciable loss of weight during more than a month of fasting and undernutrition at the outset. The diet at discharge represented almost 2 gm. protein and 36 calories per kg., reduced by the weekly fast-days to 1.7 gm. protein and 31 calories average.

Syphilis.—The diet was purposely raised to the verge of tolerance, partly because of the mildness of the case, but chiefly with a view to testing the effect of syphilitic treatment. In hospital the patient received 50 mercury inunctions, each consisting of half a Parke Davis "mercurette." He was also given 4 intravenous doses of 0.5 gm. salvarsan. There were no reactions to the first treatments, slight reactions to the later ones. After discharge, he was treated with 50 more mercury inunctions of the same kind and 4 more salvarsan injections, which continued to cause slight reactions. The former + + + Wassermann

in the blood had become negative by Sept. 2. After return to Spain the patient received treatment with neosalvarsan.

Subsequent History.—The patient went immediately upon discharge to a nearby summer resort and adhered to the weighed diet. Glycosuria remained absent. On July 12, sugar in whole blood was 0.145 per cent, in plasma 0.154 per cent; on Aug. 15, 0.132 per cent in whole blood, 0.151 per cent in plasma. The patient complained slightly of chronic hunger and weakness. An increase of diet to 40 gm. carbohydrate and 2500 calories on July 25 resulted in slight traces of glycosuria. A reduction was therefore made to 35 gm. carbohydrate and 2250 calories. The weight tended to fall; *i.e.*, on July 12, 55 kg.; on July 25, 54.8 kg. In Oct. the patient returned to Spain, having a rough voyage and showing glycosuria several times because of starch in the diet on shipboard. He has tried to continue diet, but has not been successful in remaining sugar-free, chiefly because of too high caloric intake, including alcohol.

Remarks.—Though syphilis is a possible etiologic factor in this case, it responded to dietetic treatment in the usual manner of a case of this type, whereas antiluetic treatment, sufficiently thorough to render the Wassermann negative, showed no appreciable influence upon the tolerance.

CASE NO. 68.

Male, age 23 mos. American Jew. Admitted June 13, 1916.

Family History.—Parents and one older brother living and well. A maternal great grandmother and grandmother died of "old age diabetes" developing at about the age of 75.

Past History.—A normal baby with never any illness except an occasional slight cold. Was entirely well when examined by a physician 3 months ago at time of vaccination. Weight 1 month ago 25 pounds.

Present Illness.—About 1 month ago the baby was noticed to be not quite so well, and hunger, thirst, and urine were increased. The diet had consisted of cereals, vegetables, milk, cream, butter, and occasionally eggs. During this month he has gradually lost about 5 pounds, but seemed bright and playful and not ill enough to cause worry. 4 days ago (June 9) it was noticed that the breathing was abnormally deep. Thereafter he became fretful, unwell, and somnolent. The respiration by today became alarmingly deep and rapid, and a physician diagnosed impending diabetic coma.

Physical Examination.—Height 86.4 cm. A normal child, still fairly well nourished. Cheeks flushed. Marked air-hunger. Mind clear. Tonsils enlarged, but not acutely inflamed. A very few shot-like glands in neck and axillæ. Reflexes normal. Wassermann negative. Examination otherwise negative.

Treatment.—The child was admitted at 9:30 p.m., showing intense glycosuria and ketonuria, a trace of albumin, and numerous casts. The data of the initial period are shown in Table XXI.

The child was restless and irritable and refused to take liquid of any kind. The bowels were moved by enema. Food or liquids being violently resisted, soup and water were given by stomach tube during the day, along with sodium chloride and bicarbonate. The bicarbonate seemed to act rather promptly in diminishing dyspnea. On the morning of June 14, the breathing and general condition had not changed appreciably. By June 15, the condition seemed only slightly better. Probably owing to thirst created by the salt, the child occasionally drank water voluntarily, but was still mostly treated by gavage. Albumin and casts disappeared. On June 16, the condition was better, but food and drink were still refused. On June 17, liquids were still given by tube, but the patient began to ask for food. On June 19, 100 gm. thrice cooked asparagus were given. On June 20, vegetables representing 10 gm. carbohydrate brought a return of glycosuria. On June 21, a diet of eggs, heavy cream, thrice boiled vegetables, and soup was begun, but the tolerance was so low that 20 gm. protein caused glycosuria. Diets of about 300 calories were continued, with occasional fast-days, and the assimilation gradually improved. The patient was discharged on Oct. 2, the parents having carefully learned the method of diet.

Acidosis.—While it is possible that simple fasting with fluids and salt would have averted the threatened coma, the small doses of alkali seemed to be distinctly beneficial. Even with the alkali the blood bicarbonate was rather slow in rising. The child subsequently remained free from acidosis. From Sept. 18 to Oct. 2, the total acetone in the blood plasma varied between 5 and 9 mg. per 100 cc.

Blood Sugar.—The chart shows the normal level of the fasting blood sugar. An abnormal degree of digestive hyperglycemia is not excluded.

Weight and Nutrition.—Weight at admission 8.5 kg., at discharge 8.1 kg. For the first 2 months the diet was approximately 15 to 20 gm. protein and 330 calories daily, about 2 gm. protein and 40 calories per kg. The tolerance gradually rose, so that at the end, 42 gm. protein, 22.5 gm. carbohydrate, and 600 calories could be given, (including 200 cc. milk) with the blood sugar remaining as above shown. The diet prescribed at discharge was 42 gm. protein, 15 gm. carbohydrate, and 550 calories (about 5 gm. protein and 68 calories per kg.).

Subsequent History.—The patient remained cheerful and well at home and free from glycosuria. The following blood record was obtained: On Oct. 20, blood sugar 0.125 per cent, plasma bicarbonate 60.7 per cent; on Nov. 20, blood sugar 0.125 per cent, plasma sugar 0.133 per cent. This fasting hyperglycemia was a warning of the beginning of trouble from the excessive diet, which was ignored. Nevertheless the clinical condition continued apparently favorable until an attack of gripe at Christmas. With this he had cough, fever, and heavy glycosuria. The parents partially controlled the glycosuria by fasting and reduced diet, but hastened to return the child to the hospital.

Second Admission.—Jan. 1, 1917. Weight 8.3 kg. The ferric chloride reaction was negative. The glycosuria was slight, and ceased promptly on a reduced diet of 15 gm. protein and 160 calories, without fasting. This was rapidly increased, and after an uneventful stay in hospital, the patient was dismissed on

June 21	8.4	98.8 96.6	108 102	48 24	—	21.1	18.5	4	274	800	1050	785	5.5	3.10	—	1.57	0.58	1.56	4.32	—	—	—	—
"	22	98.6 95.2	108 92	48 24	—	14.9	10.6	—	159	800	1270	725	+	—	—	1.28	0.39	0.88	2.85	0.102	60.6	30.1	0
"	23	98.6 98.0	112 100	40 24	—	15.4	20.6	0.9	257	800	1200	815	+	—	—	1.73	0.48	—	3.65	—	—	—	0
"	24	98.6 98.4	110 104	32 28	—	15.6	20.8	1.3	261	800	1175	525	2.30	—	—	2.10	0.40	0.75	4.17	—	—	—	0
"	25	98.0 98.0	100 92	24 24	—	18.2	22.8	5.0	306	800	1250	290	7.60	—	—	2.74	0.52	1.42	5.25	0.078	57.8	20.9	0
"	26	98.6 98.2	96 90	36 24	—	15.6	25.6	1.3	296	800	875	285	+	—	—	2.35	0.48	0.69	6.15	—	—	—	—
"	27	98.0 98.0	92 92	36 36	—	19.1	23.2	0.9	296	800	1305	420	0	—	—	2.12	0.34	0.41	5.60	0.125	55.1	24.0	0

Jan. 24, 1917, weighing 8.1 kg., on a diet of 35 gm. protein, 10 gm. carbohydrate, and 415 calories (4.3 gm. protein and 51 calories per kg., reduced by weekly fast-days to 3.7 gm. protein and 44 calories average). For extraneous reasons no blood analyses were performed.

Subsequent History.—The patient remained free from glycosuria except for occasional slight traces, for which minor changes in diet were advised. The weight on July 3 was still 8.1 kg. The diet was increased with a little bacon, and glycosuria gradually developed. It did not cease on withdrawal of the bacon, and the parents hesitated to employ fasting. One feature in the case was the nervous strain which the prolonged invalidism of the child imposed upon the mother. The course adopted therefore was to allow glycosuria to continue on a carbohydrate-free diet of 320 calories. The glycosuria remained moderate. There was no serious acidosis, and the child was comfortable except for the progressive weakness. Death must occur before long.¹⁰ It is noteworthy that the tendency to acidosis seems to be no greater than in an adult.

Remarks.—The attempt to force a diabetic child to grow and develop on high diet failed as usual. As the diet at first prescribed included milk and carbohydrate, and was adequate in calories and liberal in protein, the possibility of a specific inability of a diabetic child to grow and develop properly is suggested. Comparison of such a child with a normal child on an identical diet would be an interesting and valuable experiment.

A diet as excessive as this would quickly bring disaster in any adult patient with severe diabetes. It is only surprising that the baby was able to withstand the injury so long. The record of blood sugars in hospital illustrates the fact that absence of fasting hyperglycemia is not proof that the diet given is suitable. Irrespective of any laboratory findings, downward progress could be expected with certainty from such a strain upon a weakened metabolism. As usual, the diet which is not restricted at the outset from choice, is later restricted from necessity. The child does not grow or thrive, and the only result of excessive feeding is the permanent injury produced. Whether downward progress is inevitable in an infant (as it probably often may be) or not, there is little doubt that it can be delayed and both life and comfort longer maintained with a more rational limitation of food.

The failure to make the limitation, even on the appearance of warning hyperglycemia, long before the onset of glycosuria, is another serious fault in the management, which either caused or hastened disaster. It leaves the question of inevitable downward progress of infantile diabetes undecided, and merely proves that such a patient does not possess any remarkable recuperative power on account of his years.

¹⁰ Coma death occurred early in Dec., 1917.

CASE NO. 69.

Female, married, age 39 yrs. German Jew; housewife. Admitted Aug. 23, 1916.

Family History.—Father died of Bright's disease at 69. Mother died of cancer of liver at 79. Patient has had five brothers and two sisters. Three brothers are well; one has right-sided hemiplegia; one died of "creeping paralysis" at 49. Both her sisters died in infancy of unknown cause. No known diabetes, gout, obesity, tuberculosis, syphilis, or cancer elsewhere in family.

Past History.—A few ordinary childhood diseases. The only other illnesses were two attacks of "vaginal cellulitis" in 1912 and 1914. The local swelling was such that catheterization was necessary. The inguinal glands were tender and there was temperature as high as 104.5° F. She has had a healthy life, always in or near New York, but has been overwrought and neurotic and has tended to become obese. She was married 14 years ago and has been separated from husband for the past 4 years. She has been under strain as a housewife, directing a large establishment. Menstruation normal, except for some hemorrhages in recent years, said to be due to fibroids. No children; five miscarriages, all self-induced. Venereal denied. No tobacco. Only a little wine occasionally. Food taken very sparingly for a number of years in order to check the tendency to obesity. Bowels regular until onset of diabetes.

Present Illness.—On Dec. 28, 1915, there was a distinct acute onset of marked polyphagia, polydipsia, and polyuria. 2 weeks later, because of these and rapid loss of weight and strength, a physician was consulted, who immediately diagnosed diabetes and referred her to an experienced internist. She spent most of Feb. in a hospital under his care, and by fasting and very low diet became sugar-free 5 days before leaving hospital. A nurse was with her for 10 days after discharge, and freedom from glycosuria continued during this time. Glycosuria returned soon after the nurse discontinued supervision. Since then on several occasions doctors are said to have given her up because of threatening coma. There has been a tormenting pruritus vulvæ. Much of her hair has fallen out. There has been loss of weight as follows: Sept., 1915, weight 138 pounds; Dec., 129 pounds; June, 1916, 89 pounds; Aug., 1916, 82.5 pounds; *i.e.*, a total loss of 55.5 pounds.

Physical Examination.—An emaciated, neurotic looking woman with sallow, dry skin and anemic appearance, but no acute symptoms. She claims to be so weak that she can scarcely move a limb, but tests show that she is not quite so feeble. Eyes, mouth, and throat negative aside from pallor of mucous membranes. Liver edge palpable 2 cm. below costal margin. Blood pressure 70 systolic, 50 diastolic. General lymph gland enlargement. Slight edema of legs with pitting about ankles. Knee and Achilles jerks normal. Wassermann reaction negative.

Treatment.—The patient fasted Aug. 25 to Sept. 1 inclusive. In the subsequent test with green vegetables, 10 to 20 gm. carbohydrate were tolerated on Sept. 2

and 3, but glycosuria appeared with 30 gm. on Sept. 4. Corresponding to this low tolerance, it was necessary to employ very low carbohydrate-free diets thereafter. Apart from the severity of the diabetes, the greatest difficulty in hospital resulted from her excessively neurotic nature. She was subject to fits of crying or screaming and other irresponsible conduct, and though the condition improved somewhat with relief from the diabetic symptoms, it was never satisfactory. She was discharged on Nov. 27 with a view to continuing undernutrition treatment under her private physician.

Acidosis.—The highest ammonia nitrogen excretion was 1.81 gm., the lowest plasma bicarbonate 42.7 per cent. This acidosis cleared up under fasting without alkali. Thereafter the CO₂ capacity remained fully normal and the ammonia output was only slightly elevated.

Blood Sugar.—The hyperglycemia of 0.344 per cent on the morning of Aug. 25 remained unchanged 24 hours later, then gradually diminished to 0.178 per cent on the morning of Sept. 4. Thereafter, even on the extremely low diet employed, it remained persistently high, the value of 0.156 per cent in the plasma in the last analysis on Oct. 24 representing the lowest level observed. As usual with such a degree of hyperglycemia, traces of glycosuria readily occurred on any attempt to increase the diet.

D:N Ratio.—Omitting the initial ratio of 4.5, evidently due to carbohydrate of the former diet, the ratios on the fast-days Aug. 25 to 28 were 2.12, 1.85, 2.12, 1.03.

Weight and Nutrition.—Weight at admission 37 kg., at discharge 35.7 kg. Extreme undernutrition was necessary to control the severe diabetes during the entire period of 100 days in hospital. The total intake was 2864 gm. protein and 48,317 calories, or an average of 28.6 gm. protein and 483 calories daily. The urinary nitrogen record is not complete enough to permit calculating the nitrogen balance. Some of the figures for daily nitrogen output are conspicuously low; e.g., 2.72 gm. urinary nitrogen on Sept. 5, and 2.62 gm. on Sept. 13. Nevertheless, there must necessarily have been a negative nitrogen balance. Between Oct. 5 and 28, an experiment was performed showing the production of both glycosuria and acidosis by addition of fat to the diet, as described in Chapter VI. The diet at discharge was only 50 gm. protein, 10 gm. carbohydrate, and 730 calories, i.e. 1.4 gm. protein and 20 calories per kg., diminished by weekly fast-days to 1.2 gm. protein and 17 calories average. The treatment was therefore incomplete, since the patient had not been brought into equilibrium. Even with the extreme undernutrition required, she showed slight increase rather than decrease in strength, especially subjectively.

Subsequent History.—The patient continued treatment for a period not exactly known, and then was subjected to various diets by other physicians. She died Feb. 23, 1917, supposedly in coma.

Remarks.—The diabetes was of genuinely great severity, and the psychopathic disposition largely precluded success. More might have been accomplished by still more stringent undernutrition, to control the symptoms more completely within a shorter time, but the ultimate result must have been failure without greater reliability on the part of the patient.

CASE NO. 70.

Male, married, age 34 yrs. American; physician. Admitted Sept. 3, 1916.

Family History.—Mother once had a tumor of face, which was removed by operation, and did not return; nature not known. She died of cardiorenal disease. Father living and well, aged 74. Two brothers are well. One sister died of diphtheria in infancy.

Past History.—Healthy life in good hygienic surroundings. Measles in childhood. No illnesses, operations, or injuries since. Venereal denied. No excesses in food, alcohol, or tobacco. Never nervous. Life easy and pleasant without financial or other worries. Normal weight 60 kg.

Present Illness.—Began in Sept., 1914, with polydipsia and polyuria, but no polyphagia. The onset was apparently sudden and glycosuria was immediately found. For a year he was on almost carbohydrate-free diet under experienced care, with the usual quantitative restriction also in protein; nevertheless glycosuria was never absent at any time. He has since become discouraged and therefore has occasionally broken diet with bread or cake. During the past year he has lost about 8 kg. weight.

Physical Examination.—A tall, extremely emaciated young man. Skin very dry. Hair thinning rapidly. Gums receding, though teeth are well kept. Knee jerks absent. Blood pressure 85 systolic, 65 diastolic. Examination otherwise negative. Wassermann negative.

Treatment.—The severity of the case and the results of initial treatment are shown in Table XXII.

In the subsequent period on green vegetables, traces of glycosuria appeared when the intake reached 100 gm. carbohydrate. Mixed diet was then rather rapidly built up, and the patient was discharged on Oct. 16 feeling much improved in strength and comfort.

Acidosis.—The rapid clearing of the rather threatening acidosis on fasting without alkali is shown in the table. By Sept. 17, the plasma bicarbonate had reached 61.4 per cent, and acidosis remained absent thereafter, the plasma bicarbonate at the last analysis on Oct. 13 being 70.6 per cent. Analyses for acetone bodies in the plasma were made on 11 days at irregular intervals. The highest finding was 39 mg. total acetone per 100 cc. plasma on Sept. 29. Diminution followed, so that on Oct. 13 the total acetone was 11 mg. per 100 cc. plasma. The ammonia excretion in the last analyses up to Oct. 11 was 0.51 to 0.88 gm. daily.

Blood Sugar.—Though glycosuria was kept absent, hyperglycemia was present most of the time. From 0.143 per cent in whole blood and plasma on Sept. 17, the blood sugar rose during the carbohydrate test to 0.213 per cent in whole blood and 0.217 per cent in plasma on Sept. 24. It then gradually fell to 0.111 per cent in whole blood and 0.135 per cent in plasma on Oct. 9 and 0.100 per cent in whole blood and 0.135 per cent in plasma on Oct. 11. This was with 10 gm. carbohydrate in the diet. With increase to 20 gm. carbohydrate daily, the final

analysis on Oct. 13 showed 0.179 per cent sugar in whole blood and 0.189 per cent in plasma. The allowance was therefore diminished to 10 gm.

Weight and Nutrition.—Weight at admission 42.2 kg., at discharge 40.3 kg. Edema was present at certain times in hospital, raising the weight as high as 44.8 kg.; this subsided on salt-free diet. There was the usual gain in strength and comfort with undernutrition and reduction of weight. The diet at discharge consisted of 70 gm. protein, 10 gm. carbohydrate, and 1500 calories; *i.e.*, 1.7 gm. protein and 37 calories per kg., diminished by weekly fast-days to 1.4 gm. protein and 32 calories average.

Subsequent History.—The patient remained comfortable and resumed his former work. Slight glycosuria developed on two or three occasions, but was immedi-

TABLE XXII.

Date.	Diet.				Weight.	Urine.						Blood plasma.	
	Protein.	Fat.	Carbo- hydrate.	Total calories.		Volume.	Sugar.	Total nitrogen.	D:N ratio.	NH ₃ -N	FeCl ₃ reaction.	Sugar.	CO ₂
1916	gm.	gm.	gm.		kg.	cc.	gm.	gm.		gm.		per cent	vol. per cent
Sept. 4	65	127	10	1495	41.8	1990	42.8	11.55	2.83	3.92	++++	0.294	39.1
" 5	65	127	10	1495	41.6	1780	31.2	9.43	2.25	3.02	++++	—	—
" 6	65	127	10	1495	42.2	1800	33.3	9.30	2.50	3.08	++++	0.291	42.1
" 7	Fast-day.				42.4	1780	16.2	7.70	2.12	2.59	++++	—	—
" 8					42.0	1810	5.8	4.48	1.30	1.41	+++	0.238	51.0
" 9					41.1	3370	+	5.70	—	1.76	+++	—	—
" 10					41.0	2445	+	4.82	—	0.93	++	—	—
" 11					40.8	2420	0	5.20	—	1.11	+	0.208	55.7
" 12					40.6	2340	0	4.78	—	1.04	+	—	—
" 13	3.9	0.4	10	60	40.0	3540	0	6.86	—	1.32	+	0.175	52.2
" 14	7.9	1.5	20	127	40.8	2150	0	4.12	—	0.58	0	—	—

ately checked by a fast-day. There was a further slight diminution in weight. On Dec. 19, an apparently slight attack of influenza began. He was still up and attending to regular duties until Dec. 23, when severe cough developed, and fever and weakness forced him to go to bed. The highest temperature was 100.5°. The weakness increased, and on Jan. 1 the respiration was noticeably rapid, the pulse rapid and weak; unconsciousness came on about 3 p.m., and death occurred on the morning of Jan. 2, 1917. The local physician who attended him attributed the death to infection and not to diabetes, and no urine examinations were made after Dec. 23.

Remarks.—It seems possible that the terminal condition was really diabetic acidosis of the fasting type, since the patient was eating practically nothing on the final days and the tendency to acidosis with even a slight infection is well

known. If this were the case, there might have been a chance of preventing the death by simple measures. The patient may have fallen a victim to a simple influenza infection by reason of his somewhat weakened condition, but the desirability of consultation with someone having experience with diabetes is indicated in conditions of this sort.

CASE NO. 71.

Male, age 9 yrs. American. Admitted Oct. 30, 1916.

Family History.—No diabetic or other heritable disease.

Past History.—Normal and vigorous child, with no known infections or illness of any kind.

Present Illness.—2 years ago, mother began to notice polyphagia and polyuria with bed-wetting. He received early treatment from Dr. Joslin in Boston, and subsequently came to New York. Under the treatment he was continuously well and sugar-free, playing like a normal boy and going to parties, always taking his own food with him. About the 1st of Sept. he was detected in the practice of going downstairs at night to take forbidden food from the pantry. Heavy glycosuria thus came on, which was not controlled by his New York physician. Progress was rapidly downward, and recently there has been marked and increasing drowsiness.

Physical Examination.—A fairly developed, moderately emaciated boy, stuporous but not unconscious, with deep rapid grunting respiration, 30 per minute. Temperature 96° F, pulse 124. Mouth and throat normal. No lymph node enlargements. Abdomen rounded with tympanites. Testicles undescended. Knee and Achilles jerks absent. Examination otherwise negative.

Treatment.—The clinical record can be summarized in Table XXIII.

The patient was admitted at 12:50 p.m., Oct. 30. He could still be roused, but immediately went to sleep. The stomach was washed out to remove remains of previous food, and 30 cc. castor oil, 5 gm. sodium bicarbonate, and 200 cc. water were given through the tube. A high colon irrigation removed considerable feces and relieved tympanites. The bowels subsequently moved several times as the result of the castor oil. The temperature fell at first to 95.6°, but with application of heat gradually rose to normal by midnight. Notwithstanding fasting and 20 gm. sodium bicarbonate, the CO₂ capacity of the plasma on Oct. 31 was the same as at admission, and the patient was in full coma. The same treatment of fasting with liquids and bicarbonate by stomach tube was continued, and on Nov. 1 the patient became able to understand what was said to him and to drink voluntarily. On the following days he was conscious but not fully rational, and more or less hyperpnea persisted.

After 6 days of fasting, glycosuria was still present, sugar and ketones in the blood were higher than before, and the strength was plainly becoming exhausted. Accordingly, on Nov. 6, food was given to the extent of two eggs and 5 gm. carbohydrate in green vegetables, and on Nov. 7 a slightly higher diet. Bed sores began to develop at this time, and death from weakness threatened. Therefore

Nov. 3	—	98.6 104 30 98.0 90 28	2	Fast-day.	700	990 2050	800+	5.89 3.85 1.52 0.48 2.80 7.20 0.02 0.41 50.2 269.7 35.7	—	1.96	Same.	
"	4	—	3	"	750	745 1795	805+	6.25 3.64 1.72 0.35 2.58 4.54 0.24 0.56 38.8 368.4 29.4	—	"	"	
"	5	—	—	"	750	775 1825	1605	7.11 5.06 1.42 0.59 3.27 6.78 1.12	—	—	"	"
"	6	13.2	99.2 102 32 98.0 98 28	—	16.0 11.0 5.0 188	200 1050 1500	1195	5.11 4.29 — 0.59 2.52 5.38 0.67 0.55 39.0 212.5 22.7 430.0	—	—	Same. Very weak.	
"	7	12.7	100.8 116 32 99.0 85 24	—	26.0 17.0 5.0 283	— 1510	648+	7.26 3.40 — 0.49 1.94 1.74 0.08 0.50 48.5 192.5 34.0 439.0	—	—	Very weak. Unconscious.	

on Nov. 7, 200 cc. blood were taken from the father into sodium citrate, and infused into the patient. The only result was a temporary improvement of strength. Unconsciousness gradually came on, and death occurred at 10 a.m. Nov. 8 in coma.

Acidosis.—The urine gave no adequate indication of the degree of acidosis. On the other hand, acetone bodies accumulated in the blood to a remarkable degree, as if the renal elimination were defective. This renal impermeability was perhaps of decisive influence for the fatal result. Albuminuria and casts were present, as usual in such a condition. Food, even though small in amount and composed largely of protein and carbohydrate with little fat, was followed by a return of coma. Of course, it cannot be said positively that coma might not have returned even with fasting.

There is no chemical explanation for the death. The blood bicarbonate on Oct. 31, the child being in coma, was identical with that on Oct. 30, when coma was still absent. It was comparatively high on the days when coma was partially relieved, but was also far above the ordinary danger level up to the last determination. On the other hand, the acetone bodies in the plasma on Oct. 31, with coma present, showed only twice the concentration present on Oct. 30 before coma; but they rose as coma subsided, so that on Nov. 4, with coma symptoms mostly absent, the concentration was over twice that on Oct. 31; with coma present. Diminution of the ketonemia then followed as the clinical condition became worse, though the figures remained high to the end.

Lipemia.—The high lipemia at the outset was one of the striking features. It diminished under fasting, and though later analyses were not performed, the plasma in the closing days was clear.

Blood Sugar.—This also was very high in proportion to the glycosuria. Such an apparent renal impermeability for sugar may perhaps be a disturbing influence in the attempt to reckon dextrose-nitrogen ratios. Except for such impermeability, high and perhaps maximal ratios might have been found. Also, the child might have been better off if he could have excreted both sugar and acids freely. The relatively low blood sugar of Nov. 1 is remarkable in comparison with all the other figures. Otherwise the blood sugar changed little or even increased slightly on fasting.

Body Weight.—There was not the precipitous fall in weight characteristic of fasting coma and desiccation. On the other hand, bicarbonate did not cause edema. The total loss of 2.1 kg. weight is adequately accounted for by the prolonged fasting and rather free purgation, without the assumption of any abnormality of the water balance.

Remarks.—The child went into complete coma before fasting had time to exert much influence. He then came out of coma and apparently might have been saved if the strength had held out.

The treatment has not been satisfactorily worked out for patients with either dangerous weakness or extreme intensity of intoxication. With regard to alkali, some would employ larger dosage, while Joslin suspects an injurious effect and

would perhaps suggest that the great increase of acetone bodies in the blood represented such a harmful influence of the alkali. With regard to diet, there are the possibilities of simple fasting, carbohydrate feeding, and protein feeding. Fasting alone often fails in this extreme condition. Carbohydrate perhaps could not be burned at all, and the possible hyperglycemia consequent upon any large dosage of carbohydrate, with the blood sugar already 0.5 per cent and poor excretory power, presents a serious question. Pure protein diet might maintain strength and furnish ammonia to neutralize acids. At the same time it might aggravate the diabetes and nullify the possible benefit derivable from fasting. Various persons will hold various opinions, but the fact remains that while impending coma of ordinary type is generally readily cleared up, the patients presenting this exceptionally severe condition generally die.

With regard to the cause of death, the evidence in this case excludes the supposition of simple acid intoxication or deficit of alkali. Some may seek the explanation in the toxicity of certain substances of the acetone group. Others may see the cause in possible precursors of acetone bodies in the tissues. The explanation is wholly undecided. It is possible that no one substance is responsible, but that death results from a more general alteration of cellular metabolism and protoplasm.

CASE NO. 72.

Female, age 12 yrs. American; schoolgirl. Admitted Nov. 16, 1916.

Family History.—Parents living; mother rather sickly, cause unknown. One brother died in infancy. Two brothers and one sister are well. No diabetes or other hereditary diseases known.

Past History.—Measles, mumps, and possibly chicken-pox. No infections recently. Normal development, health, and habits.

Present Illness.—Patient began to feel unwell about a year ago, and a physician diagnosed diabetes. She has since been on starch-poor, fat-rich diet, and applied at the Institute on account of progressive weakness especially during the last 2 months.

Physical Examination.—A well developed, fairly well nourished child; high color in cheeks; slight edema of eyelids and ankles. Deep rapid respiration suggesting air-hunger. Tongue red and dry. Teeth poorly kept, two decayed; pyorrhea present. Enlarged lymph nodes on both sides of neck. Knee jerks very feeble. Examination otherwise negative.

Treatment.—At admission temperature was 100.2°, pulse 120, respiration 24. After the first 24 hours the temperature remained between 98 and 99, pulse about 80, respiration 18 to 20. The data of this period in hospital are shown in Table XXIV. No alkali was used.

The case was rather unusual in its slowness in clearing up. The only special incident in hospital was the uneventful removal of the two carious teeth. Complete control of the diabetes was never achieved, as shown especially by the persistent hyperglycemia. The patient was discharged Dec. 23, 1916, on a diet of 50 gm. protein, 10 gm. carbohydrate, and 600 calories.

Dec. 7	27.3	20.0	7.7	10.0	194	2500	2300	+	4.43	—	0.65	1.17	1.35	—	—	—	—	—	—
" 8	27.3	30.0	14.2	10.0	296	2500	2510	+	5.93	—	0.68	0.78	1.76	—	—	—	—	—	—
" 9	27.4	30.0	14.2	10.0	296	2500	2365	+	6.50	—	0.68	0.56	1.44	—	—	—	—	—	—
" 10	27.5	—	Fast-day.	—	—	2500	2505	+	5.09	—	0.52	0.44	1.28	—	—	—	—	—	—
" 11	26.8	30.0	30.1	—	402	2500	2125	0	5.14	—	0.54	0.62	0.79	0.270	66.0	31.0	6.60	—	—
" 12	26.5	30.0	30.1	—	402	2500	2630	0	5.44	—	0.64	0.56	0.69	—	—	—	—	—	—
" 13	26.4	40.0	35.7	—	496	2500	2450	0	6.88	—	0.73	0.51	0.29	—	—	—	—	—	—
" 14	26.5	40.0	35.7	—	496	2500	2555	0	7.61	—	0.75	0.48	0.80	—	—	—	—	—	—
" 15	26.5	40.0	34.5	5.0	305	2500	2520	0	7.05	—	0.72	0.50	1.00	0.262	60.0	23.3	11.6	—	533
" 16	26.5	40.0	32.5	7.5	497	2500	2565	0	5.86	—	0.56	0.39	0.40	—	—	—	—	—	—
" 17	26.6	40.0	31.3	10.0	496	2500	2515	0	7.41	—	0.65	0.42	2.24	—	—	—	—	—	—
" 18	26.7	40.0	42.7	10.0	602	2500	2630	0	6.96	—	0.57	0.27	2.56	—	—	—	—	—	—
" 19	26.3	50.0	43.5	10.0	650	2500	2825	0	7.70	—	0.72	0.28	3.80	—	—	—	—	—	—
" 20	26.4	50.0	43.5	10.0	650	2500	2635	0	7.70	—	0.81	0.31	4.67	—	—	—	—	—	—
" 21	26.1	50.0	43.5	10.0	650	2500	1575	0	6.40	—	0.61	0.23	3.21	0.188	58.0	22.0	11.0	—	548

Subsequent History.—The patient felt fairly well, played about with her friends, and led an approximately normal life. Sugar and ferric chloride reactions gradually returned about Mar. Particularly on Mar. 9, it is suspected that candy was obtained surreptitiously, and later in that day shortness of breath and drowsiness developed. On the morning of Mar. 10, these had increased and nausea had come on, which prevented eating, but water was still taken in large quantities on account of thirst.

Second Admission.—11:20 p.m., Mar. 10, 1917. Child pale, with flushed cheeks, semiconscious and delirious, in typical diabetic coma. Temperature 96.8°, pulse 97, respiration 36. Otherwise appearance and examination as before.

In addition to the usual urinary reactions, it was found that the CO₂ capacity of the plasma was 14 per cent, and the total acetone of the plasma 54.5 mg. per 100 cc. The stomach was washed out, and 20 cc. castor oil and 5 gm. sodium bicarbonate were given through the tube. A saline enema had little result. Sodium bicarbonate was continued in 5 gm. doses, so that 25 gm. had been taken by 6 a.m. The coma gradually became deeper. The temperature gradually rose to 100°, the pulse to 138, the respiration rate remained 36 to 38. Death occurred at 6:50 a.m. A blood sample taken shortly before death showed plasma bicarbonate 17 per cent and total plasma acetone 97.8 mg. per 100 cc.

Remarks.—With diabetes of this severity only imperfectly controlled by treatment, downward progress is inevitable. The case illustrates the necessity of prolonged and thorough hospital treatment if any results worth while are to be achieved in the severest diabetes, though it is possible that any dietetic method would have been inadequate to save this patient.

In connection with the rapid premortal rise of acetone bodies in the blood, the question may be raised whether this was due to the administration of alkali, and whether sodium bicarbonate was harmful in this case. Similar premortal increase of circulating acetone has been observed in patients receiving no alkali.

CASE NO. 73.

Female, age 3 yrs. American. Admitted Dec. 18, 1916.

Family History.—Negative except for glycosuria in a paternal grandfather.

Past History.—Entirely healthy life; no known infection. Habits normal.

Present Illness.—About 1 year ago, thirst and loss of weight attracted notice, and the patient then received fasting treatment for 3 weeks in a hospital under the best care (Dec., 1915). Glycosuria was abolished and the tolerance was high, so that she was finally able to take 46 gm. protein, 24 gm. carbohydrate, and 1000 calories. Only occasional traces of glycosuria appeared on this diet at home until Oct., 1916. Since then glycosuria has occurred every 3 or 4 days, despite increasing strictness of diet. The diet before entry contained 25 gm. protein, 5 gm. carbohydrate, and 430 calories.

Physical Examination.—Height 88.6 cm. A poorly developed, emaciated, pale and pinched looking child, without acute symptoms. Mouth and throat normal.

Abdomen slightly distended, but soft. No lymph node enlargements. Examination otherwise negative.

Treatment.—Glycosuria was very slight and the ferric chloride reaction negative. The traces of sugar persisted, however, not only on 25 gm. protein and 420 calories but even on 20 gm. protein and as little as 250 calories. In a tolerance test with green vegetables, increasing by 5 gm. carbohydrate daily, glycosuria was absent with 20 gm., but appeared with 25 gm. carbohydrate. With gradual undernutrition the food tolerance rose slightly, and the patient was discharged on Apr. 7, 1917, free from diabetic symptoms but not otherwise improved.

Acidosis.—By reason of the former treatment, this was never present. The plasma bicarbonate was normal, and the ammonia nitrogen on carbohydrate-free diet was about 0.084 to 0.42 gm. daily, with total nitrogen output of some 3 to 5 gm.

Blood Sugar.—This was 0.245 per cent at admission, and was not appreciably affected by treatment, even though freedom from glycosuria was achieved.

Weight and Nutrition.—Weight at admission 9.8 kg., at discharge 8.9 kg. With gradual undernutrition the patient became able in Jan. to take a diet of 22 gm. protein and 350 calories. It gradually became possible to increase this and also to introduce carbohydrate, so that she was discharged on a prescribed diet of 28 gm. protein, 7.5 gm. carbohydrate, and 550 calories (3.2 gm. protein and 62 calories per kg., reduced by weekly fast-days to 2.7 gm. protein and 53 calories average). The carbohydrate was in the form of milk, and no reckoning was made of the 300 gm. thrice cooked vegetables. The child showed no injury from the 0.9 kg. loss of weight while in hospital, but on the other hand was no stronger, and remained pale and puny, fairly comfortable, yet with her mind fixed on her diet, like a severely diabetic adult.

Subsequent History.—Only rare traces of glycosuria have occurred at home. There has been no sign of downward progress; neither has there been improvement in tolerance, or anything resembling normal development. The small patient merely leads an existence of semi-invalidism. She has recently been readmitted, and the blood sugar brought to normal by the method described in Chapter II. It is of interest that this was possible in a case of such extreme severity, but the ultimate result is still doubtful.

Remarks.—The case is one of the severest and most hopeless examples of juvenile diabetes. There has been no improvement in assimilation. The ability to remain free from glycosuria on a higher diet than at admission has merely been purchased at the price of the slightly reduced weight. With regard to the question of "spontaneous downward progress" in children, it is instructive to note what a great loss of tolerance took place within 10 months on high caloric diet, while no downward progress has been perceptible in the past 10 months on low diet, even though the diabetes in the latter period is at a much more severe stage than before.

CASE NO. 74.

Male, unmarried, age 23 yrs. American; plumber. Admitted Feb. 1, 1917. *Family History*.—Mother died from an operation of unknown character. Father and two brothers are well. No diabetes or other heritable disease known in family.

Past History.—Thoroughly healthy life. Never ill to his knowledge, even with childhood diseases. Appetite, diet, digestion, and bowels normal. No alcohol; moderate tobacco. Never had a medical examination before.

Present Illness.—1 year ago began weakness and excessive thirst. He consulted a physician within a month but received only a very lax diet slip. 7 months ago he was forced to give up work and has continued to grow weaker. He has lost about 45 pounds in all.

Physical Examination.—Height 173.8 cm. A rather poorly developed, emaciated young man. Skin dry and pale. Perceptibly but not seriously drowsy. Mouth and throat normal. Knee jerks absent. Wassermann reaction negative. General examination negative.

Treatment.—Fasting was begun immediately and continued Feb. 1 to 4 inclusive. 10 and 20 gm. carbohydrate were tolerated on Feb. 5 and 6, but 30 gm. caused glycosuria on Feb. 7, which increased with 40 gm. on Feb. 8. Thereafter the diet was rather rapidly built up, and on 60 gm. protein and 1100 calories there was decided improvement in general condition. In another green vegetable period beginning Mar. 19, 100 gm. carbohydrate were tolerated without glycosuria. The weight at this time was down to 40 kg. The improvement continued on an increased diet of 65 gm. protein, 10 gm. carbohydrate, and 1450 calories. The patient was discharged on Apr. 27, 1917, much improved, though still not strong enough to return to his regular work.

Acidosis.—The plasma bicarbonate of 36 per cent at admission rose steadily without the aid of alkali to 55 per cent on Feb. 3, 57 per cent on Feb. 5, and 73 per cent on Feb. 8. Thereafter it remained at a high normal level. Ammonia determinations were not made at first, so the highest ammonia nitrogen observed was that of 2 gm. on Feb. 5. The ferric chloride reaction of the urine was only slight at admission, diminished to traces on the first fast-day, and thereafter was negative. Nevertheless, the ammonia nitrogen remained stubbornly elevated, frequently as high as 1.5 gm. daily, except for a fall as low as 0.45 gm. during the second carbohydrate test. At discharge it was still 0.8 to 1.4 gm. daily. The ammonia excretion was therefore the most delicate index of acidosis and at the same time evidence of an unduly high fat ration.

Blood Sugar.—The sugar in the plasma was 0.377 per cent at admission, 0.290 per cent on the morning of the second fast-day, and thereafter gradually diminished to its lowest level of 0.137 per cent at the last analysis on Apr. 14. These values obtained mornings before breakfast showed that the hyperglycemia was inadequately controlled, though the tendency was in the right direction.

Weight and Nutrition.—Weight at admission 43.6 kg. Lowest weight 40 kg. The diet of 65 gm. protein, 10 gm. carbohydrate, and 1450 calories at discharge thus represented 1.5 gm. protein and 33 calories per kg., diminished by the weekly fast-days to 1.3 gm. protein and 28 calories average.

Subsequent History.—The patient contracted a cold with heavy cough 3 days after leaving hospital. He adhered to his diet and remained free from glycosuria, but cough and weakness increased. He returned to report on May 29, 1917, and was immediately readmitted.

Second Admission.—The patient was more emaciated and much weaker than before. Weight 38.6 kg. Sugar and ferric chloride reactions negative; CO₂ capacity of plasma 64 per cent. He was kept in hospital until June 13, and on carbohydrate-free diet of 75 gm. protein and 1500 calories showed neither glycosuria nor dangerous acidosis. The ammonia excretion was about 1 gm. daily. The temperature during the first 4 days in hospital was 102 to 103° F., thereafter 101°. Cough persisted. Physical examinations revealed nothing in the right lung beyond fine moist râles at the base. Over the left lung there was dulness from the apex to the fourth rib in front, to the fifth interspace in the axilla, and to the middle part of the infraspinous region behind, with bronchial breathing and coarse and fine moist râles. X-ray plates and the finding of tubercle bacilli confirmed the diagnosis. As such a patient could not be kept long, he had to be moved on June 13 to a public hospital, and died on July 3.

Remarks.—The susceptibility of diabetic patients to tuberculosis is well known, and this patient's weakened condition doubtless impaired his resistance to the disease. The slight or absent influence of the infection and fever in producing glycosuria or acidosis is noteworthy. With tuberculosis of this grade and such severity of diabetes, the prognosis was necessarily hopeless.

CASE NO. 75.

Male, unmarried, age 33 yrs. Irish Canadian; teamster. Admitted Feb. 21, 1917.

Family History.—Father died at 65, cause unknown. Mother alive, aged 60. Three brothers and two sisters are well. As far as known, a perfectly healthy family of laboring class.

Past History.—Measles and mumps in childhood. Never ill since. Venereal denied. Patient is slight in build, but tough and wiry. Has lived rough outdoor life with heavy work as a teamster in Hudson Bay district. Thus had a very high caloric diet, but well balanced. He has taken 5 or 6 drinks of whisky or beer daily.

Present Illness.—In June, 1914, patient noticed polydipsia and polyuria without polyphagia. Principal trouble was that all his teeth loosened and fell out. Since then he has been most of the time under fasting treatment at the Victoria General Hospital at Halifax. He has been kept alive for this time, but the normal weight of 130 pounds has fallen to 89 pounds. He was referred to this Insti-

tute because of the great severity of his case, making it almost impossible to keep him sugar-free on any living diet.

Physical Examination.—Height 162.4 cm. A short, slight, small-boned young man, extremely emaciated, but still cheerful, alert, and with a look of strong constitution and unlimited resisting power. He still shows indications of his former weather beaten life and sinewy musculature. There is a peculiar icteric tinge to the skin of the face and thorax, while conjunctivæ are clear. Hair thin and dry. Teeth missing. Throat normal. Blood pressure 110 systolic, 80 diastolic. Knee jerks not obtainable even with reinforcement. Examination otherwise negative.

Treatment.—He made the trip from Halifax to New York in this condition unattended, and had the misfortune to be detained for a week by the immigration officials. As he could not during this time receive suitable treatment, it was advised that he be fed protein and carbohydrate with as little fat as possible. Consequently, he finally arrived at the hospital with heavy glycosuria, but with no acidosis beyond a trace of ferric chloride reaction. On an observation diet of 50 gm. protein, 10 gm. carbohydrate, and 600 calories, glycosuria remained heavy. Fasting was therefore begun on Feb. 23. Glycosuria ceased in 3 days, but the fast was continued for 5 days. The tolerance was evidently too low to make an attempt at a carbohydrate test worth while. Accordingly, the first food (Feb. 28) consisted of two eggs, with coffee, soup, bran, and 300 gm. thrice boiled vegetables. This diet was increased until on Mar. 8 glycosuria appeared on 60 gm. protein and 800 calories. The patient is still in the hospital, and the tolerance has gradually improved under treatment, so that he has sometimes for brief periods taken diets as high as 95 gm. protein and 3200 calories (fat and alcohol) with little or no glycosuria. The opportunity has been taken of shifting the diet in various ways for experimental purposes. The data are partly given in Chapter VI.

Acidosis.—This has remained absent, except as slight ketonuria has been deliberately produced and abolished at times in the course of experiments.

Blood Sugar.—Hyperglycemia, though not excessive (0.2 to 0.3 per cent) proved stubborn, as usual in such a case. It has been more marked when the true tolerance was experimentally exceeded. Nevertheless, it has since been shown that the plasma sugar even in this case can be brought fully to normal (0.066 to 0.11 per cent). Whether it can be made to remain so and whether the clinical result will be beneficial is an important question.

Weight and Nutrition.—The weight at entrance was 37.6 kg. Under treatment, it touched a minimum of 33.4 kg. on Mar. 20. It has since been possible to increase the weight to 38.8 kg. with no more than faint glycosuria (Aug. 14, 1917), but it will again be reduced therapeutically. There has been no perceptible edema. The diet has varied widely for experimental reasons, but has never included more than 20 gm. carbohydrate. The above mentioned high diets must be understood as only brief and experimental, and clearly injurious if continued. In general the diet is a low maintenance ration in proportion to the emaciated condition.

Remarks.—The absence of knee jerks is supposedly attributable to neuritis or some other nervous disorder, for, in contrast to the rule with most emaciated diabetics, the muscles are not relaxed in this patient. He has remained clinically the same as at admission, always cheerful and alert, always feeling a little hungry and sometimes decidedly so, and as active as the fuel value of his diet permits. He is thus up and about all day long, occupied with reading or other recreation, and able to go on walks and visits outside the hospital when desired. He cannot live outside an institution, partly on account of lack of education. The diabetes is in the extreme stage where true recovery of assimilation has never been known to occur. But during 9 months in hospital there has been not the slightest indication of "spontaneous downward progress."

CASE NO. 76.

Male, age 4 yrs. American. Admitted Mar. 9, 1917.

Family History.—A maternal grandaunt and cousin had diabetes at the time of their deaths, aged 55 and 60 years respectively. The family history is otherwise negative for heritable disease. Parents and three older brothers of patient are well.

Past History.—Normal birth. Breast fed for 9 months; always perfectly healthy, mild whooping-cough being the only disease ever suspected. He took a prize as a most perfect baby a year or so before onset of diabetes.

Present Illness.—An earache occurred on Feb. 17, 1917. A physician found the temperature 103° F. With simple warm applications the pain promptly subsided, and the ear has been normal since. On Feb. 22 the boy, still appearing and feeling entirely well, was target shooting with his father, and intense polyuria was noticed, the father saying that the boy urinated every 15 minutes. He was immediately taken to the family physician, who made no diagnosis, but the father is convinced that the urine was tested only for albumin. In addition to intense polydipsia and polyuria, rapid loss of flesh was noticed, though the amount was not determined by weight. As the family physician continued to make light of the trouble, the father insisted on taking the boy on Mar. 6 to a New York pathologist, who found glycosuria of about 8 per cent and positive acetone reactions, and gave a prognosis of only a few months of life. The family physician then prescribed an antidiabetic diet with some oatmeal, and 2 days later the boy was brought to this hospital.

Physical Examination.—Height 106.6 cm. The child is an admirable physical specimen, fully developed and still well nourished, handsome, but with a pale waxen beauty and listless apathetic behavior which augur badly. Axillary and epitrochlear glands palpable. Reflexes lively. Blood pressure 90 systolic, 70 diastolic. Wassermann reaction negative. Physical examination normal.

Treatment.—The urine at admission showed only slight sugar and ferric chloride reactions. Fasting was begun immediately. The sugar immediately fell too low to titrate, and was absent after 24 hours. After 2 days of fasting a carbohydrate tolerance test was begun. On Mar. 21, 82.5 gm. carbohydrate were taken with-

out glycosuria, but 90 gm. on the next day resulted in glycosuria. A mixed diet was then gradually built up, and the patient showed no more glycosuria up to his discharge on May 8, 1917.

Acidosis.—This was limited to slight ferric chloride reactions, and ammonia excretion of 1.16 gm. daily. There were no clinical symptoms or lowering of the plasma bicarbonate. During the carbohydrate tolerance test the ammonia output fell as low as 0.05 gm., and there was no further evidence of acidosis.

Blood Sugar.—The usual hyperglycemia was present at admission. In subsequent treatment the blood sugar was made and kept normal throughout.

Weight and Nutrition.—Weight at admission 15 kg., at discharge 14.4 kg.; *i.e.*, undernutrition to the extent of 0.6 kg. altogether. The diet was gradually built up to 50 gm. protein, 65 gm. carbohydrate (25 gm. in milk, 30 gm. in bread, the rest in vegetables), and 900 calories. This represented nearly 3.5 gm. protein and 63 calories per kg., diminished by the weekly fast-days to about 3 gm. protein and 54 calories per kg. The child still appeared normal and well nourished but remained somewhat depressed.

Subsequent History.—The patient lived his regular normal life with the other children at home, spending most of every day in lively outdoor exercise. With this his strength and spirits improved while the urine tests, in four periods every day, remained continuously negative for sugar. Perhaps on account of the exercise the weight remained stationary. He seemed to be in favorable condition and steadily improving, and was readmitted to hospital on Sept. 12, 1917, solely for observation. One noteworthy feature of both earlier and later stages of the history has been the occurrence of occasional digestive upsets from slight or unknown causes. The question of pancreatitis is open.

Second Admission.—Height 107.5 cm.; *i.e.*, a growth of 0.9 cm. since first admission. Weight 14.7 kg.; *i.e.*, a gain of 0.3 kg. since discharge. On his prescribed diet the blood sugar was normal (0.067 to 0.099 per cent) in repeated tests, both fasting and at different periods of digestion. A carbohydrate tolerance test by the usual method resulted in a trace of glycosuria only with 250 gm. carbohydrate. It is not fully certain that improvement to this degree had actually occurred, for it is possible that the 90 gm. taken in the former test may not have represented the true limit of tolerance at that time. The patient was discharged Oct. 16, 1917, weighing 14.4 kg. (the same as at the former discharge) with both urine and blood normal in all respects. The prescribed diet was 55 gm. protein, 80 gm. carbohydrate, and 980 calories, representing 3.8 gm. protein and 68 calories per kg., diminished by weekly fast-days to about 3.3 gm. protein and 58 calories average. This diet is permitted with the idea of permitting the boy to grow if possible. A close watch is being kept, and any appearance of slight hyperglycemia will be the signal for a reduction of diet. The carbohydrate has since been increased to 100 gm., and the child is growing steadily, the blood sugar remaining normal.

Remarks.—The case was received at a favorably early stage, and the treatment has been followed with the utmost fidelity. The result in this 4 year old patient is favorable to date.

CHAPTER IV.

PANCREAS FEEDING.

Since so many factors, dietary, psychic, and others, influence the glycosuria in most cases of diabetes, the only valid material for testing the specific influence of any therapeutic agent must consist of cases in which the food tolerance is accurately known under exact dietetic management for considerable periods of time. The use of drugs and other agencies credited with power to influence diabetes has never been supported by reliable tests of this character. Since diabetes is accepted as a deficiency of the internal secretion of the pancreas, and since a few other internal secretory deficiencies can be more or less compensated by administering preparations of the organ in question, the attempt to supply the internal pancreatic secretion in this manner has appealed to investigators since the time of von Mering and Minkowski. Such attempts have uniformly failed in both animals and patients. It seemed worth while, if only for the sake of negative results, to make a few tests with the administration of fresh pancreas to patients whose assimilative power was accurately known. As pancreas preparations are toxic when administered parenterally, the fresh gland was given by feeding.

By reference to the graphic chart of patient No. 1 (Chapter III) it will be seen that diets of 75 to 100 gm. carbohydrate and 40 to 60 gm. protein had been tolerated in May and June without glycosuria, or with only small quantities of glycosuria toward the close of June as the calories were increased by addition of fat. Pancreas feeding was tried for a week, following the fast-day of July 9. The diet was the same as during the previous 2 months; *viz.*, nothing but vegetables with the addition of a little cream, butter, or bacon on certain days. The calories were thus kept very low and the only protein, aside from that of the green vegetables, was in the form of pancreas. This consisted of 100 gm. pancreas on July 10, 150 gm. daily on July 11-12, and 200 gm. daily on July 13-14. The pancreas was obtained fresh

from the slaughter house each day, so that the first portions were eaten only a few hours after killing, and that taken at supper was still less than 12 hours old. The pancreas was kept on ice except during the messenger's trip, and was served raw with vegetables in the form of a salad. It can be seen from the graphic chart that glycosuria was absent with 80 gm. carbohydrate on July 10 and with 117 gm. carbohydrate on July 11. On July 12, with 143 gm. carbohydrate, there was glycosuria of 9.59 gm.; on July 13 with 92 gm. carbohydrate a glycosuria of 5.54 gm.; on July 14 with 83 gm. carbohydrate, a glycosuria of 7.39 gm. This record may be compared with that of the preceding 2 months. For example, on May 23, 140 gm. carbohydrate had been taken without glycosuria, and the total calories on that day were higher than on any day during the pancreas period. There was also no subsequent improvement of tolerance, owing to the week of pancreas feeding, because, beginning July 16, diets somewhat lower in carbohydrate, but with the addition of considerable fat, soon brought on continuous glycosuria.

Patient No. 4, a 12 year old boy, developed a liking for raw pancreas, and the opportunity was taken to carry out several feeding tests. One series is described in detail in his history (Chapter III), and the conclusion was there drawn that the pancreas did not improve the carbohydrate tolerance to the extent of a trivial quantity of sugar, and did not improve the protein tolerance to the extent of one egg. Another test was undertaken in August and September. It will be seen in the graphic chart (Chapter III) that there was a gradual increase of carbohydrate-free diet beginning August 26. This diet consisted of eggs, steak, olive oil, butter, and whisky, with no vegetables or other food. It will be noted that sugar and ferric chloride reactions remained negative until the diet reached 58 gm. protein and 1300 calories on August 30. Ferric chloride reactions then developed, followed by glycosuria of 0.75 gm. on September 1. The glycosuria and ketonuria were continuous on the following days, until checked by the alcohol days of September 5 and 6. Beginning September 7 a similar carbohydrate-free diet was resumed, which on September 8 and 9 amounted to 60 gm. protein and 1600+ calories. On September 10, 100 gm. pancreas were substituted for the former 100 gm. beefsteak. This happened to be the day on which a glycosuria of

0.32 gm. appeared. The pancreas was continued in the same quantity on the subsequent days, and it is seen that glycosuria was continuous. Also the ferric chloride reactions were actually heavier than before, due doubtless to the gradual impairment of tolerance. It was necessary on September 16 to stop this diet, and then two alcohol days were inadequate to clear up this glycosuria and ketonuria which had developed on pancreas feeding. Beginning September 18, very low diets, generally below 500 calories daily, were employed, and the attempt was made to compare successive days of pancreas and steak feeding. The results were interfered with because during this time the patient obtained small quantities of food surreptitiously. All that can be said is that these tests, which continued up to September 27, showed no perceptible advantage of the pancreas. What is certain is that even on these very low diets the pancreas feeding did not avail to prevent glycosuria from even a few grams of bird-seed eaten by stealth.

The possibility was also considered that some portion of the benefit in the way of improved assimilative power from fasting might be due to the digestive rest involved. For example, it might be supposed that the internal secretory function of the pancreas is more or less inhibited during activity of the external secretory process, while perhaps the nervous, secretory, or glandular condition during the resting state of the acinar tissue might be most favorable for the internal secretory function. Inasmuch as the special stimulus to the formation of pancreatic juice is furnished by the hydrochloric acid of the stomach, experimental or practical results might be hoped for by administering food in some way which would not call forth acid secretion in the stomach. Since rectal or parenteral feeding did not appear promising, a trial was made with a tube like an ordinary Einhorn duodenal tube, but over one meter in length, so that food might be delivered through it to a point low enough in the intestine to avoid regurgitation into the stomach if possible, yet high enough up to permit favorable absorption. Patient No. 8 was chosen as a suitable subject. The method of procedure consisted in his swallowing the tube slowly in the morning; after 2 or 3 hours the tube was generally found in proper position for the first feeding, and was retained until bedtime. The patient was very little inconvenienced by the presence of the tube. The position of the tube was tested in various ways:

TABLE I.
Patient No. 8.

Date.	Diet.							Urine.				Remarks.
	Protein.	Fat.	Carbohydrate.	Alcohol.	Calories.	Sodium bicarbonate.	Weight.	Volume.	Sugar.	Total nitrogen.	NH ₄ .	
	gm.	gm.	gm.	cc.		gm.	kg.	cc.	gm.	gm.	gm.	gm.
1914												
Dec. 6....	67	198	—	50	2462	3	44.4	1960	0	7.32	0.29	—
“ 7....	89	289	—	33	3277	3	43.4	2262	0	11.20	0.68	1.74
“ 8....	89	289	—	20	3190	3	42.8	1825	0	10.70	1.05	0.82
“ 9....	88	289	10*	25	3252	3	42.8	940	++++	5.94	0.71	0.36
Dec. 10....	—	—	50*	70	695	3	42.4	670	++++	3.36	0.24	0.28
“ 11....	87	253	—	25	2884	3	43.2	623	++++	7.35	0.42	0.33
“ 12....	Fast-day	—	—	70	490	3	43.4	2091	1.47	5.95	0.14	—
“ 13....	89	289	—	20	3190	3	42.4	852	1.70	—	0.32	—
“ 14....	60	192	—	55	2418	3	42.8	1317	4.37	9.62	0.69	—
“ 15....	Fast-day	—	—	70	490	3	42.6	2255	1.09	6.80	0.36	—
Dec. 16....	45	152	—	48	1926	3	42.6	1225	0	5.90	0.26	—
“ 17....	89	264	—	20	2957	3	42.8	1272	0	2.49	0.57	2.34
Dec. 18....	82	233	—	20	2645	3	42.4	1162	0	10.50	1.15	0.76
“ 19....	67	146	44.0	28	2005	4	42.4	2423	21.78	10.28	1.50	0.70
“ 20....	45	132	—	50	1758	2	42.2	1106	8.55	8.50	1.25	—

Eggs and olive oil by tube. Whisky by mouth.

Diets eaten.

Tube feeding, except whisky.

Tube feeding, (except whisky) with 14 gm. pancreatin daily.

Dec. 21.....	15	61	—	75	1139	—	42.8	775	+	4.95	0.56	—
" 22.....	35	96	—	70	1524	—	42.0	495	0.62	5.25	0.84	—
" 23.....	18	79	—	68	1217	—	42.8	1370	0.44	—	1.42	—
" 24.....	45	152	—	75	2119	—	42.2	1605	0	—	1.17	—
" 25.....	60	202	—	68	2608	—	42.4	1260	0	6.44	1.22	—
" 26.....	45	152	—	50	1944	—	42.2	945	+	—	—	—
" 27.....	45	152	—	35	1839	—	41.8	1095	0	6.70	1.78	—
" 28.....	45	152	—	30	1804	—	41.4	495	0.50	—	1.25	—
" 29.....	15	51	—	70	1021	5	41.4	500	+	4.80	0.98	—
Dec. 30....	141	210	—	80	3091	6	42.6	1260	0.45	5.30	1.23	—
" 31....	29	40	—	75	1016	15	42.4	1465	3.52	6.46	1.37	—

Diets eaten.

Tube feeding (except whisky), with pancreas mixture.

* Caramel.

by fluoroscopic examination for the olive or injected bismuth paste; by the character of the fluids aspirated; by the absence of the feeding mixture from the stomach when the tube was withdrawn after the last feeding; by the fact that air injected with the olive in the stomach was soon belched up, whereas with the olive in the intestine it was before long passed by rectum; and, to some extent, by the sensations of the patient.

The mixture used for feeding consisted of an emulsion of eggs, olive oil, and small quantities of sodium bicarbonate. On other days the patient drank these same foods in the raw condition for comparison with the results of tube feeding. Whisky was never given through the tube but was always drunk in 10 cc. doses at intervals during the day. This allowance of whisky could not impair the results, since whisky used during fasting does not spoil the benefit of fasting. Some details are supplied by Table I and in the graphic chart (Chapter III).

It was evident that the feedings by tube did not cause glycosuria to such an extent as lower diets taken by mouth, but weight was lost, the patient was markedly weaker, the urinary nitrogen did not correspond to the protein administered, and the feces though formed, were unduly bulky, so that it seemed probable that the results were due to poor absorption of the food given by tube. Accordingly, on December 18 similar emulsions were given freshly mixed with powdered commercial pancreatin. Acidosis was manifested not only by the ammonia nitrogen above 1 gm. (notwithstanding the alkali dosage) but still more by weakness and malaise on the part of the patient. Accordingly on December 19, oatmeal gruel representing 44 gm. carbohydrate was added to the feeding mixture, with a view to testing both the assimilation of carbohydrate administered by tube and the possibility of any special virtues of oatmeal. Heavy glycosuria promptly resulted, the ammonia excretion slightly increased, and a period of undernutrition was necessary to clear up the symptoms. On December 30–31 the tube was retained by the patient both day and night for the purpose of maximal feeding. Only two eggs were given on December 30 and none on December 31; otherwise the feedings consisted of olive oil emulsified with 5 gm. pancreatin and large quantities of extract of fresh pancreas. Over 2 kilograms of pancreas were used for this purpose. The glands

from cattle were obtained within a few hours after slaughtering, minced in a meat grinder, and then subjected to a pressure of 4000 pounds per square inch in a hydraulic press. The thick, almost pulpy extract thus obtained was diluted slightly with water, and partly used fresh. The solid residue of the glands was incubated with water, olive oil, and a trifle of sodium bicarbonate, and pressed again after digestion. The emulsion of this material was also administered by tube. Glycosuria and acidosis persisted, though apparently absorption of the material was poor. This large feeding caused only diarrhea without benefit, and the experiment was therefore discontinued.

The experiments with feeding fresh pancreas confirm the accepted view that it possesses no value in diabetic treatment. As far as a conclusion is possible from the experiments with tube feeding, they indicate that there is no benefit in this method. There is no evidence that simple avoidance of the production of hydrochloric acid in the stomach, or of stimulation of the external secretion of the pancreas, has any influence upon either glycosuria or acidosis in diabetes.

CHAPTER V.

EXERCISE.

The existing literature may be summarized as having led to conclusions as follows: that in normal persons, moderate exercise slightly elevates the blood sugar while severe exercise lowers it, but in either case the sugar tolerance is increased; that in mild diabetes, exercise may elevate the blood sugar even more than normally, but nevertheless the carbohydrate tolerance is raised; while in severe diabetes, exercise can no longer improve tolerance and must be avoided because of exhaustion of the patient and dangerous increase of acidosis. The onset of coma after slight or severe exertion has especially been known and dreaded.

The use of exercise in the present work was based upon experiments on dogs, which were carried out with the necessary completeness and controls, and will be published in detail in the near future. Though circumstances prevented carrying out corresponding comprehensive tests upon patients, nevertheless exercise has been employed for the past 2 years as part of the treatment of diabetic cases, most of them severe beyond the degree formerly considered to contraindicate exercise. A few definite experiments were conducted at the outset, and some empirical experience has been gained since. The observations may be grouped under the following four heads:

- A. Immediate effect of exercise on blood sugar.
- B. The effect upon carbohydrate tolerance and glycosuria.
- C. Its use in various classes of patients.
- D. The more permanent effects upon assimilation and the diabetic condition.

A. THE IMMEDIATE EFFECT OF EXERCISE ON THE BLOOD SUGAR.

Observations on Patient No. 18.

This patient represented the early mild stage of potentially severe diabetes. By reference to the graphic chart (Chapter III), it will be noted that the test with vegetables alone, ending August 4, showed a

tolerance above 350 gm. carbohydrate. On August 6, a mixed diet was begun of 100 gm. protein, 100 gm. carbohydrate, and 2600 calories. Beginning August 10, carbohydrate was gradually substituted for fat until 170 gm. carbohydrate were taken, which caused no glycosuria on August 12 but a trace on August 13. After the fast-day of August 14, the increase of carbohydrate was continued up to

TABLE I.
Patient No. 18.

Date.	Blood.					Urine.		Body temperature.
	Blood sugar.	Plasma sugar.	Corpuscle sugar.*	Hemoglobin.	Corpuscle.	Sugar.	FeCl ₃ reaction.	
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>			<i>°F.</i>
<i>1915</i>								
Aug. 19 (rest) 2:20 p.m.	0.256	0.213	0.286	—	—	++	++	
8:00 p.m.	0.250	0.250	0.250 (calc. 0.244)	100	37.0			
Aug. 20 (exercise) 10:00 a.m.	0.150	0.156	0.133	100	—	0	+	98.2
10:50 a.m.	0.100	0.105	0.093 (calc. 0.094)	108	42.8			100.6
2:20 p.m.	0.099	0.116	0.100 (calc. 0.075)	105	41.2			100.4
8:00 “	0.222	0.238	0.182 (calc. 0.197)	110	39.7			98.8
Aug. 21 (exercise) 10:00 a.m.	0.111	0.111	0.109 (calc. 0.111)	100	41.5	0	+	98.6
10:50 a.m.	0.098	0.080	0.115 (calc. 0.120)	105	44.8			99.9

* The top figures for corpuscle sugar in all the tables are those obtained by direct analysis. The figures in parentheses are those calculated from the relations of whole blood and plasma.

200 gm. on August 18. With this, slight glycosuria appeared, and continued on August 19. Keeping the diet unchanged, the following observations were made.

No breakfast was taken. The two meals were eaten at fixed hours, 12:45 to 1:20 p.m. and 5:30 to 6 p.m. daily. It will be noticed in Table I that the diet with 200 gm. carbohydrate had produced a

marked hyperglycemia, in blood samples taken 1 hour after lunch and 2 hours after supper on August 19, the patient having been up and dressed but otherwise as quiet as convenient up to this time. Under the dietary conditions stated, the hyperglycemia could safely be expected to continue or probably to increase. On August 20, without food, the boy exercised between 10 and 10:50 a.m. to the limit of strength, running up and down 80 flights of stairs and walking briskly between times. He then rested and took food as stated. During the hour after lunch (1:20 to 2:20 p.m.) he performed the hardest exercise of the day, and continued with only short rests until supper time, the afternoon's work amounting to 160 flights of stairs and almost continuous brisk walking between. No exercise was performed after supper. On August 21, exercise was performed between 10 and 10:50 a.m., comprising 88 flights of stairs and walking as usual.

Each flight of stairs counted includes both ascent and descent. A flight was composed of 24 steps, each 16 cm. high. The boy ran rapidly up and down, and by walking between times avoided stopping for rest. He was strong and active, and though considerably tired by the exertions, was never exhausted and always felt able to do more.

It is evident from the table that violent exercise stopped the existing glycosuria and markedly lowered the blood sugar.

Ketonuria, as far as could be judged by the ferric chloride reaction, diminished rather than increased. This reaction alone is obviously not a safe index. The possible alterations in blood bicarbonate were not studied; but if there was a lowering it was evidently soon restored by rest, for a single determination at 8 p.m. on August 20 showed 63.6 per cent.

Exercise concentrated the blood, as indicated by the higher hemoglobin (Fleischl-Miescher) and hematocrit readings. Sugar analyses were performed directly upon the corpuscles, after 15 to 20 minutes centrifugation at 3000 revolutions per minute. These furnish interesting controls, but are subject to errors, on the one side from adherent plasma, on the other side from possible imperfect laking of the corpuscle mass in analysis; so that the calculated values are to be preferred. No special effect of exercise is apparent upon the distribution of sugar between plasma and corpuscles. If there was, for example, any such thing as a longer retention of sugar in the

corpuscles than in the plasma, equilibrium evidently was reached within an hour, for analyses an hour or more apart failed to reveal any such phenomenon. There was no tendency to any special elevation of blood sugar after it had been lowered by exercise, neither was the lowering due apparently to mere delay in the absorption of food, for the blood sugar remained lower at 8 p.m. and on the following morning than after a day of rest.

After the morning experiment of August 21, the diet was abruptly made almost carbohydrate-free (only 5 gm. in vegetables daily). The patient continued at rest during the remainder of August 21 and throughout August 22. The hours of eating were as before. With this diet, slight but distinct ferric chloride reactions were continually present, but the blood sugar by the morning of August 23 was found normal. The graphic chart (Chapter III) shows some of the data, but omits the 30 gm. glucose which were taken on 4 days as follows:

August 23, the patient exercised 10 to 10:50 a.m. as described in Table II. Between 10:50 and 11 a.m. he ate 30 gm. Merck anhydrous glucose. Between 11 and 11:45 a.m. he did 64 flights of stairs, and between 11:45 a.m. and 12:45 p.m. 72 more flights, with the usual walking between. He rested for the remainder of the day.

August 24 was a rest-day. Between 10 and 10:10 a.m. the patient ate 30 gm. Merck glucose.

August 25, without exercise, the effect of low temperature was tested, the point being of interest in connection with three questions: (1) the hyperglycemia caused by cold environment according to reports in the literature; (2) the clinical impression that diabetics do better in warm weather and climates than in cold; (3) the conception of diabetes as a defect of general metabolism, and the influence of alterations in total metabolism upon the assimilative function. Accordingly, at 9:30 a.m. the patient entered a refrigerator room at a temperature of 45°F., and sat there quietly in a chair until 12:45 p.m. At 10 a.m. he ate 30 gm. glucose as usual. He was clad in thin summer underwear, light khaki coat and trousers, thin socks, and bathroom slippers. The change from the hot summer weather to the cold room was about as great as could be borne without serious discomfort or danger. The patient maintained muscular rest under orders. He was uncomfortably chilly, complained especially of cold

TABLE II.
Patient No. 18.

Date.	Blood.					Urine (24 hr.).		Body temperature. °F.
	Blood sugar. <i>per cent</i>	Plasma sugar. <i>per cent</i>	Corpuscle sugar. <i>per cent</i>	Hemoglo- bin. <i>per cent</i>	Corpuscle. <i>per cent</i>	Sugar.	FeCl ₃ reaction.	
Aug. 23 (exercise day) 10:00 a.m.	0.083	0.083	0.083 (calc. 0.083)	102	39.1	0	+++	98.0
10:50 a.m. Ate 30 gm. dextrose.	0.099	0.100	0.097 (calc. 0.096)	100	40.5			99.8
11:45 a.m.	0.154	0.200	0.143 (calc. 0.094)	92	43.6			99.8
12:45 p.m.	0.101	0.111	0.099 (calc. 0.081)	100	39.0			99.8
Aug. 24 (rest day) 9:15 a.m.	0.097	0.105	0.068 (calc. 0.077)	90	39.0	0	++	97.6
10:00 a.m. Ate 30 gm. dextrose.	0.097	0.099	0.092 (calc. 0.094)	88	36.0			
10:50 a.m.	0.192	0.222	0.178	—	—			
11:45 "	0.170	0.213	0.117 (calc. 0.090)	80	33.0			
12:45 p.m.	0.169	0.196	0.170 (calc. 0.123)	81	36.5			
Aug. 25 (low temperature) 9:15 a.m.	0.077	—	—	—	42.0	0	++	98.0
9:30 a.m. (entered cold room).								98.3
10:10 a.m. Ate 30 gm. dextrose.	0.100	0.103	0.095 (calc. 0.095)	90	41.6			
10:50 a.m.	0.164	0.196	0.116 (calc. 0.124)	90	45.0			97.5
11:45 "	0.175	0.196	0.149 (calc. 0.142)	85	38.0			98.0
12:45 p.m.	0.170	0.178	0.152 (calc. 0.175)	85	42.0			97.8
Aug. 26 (exercise day) 9:15 a.m.	0.091	0.096	0.090 (calc. 0.082)	103	40.0	0	++	98.4
10:00 a.m. Ate 30 gm. dextrose.	0.092	0.092	0.092 (calc. 0.092)	103	38.1			99.6
10:50 a.m.	0.143	0.156	0.127 (calc. 0.111)	103	34.2			100.0
11:45 "	0.095	0.095	0.095 (calc. 0.095)	100	38.7			100.5
12:45 p.m.	0.052	0.058	0.049 (calc. 0.043)	103	42.0			99.5
2:15 "	0.102	0.121	0.050 (calc. 0.066)	80	33.1			

feet, and shivered slightly toward the close of the experiment. He was comfortable immediately upon leaving the cold room, and went for a street-car ride after lunch.

August 26 was another exercise day. After the blood sample was taken at 9:15, the patient did 64 flights of stairs, with the usual walking, up to 10 a.m. Between 10 and 10:10 a.m. he ate the usual 30 gm. glucose. Then, between 10:10 and 10:50 a.m., he covered 72 flights of stairs; between 10:50 and 11:45, 72 more flights; between 11:45 a.m. and 12:45 p.m., another 72 flights. He then ate lunch as usual (12:45 to 1:20) and remained at rest thereafter. An additional blood sample was taken at 2:15 p.m., to give an idea of the behavior of the blood sugar after eating and rest on an exercise day.

The observations recorded in the table show the following effects of exercise in this case.

Blood Sugar.—The repression of hyperglycemia by exercise is very evident. No uniform law of distribution of sugar between plasma and corpuscles is discernible; if one gains or loses sugar in advance of the other, the process is not revealed under the conditions of the experiments.

Blood Volume.—The hemoglobin and hematocrit readings are rather irregular. It is known that these methods are subject to errors. Also discrepancies between the two, seemingly not accidental, are a not unusual experience in carrying out long series of parallel determinations; e.g., at 11:45 on August 23 the percentage of hemoglobin is diminished and the percentage of corpuscles increased. The impression obtained is that as the individual corpuscles were subject to change in volume. In general, the hemoglobin readings indicate slight dilution of the blood with hyperglycemia on August 23, 24, and 25. An opposite process must be borne in mind; viz., the concentration of the blood by exercise, as noted under Table I. These two processes may be expected to neutralize each other in varying degrees, and possibly at the same time to be associated with unknown changes in the volume of individual corpuscles. The one definite demonstration is that, as far as hemoglobin and hematocrit determinations can decide, the changes in blood sugar are not accounted for by simple dilution or concentration of the blood.

Body Temperature.—Slight elevation of temperature, up to 99.8°F., was produced by exercise on August 23, and up to 100.5° by the live-

lier exercise on August 26. In this respect the human experiments serve as a useful control to those on dogs. Since in the former the pyrexia is so slight and in the latter so extreme, while the repression of hyperglycemia and glycosuria is similar in both, the conclusion can be drawn that elevation of temperature is not the sole or essential cause of the improved utilization of sugar.

Acidosis.—Though the diet was poor in carbohydrate and rich in fat, and the heavy exercise must have depleted body glycogen considerably, no acidosis was produced in this diabetic patient to the extent of any clinical symptoms or any perceptible change in the ferric chloride reaction.

The Influence of Cold.—It appears that the environment of 45°F. raised the blood sugar from 0.077 to 0.100 per cent. Nevertheless it must be recognized that this level of blood sugar in the cold at 10 a.m. on August 25 is not significantly higher than that at summer temperature at 9:15 on the previous morning (August 24). The patient's body temperature was not appreciably affected. The differences in blood sugar after glucose ingestion on the two days are perhaps within the limits of accidental variation, especially since the possibility of a slight alteration of assimilation by repeated doses of glucose or by the continuance of carbohydrate-poor diet cannot be wholly excluded. If any real difference exists, it is in favor of the cold environment, and might indicate that increased muscular tone, shivering, and the stimulation of metabolism slightly facilitated sugar combustion. Though no harmful effect was here demonstrated, a brief experiment of this sort in no wise opposes the belief in a harmful influence of cold upon diabetes.

Observations on Patient No. 34.

This case represented a slightly more severe stage than the preceding, and the tolerance was somewhat lower. The diet consisted of 50 gm. protein, 20 gm. carbohydrate, and 1300 calories, taken in three meals, 7:30 to 8 a.m., 12:30 to 1 p.m., and 5:30 to 6 p.m. On this diet there was a decided tendency to hyperglycemia during digestion, as shown first by the blood sugar of 0.147 per cent at 3:05 p.m. on September 3. On this day a preliminary experiment was performed as shown in the table, and the marked lowering of blood sugar found at 4:10 p.m. must be attributed to the exercise.

TABLE III.

Patient No. 34.

Date.	Blood.						Urine.		Remarks.
	Sugar.	Plasma sugar.	Corpuscle sugar.	CO ₂	Hemoglobin.	Corpuscle.	Sugar.	FeCl ₃ reaction.	
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>			
1915									
Sept. 3									Blood taken after lunch at 12:30 p.m. 3:05 to 4:10 p. m. exercised, climbing 88 flights stairs, walking corridors between times.
3:05 p.m.	0.147			56.7	111	41.4	0	0	
4:10 "	0.100			38.5	111	41.4			
Sept. 12									No exercise; fast-day.
2:40 p.m.	0.128	0.139	0.128 (calc. 0.108)	56.7	97	36.1	0	0	
Sept. 13									No exercise.
Before breakfast.	0.105	0.121	0.105 (calc. 0.076)	52.3	96	36.1	0	0	
Sept. 14									No exercise.
11:20 a.m.	0.210	0.200	0.180 (calc. 0.228)	50.4	95	35.5	0	0	
2:40 p.m.	0.191	0.195	0.191 (calc. 0.184)	—	95	37.1			
5:20 "	0.200	0.195	0.211 (calc. 0.210)	53.8	92	34.0			
Sept. 15									Light work in forenoon. 11:20 a.m. to 12:20 p.m. Climbed 72 flights stairs and walked as usual. 12:20 p.m. Lunch. Rested until 1:50 p.m. 1:50 to 2:40 p.m. Climbed 80 flights stairs besides walking. 2:40 to 4:20 p.m. Rested. 4:20 to 5:20 p.m. Climbed 88 flights stairs and walked in addition.
11:20 a.m.	0.119	0.118	0.119 (calc. 0.090)	47.6	95	34.0	0	+	
12:20 p.m.	0.100	0.103	0.105 (calc. 0.097)	29.0	86	36.0			
2:40 "	0.105	0.105	0.102 (calc. 0.105)	42.2	85	37.0			
4:20 "	0.122	0.122	0.122 (calc. 0.125)	50.3	85	32.0			
5:20 "	0.100	0.091	0.118 (calc. 0.115)	37.6	86	33.8			

September 12 was a fast-day. It is seen that the high blood sugar was still persistent at 2:40 that afternoon, but by the following morning had come down to a high normal level. Marked hyperglycemia was present on the rest-day of September 14. On the next day after breakfast the patient was engaged in duties involving light continuous exercise, and an effect is apparent in the decidedly lower blood sugar found at 11:20 a.m. Thereafter, heavy exercise reduced the blood sugar to normal and held it there during the exercise periods, but during the resting period from 2:40 to 4:20 p.m. the tendency to hyperglycemia manifested itself plainly. The most striking feature of the experiment is the immediate lowering of blood sugar by exercise as compared with the slow reduction by fasting.

Acidosis.—The trace of ferric chloride reaction which appeared on September 15 is presumably attributable to the exercise, for this reaction had been negative for over a month preceding on practically the same diet. The plasma bicarbonate was reduced by exercise on each occasion. At 12:20 p.m. on September 15 it was down to 29 per cent, which is as low as in many patients close to coma; yet the dyspnea was very transient and the patient entirely comfortable, with none of the weakness, malaise, and other symptoms generally found in diabetic acidosis. With rest, the rise of blood bicarbonate was rather rapid but not immediate; for example, in the period of rest between 2:40 and 4:20 p.m. on September 15 the CO_2 capacity of the plasma rose from 42.2 to 50.3 per cent.

Observations on Patient No. 46.

From the history and graphic chart (Chapter III) it will be seen that this patient was a frail little man, whose diabetes, though only moderate in severity, was accompanied by weakness and prostration, more marked in the subjective feelings than in actual strength tests. Beginning September 1, this patient fasted (with whisky) through September 5. On September 6, 3 gm. carbohydrate were given, and on September 7, 6.5 gm. At this point, when the weak patient had been through practically 7 days of fasting, and glycosuria and acidosis had only recently subsided, he was subjected on September 8 to a day of exercise to the full limit of his strength. He could not run rapidly like the

TABLE IV.
Patient No. 46.

Date.	Diet.						Blood.						Urine.		Remarks.
	Total calories.	Protein.	Fat.	Carbohydrate.	Alcohol.		Sugar.	Plasma sugar.	Corpuscle sugar.	CO ₂	Hemoglobin.	Corpuscle.	Sugar.	FeCl ₃ reaction.	
	gm.	gm.	gm.	gm.	gm.	gm.	per cent	per cent	per cent	vol. per cent	per cent	per cent	gm.		
1915															
Sept. 8	236	4.3	1.0	12.7	22.5	0.161	0.154	—	50.0	118	35.2	0	0	2:30 to 3:30 p.m. 56 flights stairs; rested after 3:30.	
3:30 "						0.139	0.134	—	31.9	120	43.8				
4:30 "						0.179	0.182	0.137	39.5	117	41.0				
5:30 "						0.156	0.166	(calc. 0.180) 0.143	53.8	115	41.0				
Sept. 18					10.0	—	—	—	—	—	—	—	0	0	
Sept. 19	1147	99.6	42.4	50	20.0	—	—	—	—	—	—	—	0	0	
Sept. 20	1420	99.9	69.7	50	22.5	—	—	—	—	—	—	—	0	0	
Sept. 21	1640	100.0	96.2	50	20.0	—	—	—	—	—	—	—	+	0	
Sept. 22	1915	100.0	122.9	50	22.5	—	—	—	—	—	—	—	+	0	
Sept. 23	2200	100.0	153.6	50	22.5	—	—	—	—	—	—	—	++	0	
Sept. 24	2438	150.0	179.0	50	22.5	—	—	—	—	—	—	—	27.75	+	
Sept. 25															
9:40 a.m.	2687	100.0	206.0	50	22.5	0.244	0.371	0.200	59.4	109	42.0	2.77	+	9:40 to 10:50 a.m. Exercise. 10:50 a.m. to 12 m. Rest.	
10:50 "						0.161	0.193	0.143	42.2	111	42.0			Exercise to limit of strength continued afternoon and evening.	
12:00 m.						0.147	0.167	0.143	51.3	111	37.0			Total day's work 176 flights stairs and considerable walking.	

preceding patients, but he plodded faithfully up and down stairs and by sufficient exertion covered a surprising number of flights. The experiment was useful as a control to those upon diabetics of the severest type, because this patient was as weak as many of the latter. Also, the effect of marked strain and exhaustion was thus tested. These have been feared and warned against, as tending to injure assimilation and create serious danger of coma in patients with anything like a severe form of diabetes, and it was conceivable that there might be an actual influence of these factors, particularly through the nervous system. Also, from the standpoint of acidosis, it was of interest to observe the effect of exercise upon a patient who had recently had a considerable acidosis, whose plasma bicarbonate was still below normal, and whose glycogen reserves were supposedly depleted by glycosuria and fasting with only a trivial carbohydrate intake.

It is seen in Table IV that during the hour of exercise the blood sugar fell unmistakably, but in the succeeding hour of rest rose decidedly higher than at the outset. At the end of a second hour of rest it returned to near its original level. Therefore no benefit is perceptible from exercise at this stage of treatment. If exhaustion was possibly responsible for the hyperglycemia to any extent, it at least did no appreciable harm from the standpoint of acidosis. The ferric chloride reaction was negative. It is not improbable that the traces present on September 9 and 10 were due to this exercise on September 8. The plasma bicarbonate fell during the hour of exercise from 50 to 31.9 per cent, a figure generally indicative of severe acidosis; but there were no threatening symptoms and no distress beyond that of any very tired person. The CO_2 capacity then rose steadily, until after 8 hours of rest it was 53.8 per cent, or slightly higher than before the exercise.

Period from September 19 to 25.—In this period the patient was placed on a fixed ration of protein, carbohydrate, and alcohol, with daily increase in fat (see graphic chart). Starting with a total intake of 1147 calories on September 19, sugar and ferric chloride reactions were negative. A trace of glycosuria appeared with 1640 calories on September 21, and increased slightly with 1916 calories on September 22 and 2200 calories on September 23. Then, with 2438 calories on September 24, heavy glycosuria developed suddenly to the extent of

27.75 gm., and at the same time a faint ferric chloride reaction appeared. On September 25, the fat was still further increased to make 2687 calories, and exercise was employed to the limit of strength. The purpose of the experiment was to test the effect of exercise upon such a condition brought on by overfeeding with fat.

As shown in the table, there was a remarkable drop in glycosuria, down to 2.77 gm. The blood sugar fell in the exercise period 9:40 to 10:50 a.m. from 0.244 to 0.161 per cent, and then on resting till 12 noon fell further to 0.147 per cent. The patient was slightly stronger than before, but the factor of overstrain was still present. This in itself seemed to have no demonstrable importance. The initial blood sugar was higher than on September 8, but this was merely incidental to the diet. The actual diabetic condition was better in consequence of the longer treatment. The better assimilation was indicated by the far greater fall of blood sugar during exercise, and by the continued diminution during rest.

In Table IV, as in Table III, the hemoglobin and hematocrit figures permit no uniform interpretation, aside from the fact that the changes in blood sugar are not accounted for by changes in blood volume so far as these methods can reveal. Also it is not possible to distinguish any rule governing the distribution of sugar between plasma and corpuscles.

Though the condition had been produced by feeding fat, and the exercise presumably depleted the carbohydrate supply, there was no appreciable tendency to acidosis. The existing faint ferric chloride reaction was unchanged. The fall in the plasma bicarbonate from 59.4 to 42.2 per cent during the exercise period 9:40 to 10:50 is no greater than ordinary, and in the rest period up to 12 noon there was a rise as usual, up to 51.3 per cent. The patient recovered easily from his weariness and experienced no unpleasant symptoms.

The impression is given that the condition created by excessive calories was in large measure relieved by the increased combustion due to exercise. It is evident also that the same patient can react differently to exercise at different stages of treatment.

Observations on Patient No. 2.

This patient was an Italian girl aged 17 years, whose diabetes at the time of these observations was somewhat more severe than any of the preceding cases. At the same time her strength was such that she could carry on heavy muscular labor continuously without difficulty. Two new features were tested here: (1) a comparison of fast-days with and without exercise in a case of this severity; (2) the effect of heavy exercise upon the tolerance over a long period of time (8 months).

First may be mentioned the comparison of the two fast-days, September 12 and 16. The former was a day of practically no exertion. It may be that the slight activity and excitement of the street-car ride and visit were responsible for the slightly higher sugar in the afternoon, immediately after returning from the trip, as compared with the forenoon. The blood and plasma sugars before breakfast on September 13 were practically identical with those on the morning of September 12, showing no perceptible influence of the single fast-day toward reducing hyperglycemia. The regular diet being slightly in excess of the true tolerance, the plasma sugar on the morning of September 16 had reached 0.172 per cent, as compared with 0.139 per cent on September 12. It is observed that exercise on this day was effective in reducing the hyperglycemia, to 0.151 per cent in plasma at 10:50 a.m. and to 0.120 per cent at 12:10 p.m. But the patient bore the exercise on this fast-day badly, and was compelled to sit or lie down the entire afternoon. The sugar then rose to 0.128 per cent at 3:50 p.m. and to the notably high level of 0.220 per cent at 5:10 p.m. The symptoms of weakness and dizziness were characteristic of acidosis, and this was verified by the CO_2 capacity of the plasma. This fell as usual during the heavy exercise between 9:15 and 10:50 a.m., and rose somewhat as usual during the lighter exercise up to 12:10 p.m. Then, instead of rising with rest, it continued to fall as the blood sugar rose, so that at 5:10 p.m. the plasma bicarbonate was only 40 per cent. After a night's rest, however, it was found on the next morning that matters had adjusted themselves. The blood sugar was distinctly lower and the plasma bicarbonate a trifle higher than on the morning of September 16. There had been a temporary upset from the exercise; in particular, this patient's usual tendency to acidosis on fast-days had

been increased; but the final outcome of the fast-day with exercise was a diminution of hyperglycemia, while a fast-day without exercise had not reduced hyperglycemia. It cannot be supposed, however, that this effect upon the blood sugar was worth the disturbance and risk under the conditions.

Turning to the general and prolonged features of the experiment, it can be seen by reference to the patient's graphic chart (Chapter III) that between May 27 and July 24 she was on a carbohydrate-free diet of 1500 to 1800 calories. This was in excess of the tolerance, for ferric chloride reactions were almost continuous and glycosuria altogether too frequent. The plasma sugar of 0.208 per cent on the morning of the fast-day of July 25 may be taken as typical of the hyperglycemia produced by this diet. After the carbohydrate tolerance test which ended August 9, carbohydrate-free diet was resumed with 1400 to 1600 calories daily. Again on September 4, it is seen in the table that the plasma sugar was 0.238 per cent. The patient performed moderate exercise for an hour, then rested 15 minutes; there was a very marked reduction of sugar, to 0.152 per cent in the plasma. No discomfort or acidosis symptoms resulted, and any lowering of plasma bicarbonate during the moderate exercise was compensated in 15 minutes of rest, for the carbon dioxide capacity was the same at 12:30 as at 11:15.

Thereafter the comparison of the two fast-days of September 12 and 16 was carried out with the results above described. The acidosis resulting on a fast-day in contrast to a feeding day may again be mentioned.

Another feature was incidentally noticed, the significance of which is unknown. On September 17 the patient weighed 38.3 kilograms without edema. With the beginning of heavy exercise on that day, there was an immediate rise in weight to 40 kilograms on September 18, with marked visible edema of face and ankles. The edema passed off within a few days and the weight remained approximately what it was before. It will be observed in the table that the hemoglobin and hematocrit readings after September 17 showed a fall decidedly beyond any possible experimental error, and the former values were not regained until September 29. In other words, the blood appeared to be diluted during the period of edema. Accidentally or otherwise, the

TABLE V.
Patient No. 2.

Date.	Diet.				Urine.		Blood.						Remarks.					
	Protein.	Fat.	Carbohydrate.	Total calories.	Sugar.	FeCl ₃ reaction.	Sugar.	per cent	Plasma sugar.	per cent	Corpuscle sugar.	vol. per cent		Plasma CO ₂ .	Hemoglobin.	per cent	Corpuscle.	per cent
1915																		
July 25 11:10 a.m.	Fast-day.				0	0	0.192	0.208	0.123 (calc. 0.165)			53.2		100	38.1			
Sept. 4 11:15 a.m. 12:30 p.m.	55.6	93.6	—	1098	0	+	0.228	0.238	0.218			52.8		98				11:15 a.m. to 12:15 p.m. Exercised climbing stairs, walking corridors.
Sept. 12 9:30 a.m. 5:20 p.m.	Fast-day.				0	0	0.134	0.139	0.145 (calc. 0.140)			52.8		98	40.0			12:15 to 12:30 p.m. Rested. No breakfast; first meal 12:30 p.m.
Sept. 13 9:00 a.m.	97.8	113.3	—	1455	0	0	0.132	0.137	0.137 (calc. 0.129) 0.147 (calc. 0.123)			53.8		102	45.0			Visited home in afternoon; otherwise remained at rest.
Sept. 16 9:15 a.m. 10:50 "	Fast-day.				0	0	0.156	0.172	0.147 (calc. 0.128) 0.116 (calc. 0.122) 0.107 (calc. 0.105)			52.3		96	37.5			9:15 to 10:50 a.m. Exercised by climbing 72 flights stairs and walking corridors.
12:10 p.m. 3:50 " 5:10 "					0.128	0.128	0.128	0.128	0.128 (calc. 0.117)			45.2		105	40.3			10:50 a.m. to 12:10 p.m. Walked corridors. Rested remainder of day, exhausted and dizzy.

EXERCISE

Sept. 17 9:00 a.m.	97.8	113.3	—	1455	0	0	0.145	0.156	0.139 (calc. 0.129)	56.4	95	41.0	Walked 30 blocks.
Sept. 21 11:45 a.m.	100.1	111.5	—	1447	0	0	0.133	0.133	0.111 (calc. 0.133)	52.0	65	32.0	Blood taken after breakfast and 32 flights stairs; has exercised large part of each day since Sept. 17; 33 flights stairs.
Sept. 22 12:15 p.m.	97.8	108.4	—	1409	0	0	0.109	0.089	0.122 (calc. 0.145)	49.6	67	35.3	Blood taken after 32 flights stairs and jumping rope 25 min.
Sept. 25 12:00 m. 4:45 p.m.	103	122.0	.25	1565	0	0	0.118	0.118	0.118 (calc. 0.119) 0.143 (calc. 0.109)	49.6 63.5	81 81	32.0 32.0	Blood taken after 32 flights stairs; 25 gm. carbohydrate in wheat flour added to lunch; 32 flights stairs and 60 blocks walking between lunch and 4:45 p.m.
Sept. 29 12:00 m.	80	125.3	.25	1595	0	0	0.125	0.128	0.119 (calc. 0.119)	—	100	38.5	
Oct. 29	39.8	5.7	140	788	+	0	0.312	0.357	—	59.5	—	—	Carbohydrate test, with diet limited to green vegetables, Oct. 11 to 30.
Nov. 2	110.6	130.8	10	1710	0	0	0.278	0.222	—	59.7	—	—	Mixed diet commenced Nov. 1.

TABLE V—Concluded.

Date.	Diet.				Urine.		Blood.						Remarks.	
	Protein.	Fat.	Carbohydrate.	Total calories.	Sugar.	Recl. reaction.	Sugar.	per cent	Plasma sugar.	Corpuscle sugar.	Plasma CO ₂	Hemoglobin.		Corpuscle.
	gm.	gm.	gm.					per cent	per cent	per cent	vol. per cent	per cent	per cent	
1915														
Nov. 5	108.3	132.6	10	1718	0	0	0	0.322	0.270	—	49.9	—	—	
Nov. 6	108.3	132.6	10	1718	0	0	0	0.270	0.250	—	57.0	—	—	
Nov. 8	108.3	163.0	10	2000	0	0	0	0.333	0.356	—	58.6	—	—	
Nov. 10	108.3	163.0	10	2000	0	0	0	0.333	0.370	—	44.5	—	—	
Nov. 11	108.3	163.0	10	2000	0	0	0	0.278	0.278	—	52.5	—	—	
Nov. 13	108.3	163.0	10	2000	0	0	0	0.200	0.208	—	52.5	—	—	
Nov. 15	108.3	183.7	10	2193	0	0	0	0.250	0.217	—	56.6	—	—	
Nov. 18	108.3	183.7	10	2193	0	0	0	0.208	0.208	—	53.2	—	—	
Nov. 20	108.3	183.7	10	2193	0	0	0	0.227	0.227	—	55.0	—	—	
Nov. 22	108.3	216.2	10	2495	0	0	0	0.294	0.294	—	57.9	—	—	
Nov. 24	103.7	222.7	—	2496	+	+	+	—	0.333	—	48.6	—	—	
Nov. 27	103.7	222.7	—	2496	+	+	+	—	0.278	—	50.4	—	—	
Nov. 29	103.7	223.3	—	2501	0	0	0	—	0.230	—	58.9	—	—	
Dec. 2	103.7	223.3	—	2501	+	+	+	0.256	0.270	—	48.4	—	—	
Dec. 4	103.7	223.3	—	2501	+	+	+	0.213	0.244	—	52.8	—	—	
Dec. 6	103.7	168.8	—	1995	0	0	0	0.227	0.344	—	55.2	—	—	
Dec. 9	103.7	168.8	—	1995	0	0	0	0.182	0.250	—	58.8	—	—	
Dec. 11	103.7	168.8	—	1995	0	0	0	0.227	0.227	—	56.6	—	—	

Exercise during the period very severe.

edema was coincident with the beginning of exercise. The changes in hemoglobin and corpuscles were not parallel to alterations in the sugar concentration. There have been no other observations on diabetic patients to indicate whether the blood volume is ordinarily increased in the period of edema to which such patients are often readily subject.

The regular diet through this time remained at 1450 to 1600 calories. After September 16, increasing exercise was carried out daily as the patient's endurance improved with training. Only on fast-days moderate exercise or none at all was required. It is seen in the table that on September 17, after walking, the blood sugar on this same diet was lower than it previously had been, without exercise. On September 21, after heavy exercise, it was lower still. On September 22, it was the lowest yet observed. On September 25, with the blood sugar approximately normal (0.118 per cent) just before lunch, the experiment was performed of adding 25 gm. carbohydrate in the form of wheat flour to the noon lunch. Although this patient had previously been subject to repeated glycosuria on carbohydrate-free diet with the same protein and total calories, glycosuria remained absent with this quantity of carbohydrate with heavy exercise, and the plasma sugar at 4:45 p.m. was only 0.162 per cent, in contrast to the above mentioned values of 0.208 and 0.238 per cent observed on fasting before exercise was inaugurated. The use of carbohydrate was continued, but the form was changed to green vegetables. On September 29, with 25 gm. carbohydrate in the diet, and after breakfast had been taken about 7:30 a.m. as usual, the plasma sugar at noon was 0.128 per cent. The hyperglycemia of 0.357 per cent in the plasma on October 29 was the result of the carbohydrate tolerance test at that time, with 140 gm. carbohydrate in the diet and glycosuria present. The diet up to this time had involved slight undernutrition, especially in view of the exercise. This was evidenced by the weight, 41.3 kilograms on June 27, 40.4 kilograms on October 30. After October 30 the carbohydrate allowance was diminished to 10 gm., and the attempt was made to build up weight by steady increase of total calories. The exercise at the same time was pushed to a maximum, with the idea that the patient might be made to lose fat while building up her muscles to the greatest possible size and functional power on a diet abundant in protein and total calories. Her day's work frequently consisted of 200 flights of

stairs, walking 75 blocks, 30 minutes roller-skating, and 30 minutes hard work with the medicine ball. In addition she carried on minor activities, so that she was fully resting only during the hours of sleep. The strength was greatly increased by this program. The patient had the full strength and endurance of the most vigorous working girl and could outdo the average normal girl. It is evident from Table V, however, that the attempt thus to use exercise to compensate for an excessive caloric ration was a failure. As the calories were increased, the blood sugar rose in proportion, and the rise was not checked by omitting all carbohydrate after November 24. Glycosuria also became rather frequent, as shown in the graphic chart. The ultimate outcome was that the patient was dismissed on February 2, 1916, weighing only 39.2 kilograms, on a carbohydrate-free diet of 75 gm. protein and 1500 calories; *i.e.*, a reduction in both weight and food. No blood sugar analyses were performed later than January 15, but in view of the glycosuria present as late as January 29, it is certain that hyperglycemia was persistent.

Reference may be made also to the three formal tests of carbohydrate tolerance performed during this period (July 26 to August 9, October 11 to 30, December 13 to 20). The point to be determined was whether the building up of the muscles in mass and function would bring about any noteworthy improvement in the carbohydrate tolerance. It was clearly evident that the patient gained in size and power of her muscles, but it is also evident from the history and the graphic chart that the carbohydrate tolerance by accurate tests remained unchanged. In addition, it can be observed from the graphic chart that the attempt to introduce as much as 30 gm. carbohydrate in the diet in January was borne for a few days by virtue of hard exercise, but terminated in marked glycosuria. The tolerance meanwhile was injured, since glycosuria resulted thereafter from smaller quantities of carbohydrate, so that on January 26 to 29 glycosuria was present on diets of 77 gm. protein, 25 to 0 gm. carbohydrate, and 1200 to 1400 calories.

The behavior as respects acidosis is also of interest. Some of the fluctuations in the plasma bicarbonate in this period, shown particularly in the graphic chart, were due to exercise. In general this curve remained close to the lower border of normal. The ideas concerning

the carbohydrate supply and the glycogen reserve as governing acidosis are so firmly entrenched in the literature that attention may profitably be called to these results with prolonged heavy exercise on diets always poor in carbohydrate and completely free from carbohydrate for months at a stretch. The ration of approximately 100 gm. protein could furnish approximately 60 gm. potential carbohydrate, but it is known that normal persons generally exhibit more or less acidosis, at least temporarily, when placed upon diets of this character. Two questions may be raised. First, what effect will exercise have upon the acidosis of carbohydrate-free diet? Second, if the introduction of carbohydrate into the diet is made possible by exercise, will this carbohydrate, which is consumed by the exercise, have the usual effect in diminishing acidosis? Contrary to some existing preconceptions, it will be seen that exercise produced no perceptible tendency to acidosis, except on the fast-days as above mentioned. The evidence on the point is as follows: (a) Practically continuous ferric chloride reactions had been present throughout the earlier months in the hospital. They were thus present on the carbohydrate-free diets of 1600 calories or more prior to August, and on the lower carbohydrate-free diets, *viz.* about 1500 calories, they had ceased in September, shortly before exercise was begun. Exercise did not bring back such reactions; on the contrary, they were negative or limited to indefinite traces on the carbohydrate-free diet of 2500 calories, November 24 to December 4, and entirely negative on the carbohydrate-free diet of 2000 calories December 6 to 11. There was thus if anything a diminution of ferric chloride reactions after exercise as compared with the period before exercise. (b) The data for ammonia nitrogen are best seen by a glance at the graphic chart. It is evident that the ammonia determinations after December 2 show no striking tendency to acidosis as compared with those before June 25. The question of the usefulness of carbohydrate in lowering acidosis during exercise cannot be answered from the data in this record. With the same number of calories in the diet there is no essential difference in the ammonia excretion on December 31 and January 6 with 30 gm. carbohydrate and on January 15 without carbohydrate, but here the proper utilization of the carbohydrate is made questionable by the glycosuria and marked hyperglycemia.

B. THE EFFECT UPON CARBOHYDRATE TOLERANCE AND GLYCOSURIA.

It was noted in several of the above studies that glycosuria was either prevented or checked after it had begun, and this rule applied also to the glycosuria resulting from carbohydrate-free diet or (patient No. 46, Table IV) from simple addition of fat to a diet.

From the standpoint of clinical experience, patients may be divided into three groups on the basis of their reaction to exercise: I, those showing more or less improvement in food tolerance; II, those showing little or no change in tolerance; III, those in whom the effect is injurious.

I. A number of tests were performed of which the following is typical. Patient No. 34 (see Table III above; see also graphic chart, Chapter III) was started on a carbohydrate tolerance test on October 11. With a steady increase of 10 gm. daily in the carbohydrate intake, glycosuria appeared with 200 gm. carbohydrate on October 28, and increased slightly with 210 gm. carbohydrate on October 29. The patient had been at rest up to this time. The daily increase of carbohydrate was continued, but exercise was imposed in the form of 72 flights of stairs and 30 minutes lively rope-jumping daily. The glycosuria ceased immediately, and reappeared only with 260 gm. carbohydrate on November 3. A similar observation is described in the history of patient No. 49. This improvement in tolerance belongs to the milder cases, and may practically be said to vary with the degree of mildness. It is well known that diabetics of milder type than those represented in this series may assimilate much larger quantities of carbohydrate with exercise than without, and this fact has been counted as an advantage in the dietetic management of patients of the poorer class, who must live by hard manual labor. As was shown above (patient No. 46, Table IV) the reaction to exercise varies with the time and degree of treatment. Patients with active diabetes may show no improvement of assimilation, and only injurious and perhaps dangerous consequences from exercise, but later, after a sufficient period of sufficiently thorough treatment, may reach the condition in which exercise is clearly beneficial.

II. Patient No. 26 (see graphic chart, Chapter III), a girl of 14 years, began a carbohydrate tolerance test on October 6. A trace of

glycosuria appeared with 130 gm. of carbohydrate on October 19. Exercise was then introduced in the form of stair-climbing and rope-jumping to the point of exhaustion daily. The glycosuria continued, and increased slightly on the ensuing days up to October 23 as the carbohydrate was slightly increased. Even with exercise, two partial fast-days (October 24 and 25) were necessary to abolish it. This instance is typical of cases in which exercise shows no appreciable effect upon the tolerance one way or the other.

Patient No. 43 (see graphic chart, Chapter III), a young woman of 27 years, beginning August 1, 1915, took a diet of 100 gm. carbohydrate and 2150 to 2500 calories. On this she remained free from glycosuria during the week ending August 7. In the following week (August 9 to 14) she was sent on long walks, as much as 8 miles daily, which, though taken slowly, were enough to tire her thoroughly. On August 10 and 11, she happened to have crying spells which brought on glycosuria. A walk was taken immediately after the one on August 10, and it was found that the urine became immediately free from sugar. Nevertheless glycosuria recurred from time to time subsequently; *viz.*, on August 19 to 20, 23 to 25, and September 11. After the fast-day of September 12 exercise was temporarily discontinued, to determine the effect of the omission upon the tolerance. Traces of glycosuria occurred on September 14 to 15.

On September 16, blood was taken at 9:15 a.m., as shown in Table VI. The patient then ate breakfast and went for a walk of 54 blocks. The marked rise in blood sugar found upon her return at 12:20 p.m. may be attributable to the breakfast; the walking had not availed to prevent this increase of hyperglycemia. The hemoglobin and hematocrit readings seemed to indicate that the exercise was sufficient to concentrate the blood appreciably. Notwithstanding the hyperglycemia, however, the glycosuria which had been present on the two previous days ceased promptly with this exercise, and remained absent as exercise was continued on the succeeding days. The data do not permit decision whether the cessation was due to a simple diminution of renal permeability or (as is more probable) at least partly to a slight lowering of blood sugar (as compared with corresponding hours on the preceding days, when no analyses were made).

In the 3 weeks between September 19 and October 10, severe exercise was discontinued, and the patient took only a short walk daily. Nevertheless glycosuria was fully as rare as before, the only trace in this period being on the last day. Mild exercise was employed during the carbohydrate test, October 11 to 30, and, as evident from the graphic chart, the assimilation was not quite so high as shown in the previous test in July. The slight difference between the tests may be attributed to the unduly high diets of the intervening period. It is evident that exercise failed to build up the tolerance or to prevent the injury resulting from such diets. On the whole, the influence of

TABLE VI.
Patient No. 43.

Date.	Blood.						Urine (24 hr.).	
	Sugar.	Plasma sugar.	Corpuscle sugar.	CO ₂	Hemo-globin.	Corpus-cle.	Sugar.	FeCl ₃ reaction.
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>gm.</i>	
1915 Sept. 12, 11:30 a.m.	0.154	0.154	0.154 (calc. 0.154)	37.1	101	46.0	0	0
Sept. 16, 9:15 a.m.	0.167	0.164	0.137 (calc. 0.173)	39.2	88	33.0	0	0
12:20 p.m.	0.185	0.188	0.147 (calc. 0.180)	42.0	95	38.8		

exercise upon the tolerance of this patient was so slight as to be barely recognizable.

Occasional ferric chloride reactions were present both before and after the inauguration of exercise. Their occurrence was not governed solely by the quantity of carbohydrate in the diet, as may be seen by comparing the periods July 27 to 31, August 26 to 28, and November 7 to 25 in the graphic chart. Exercise had no perceptible influence in this respect. The plasma bicarbonate is seen also to hold generally a normal level. Nothing can be concluded beyond the fact that exercise failed to produce any appreciable tendency to acidosis, and as far as carbohydrate served to prevent acidosis, it was apparently as effective with exercise as without.

III. No observations have been recorded which show the injurious effect of exercise in patients with the severest diabetes. The injurious effect easily demonstrable in cases even of milder type under inadequate treatment is, as above mentioned, another matter. The carbohydrate tolerance of the patients properly belonging in this group is practically nil, even under the most rigorous treatment. Their tolerance for protein and total calories is likewise excessively low. Experience has clearly and repeatedly demonstrated that their tolerance cannot be built up by exercise. Experiments such as described in patient No. 46 (Table IV above) will have different and sometimes dangerous results if performed upon these severest cases. In view of their great proneness to glycosuria, it is a difficult matter to show conclusively that a given patient of this type has glycosuria on exercise, and is free from glycosuria at rest. The existing evidence is of two kinds:

(a) The demonstrable changes in the blood sugar, which can be shown to be increased instead of diminished by exercise, as above mentioned.

(b) The general clinical experience that patients of this sort are badly affected by heavy exercise. They are weak and worn out, nervous and unwell on even moderate exertion. Those with diabetes even of a somewhat milder type sometimes reach this condition temporarily when they overdo exercise without supervision. Such patients have been treated with complete bed-rest for periods of one to several weeks continuously, and the effect of such rest has been good, certainly upon the general health and seemingly also upon the tolerance.

C. THE USE OF EXERCISE IN VARIOUS CLASSES OF PATIENTS.

From the standpoint of practical usefulness, the experience with exercise in the present series of diabetic cases may be expressed by grouping patients into the following six classes.

1. It is obvious that some patients are received in very critical condition and die before there can be any possible use of exercise. There were six such cases in the present series; *viz.*, Nos. 11, 15, 30, 38, 45, and 71.

2. Exercise is necessarily limited or impossible in the youngest and the oldest patients, also in those with organic disability of some kind. In the present series, Nos. 55 and 68 were infants too young for any considerable exercise, and not much was possible for patient No. 73, a girl of 3 years, already weak with advanced diabetes. Senile patients have, as a rule, not been taken. Therefore patient No. 17, with arteriosclerosis and tendency to gangrene, and No. 58, senile and nearly blind, are the only ones falling in this category. The only ones exempted from exercise for complicating disease were patients Nos. 25 and 61, whose cardiorenal conditions were far more serious than the diabetes. Milder disabilities in other patients have not prevented prescribing exercise in keeping with their capabilities.

3. Exercise is sometimes inadvisable, as mentioned, because of the actual severity of the diabetes. In the great majority of cases this applies only to a transitory stage, and under proper treatment exercise later becomes feasible. The cases in this series which were too severe for the use of any important amount of exercise from the time they were received, are Nos. 8, 54, 69, and 75. A number of other patients in the series have shown downward progress, so that they have finally reached this stage in which exercise is impracticable on account of the severity of the diabetes and the accompanying weakness. In some instances at least this downward progress has been due to the wrong use of exercise in an attempt to maintain the patients at higher strength and on higher diets than advisable. Both children and adults are deficient in muscular power and disinclined to exertion on the minimal diets required for the severest diabetes, and obviously neither diet nor activity should be forced in such cases.

In contrast with these three classes stand three other more numerous classes in which the clinical results of exercise have been gratifying. Nearly all these patients are of the type in which exercise is impossible or injurious under former methods of treatment. One thing accomplished by the present dietary method has been to make available the benefits of exercise to the large number of patients of this group. The effects upon the general health are far more important than the influence upon the tolerance.

4. First may be mentioned its use in the great mass of severe cases in adults. Exercise was not employed for patient No. 1, and she was

clearly the worse for having been kept at rest, according to the former traditions for this type of case. She is included in the group suitable for exercise, which also comprises cases Nos. 2, 3, 5, 6, 7, 9, 10, 14, 16, 18, 19, 20, 22, 24, 27, 29, 31, 32, 34, 36, 37, 39, 40, 43, 44, 47, 48, 49, 50, 52, 56, 59, 67, 70, and 74. For this large body of patients, exercise is the most powerful deliverer from ennui, depression, neurasthenia, and invalidism. Exercise and fresh air make the most of whatever strength is possible under the conditions of the disease, and doubtless aid in raising resistance against intercurrent infection. In contradiction to the fears of those who hesitate to employ diets as low as the tolerance requires, the contrast between patients confined and stuffed with fat under former methods, and those with restricted calories and the benefits of exercise and outdoor freedom, is manifestly in favor of the latter with respect to immunity from complications and comfort and efficiency in all respects.

5. Most cases of diabetes in children are distinctly benefited by exercise on a diet which makes this possible. Such are cases Nos. 4, 13, 26, 28, 42, 51, 53, 62, 63, 64, 66, 72, and 76, in the present series. It means much to a child to be able to indulge in active play, especially outdoors. When growth and development are possible at all, these are doubtless aided by healthful exercise. Even when they are impossible, on account of the severity of the diabetes, the child's looks, spirits, and attitude toward life have been improved by active play within the limits of easy endurance.

6. Perhaps the greatest usefulness of exercise has been manifested in a group of milder cases. This applies theoretically to cases such as Nos. 40 and 65, on account of their mildness; but the group particularly referred to comprises certain middle-aged or elderly patients, including those with obesity. Graduated exercise, sometimes carried to a high point, has proved beneficial not merely in raising the carbohydrate tolerance, but also in correcting invalid tendencies associated with advancing years or sedentary habits. Patients Nos. 35 and 41, though sound in wind and limb, were drifting toward invalidism, and when the diabetes was brought under control by diet, exercise aided materially in restoring them to normal life. Patient No. 12 was elderly, sedentary, poor, and seriously debilitated. Rigid undernutrition was necessary to control his diabetes. Exercise and

fresh air, combined with undernutrition, gradually restored his working power. He was one of the obese group. In other patients, such as Nos. 21 and 57, exercise was obviously an aid in controlling the tendency to obesity, and thus benefiting both the diabetes and the general health. Though such patients are better off in all respects if they can really carry on exercise successfully, a question frequently met is how far complicating ailments contraindicate exercise. Patient No. 46 had slight arteriosclerosis and large double inguinal hernia, but nevertheless proved able to perform moderate exercise, especially in the form of regular walking. Though it did not save him from a final pulmonary infection, it was evidently beneficial as to comfort, strength, and resistance. Patient No. 33 presented the most doubtful problem, for she had blood pressure of 190 mm., uterine hemorrhages, and a variety of complaints suggesting organic disease. With these, she was fat and flabby, with the usual relaxed abdomen and neurasthenic disposition. It was decided to make a trial of exercise, and as shown in her history, the ultimate outcome was good in all respects. The tolerance was raised, the obesity and neurasthenic troubles were relieved, and even the blood pressure returned to normal with the general improvement. It is believed that in this case exercise was of decisive importance, and that the psychic factor would have precluded success from purely dietetic management. Obviously this policy and result would have been impossible in the presence of serious organic disease. Exercise was carried to its highest point in patient No. 23. He has been turned into a real athlete, and subjectively has enjoyed the best health of his life. Exercise to this degree must be considered inadvisable for the great majority of patients.

In summary, exercise has been impracticable because of acute terminal conditions, complicating factors, or severity of the diabetes and bodily weakness in altogether 17 patients of this series. In the other 59 cases exercise has found some place in the treatment at earlier or later stages, and has been beneficial when properly employed.

D. THE MORE PERMANENT EFFECTS OF EXERCISE UPON ASSIMILATION AND THE DIABETIC CONDITION.

The question of exercise has possessed considerable practical and theoretical interest in connection with the conception of diabetes as a weakened function involving the total metabolism, rather than the mere utilization of carbohydrate. From this standpoint the transitory reduction of glycosuria and hyperglycemia by exercise is of minor importance. The two chief theoretical aspects of the problem and their practical applications may be stated as follows:

1. One question touches the relation of the pancreas and the muscles as the two factors chiefly involved in the combustion of sugar or other foods. Combustion being deficient because of deficiency of the pancreatic factor, the question is to what extent this deficiency can be compensated by increasing the muscles in mass and function. The answer furnished by the present series of observations is that the apparent compensation actually runs parallel to, and is governed by, the strength of the pancreatic factor alone. With milder diabetes, the organism still possesses a considerable metabolic capacity. Combustion of sugar is accelerated in correspondence to the increased needs of the muscles in a manner more or less similar to the condition in health, and the apparent carbohydrate tolerance is thus increased. As the pancreatic function falls more and more below the normal, the response to exercise diminishes in proportion, until the point is reached at which no perceptible alteration of carbohydrate tolerance is possible. In more severe diabetes, the increased mobilization of food substances resulting from exercise is greater than can be provided for by the feeble pancreatic function, and injury is evident in the increase of both sugar and acetone bodies. These more severe states in which lack of benefit or actual injury by exercise occurs may be transitory or permanent. In the former instance the pancreatic function, which under improper diet is unable to respond to exercise, may be considered to be strengthened by suitable treatment, so that exercise later proves beneficial. The essential points at issue were the following: (a) With a given pancreatic function, is there a specific improvement of food assimilation with increased mass and function of the muscles? The answer from these observations is that food combus-

tion is accelerated and increased in proportion as the power of combustion is retained, but there is no evidence of specific improvement in this power. (b) Will the increased mass and activity of the muscles, through hormone or other agencies, stimulate the pancreas in such manner as to increase its internal secretion, thus strengthening the deficient pancreatic factor? The general result of the observations speaks against any demonstrable influence of this character.

2. If the entire metabolism is affected in diabetes, and injury results from feeding all classes of foods beyond the tolerance, the question arises how and why this injury is produced. Is every increase of total metabolism injurious? If so, exercise must in the long run be injurious. On the other hand, does the injury possibly result from the burden of an excess of food substances present, either stored foods such as glycogen, protein, or adipose tissue, or circulating foods, as represented by the hyperglycemia and hyperlipemia of diabetes? In this case exercise, by reducing bodily reserves and also relieving the glut of mobilized materials, may act in a truly beneficial manner on the same principle as fasting. Exercise could to some extent serve as a convenient and agreeable substitute for fasting and reduced diet, the patient keeping down his weight and his blood sugar while taking a more satisfying diet and maintaining a higher degree of physical efficiency. The question may be otherwise put as follows: If a diabetic patient can tolerate a given diet, is it permissible to increase this diet by a given number of calories while taking care to burn up these added calories by exercise? Will the condition thus be the same as though the extra food had not been taken, or will injury still be produced by the increased metabolism? Present experience with both patients and animals indicates that neither of the two extremes represented in these questions is correct. Even in the cases where exercise acts favorably it can be shown, as in the prolonged study of patient No. 2 (Table V), that even the heaviest exercise cannot atone adequately or permanently for a high diet. Such use of exercise has proved disastrous in every case in which it was attempted in the present series. This fact is illustrated in cases such as Nos. 2, 32, 36, 37, 39, 42, 47, and others. In many of these cases it will be noted that the blood sugar could not be made or kept normal by even the heaviest exercise. In other cases, such as Nos. 37 and 42, the blood sugar was brought to

normal on liberal diets, and the patients were normal to the routine tests for considerable periods. Nevertheless hyperglycemia and other symptoms returned later, and the end result was fatal. On the other hand, the use of exercise has not proved harmful, except in the few severest cases mentioned. In cases of decidedly mild character, exercise, by keeping down weight and improving tolerance, may serve to a limited degree as a substitute for fasting and reduced diet. It has thus been used with benefit in the group of elderly patients above mentioned. Nevertheless, histories such as those of patients Nos. 23 and 41 show that even in these milder cases exercise is limited in its usefulness in the long run, and restriction of total calories must always be the essential reliance for the permanent control of hyperglycemia and other symptoms. The general conclusion on the questions mentioned may be expressed as follows. The greatest and most rapid injury from excessive diet occurs when weight and food materials are allowed to pile up without restraint. Exercise, by reducing weight and food accumulation, diminishes this injury, and the relief is genuine to this extent, even though obtained at the price of increased metabolism. Nevertheless the burning up of surplus food by exercise is not equivalent to withholding such food, and in severe cases the disastrous result is merely delayed and not prevented.

Though exercise cannot atone for the damage of excessive caloric feeding, it apparently can make possible the use of a higher proportion of carbohydrate in suitable cases. Its well known power of diminishing glycosuria and hyperglycemia can probably be used for this purpose without injury, provided only the total calories are kept sufficiently low. Further information concerning the effect on acidosis when carbohydrate is thus used would be of interest, but with a suitable caloric intake acidosis is a matter of only minor practical importance. The disappointment of the hope that exercise might permit of higher diets and correspondingly higher bodily efficiency in severely diabetic patients is of practical importance for the treatment, especially of patients of the poorer class. Repeatedly in the present series the attempt has been made to build up such patients so that they could work with maximum efficiency. The final result has always been disastrous, no matter how well the patient might seem to thrive for the time being on high diet with the aid of exercise. It may be

urged that such patients must work to make their living, and require high diets for this purpose. A comparison with cardiac disease is proper. A patient with mild diabetes, like the one with mild heart trouble, may carry on more or less manual labor without injury. The patient with more severe diabetes is as unfit for heavy manual labor as the corresponding cardiac patient. As long as there is no cure for diabetes, such patients must necessarily conduct themselves as sick persons and not as well persons, and financial conditions should be adjusted accordingly, with public aid if necessary. Granting a suitable low diet, diabetics in general, with the comparatively uncommon exceptions mentioned above, are benefited by healthful exercise within the limits imposed by the diet. In the preliminary communication concerning exercise,¹ warning was given against its use as a substitute for dietetic measures, and this warning has been justified by the more prolonged experience. On the other hand, the benefits to the strength, spirits, and general health have also been substantiated, and it would be a gloomy prospect to return to the former practice of strict rest for severely diabetic patients. In the final outcome, over-strenuous or exhausting exercise in the endeavor to build up a true increase of tolerance has been abandoned, and muscular activity has been employed within the easy limits of strength for its beneficial influence upon the general health and spirits of the patients.

Conclusions.

1. The diminution of glycosuria and hyperglycemia by exercise described by former authors in milder diabetes has been found to obtain also in more severe cases under suitable dietetic management. In cases of still more severe type, this effect of exercise may be lacking, and the blood sugar and general condition may even be affected injuriously.

2. In suitable cases the effect of exercise in diminishing glycosuria and hyperglycemia is demonstrable when these have resulted from the addition of fat to the diet.

3. No appreciable tendency to acidosis has been produced by exercise under the ordinary conditions of proper dietetic management.

¹Allen, *Boston Med and Surg. J.*, 1915, clxiii, 743-744.

A distinct tendency to acidosis may be produced in patients inadequately treated by diet, or in the severest cases, or sometimes on fasting or very low diet. Under such conditions exercise must be used with caution.

4. No special relation has been observed between the changes in blood sugar concentration produced by exercise and the blood volume (as judged by hemoglobin and hematocrit readings) or the distribution of sugar between plasma and corpuscles.

5. Exercise may perhaps be useful as a means of introducing a higher proportion of carbohydrate in the diet in some cases, but cannot serve as a substitute for total caloric restriction in cases at all severe in character.

6. Most of the cases in which exercise has been beneficially employed in the present series are of a grade of severity which precluded the use of exercise under former methods of treatment. The present dietetic management has served to make available the benefits of exercise to this numerous group of patients. At the same time the observations carry a warning against the abuse of exercise even in milder cases, whenever an undue total caloric burden is thereby involved. In the final outcome, muscular exercise and development have exhibited no specific influence upon the diabetic condition, but can be recommended within proper limits for their beneficial effects upon the general health and spirits of diabetic patients.

CHAPTER VI.

THE INFLUENCE OF FAT IN THE DIET.

Some references to the literature on this topic will be found in preceding chapters. It suffices here to mention that the accepted doctrines in practice have been as follows: that fat is the most useful food in diabetes; that it is responsible for little or no glycosuria; that its use need not be restricted even from the standpoint of acidosis unless in the presence of threatened coma, because deficiencies of fat in the diet are made up by the use of body fat in metabolism; that diabetic patients should be built up in weight if possible and their nutrition maintained at a maximum by a full caloric ration, especially of fat, the calories lost as sugar and acetone bodies in the urine being also replaced by fat in the diet; and that undernutrition should be employed only in the slight degree and brief duration recommended by Naunyn. In opposition to these beliefs and this usage, the conclusion has been reached, especially from animal experiments, that diabetes is a disorder of the total metabolism and that any increase of weight or of total diet increases the strain upon the weakened function. According to this assumption, rational treatment would consist in first cutting down the metabolic strain to a minimum by fasting until active symptoms are controlled, and thereafter in permanently maintaining a reduced level of weight and metabolism to correspond to the weakened function. To some extent the question at issue is divisible into the influence of body weight in itself and the influence of the diet in itself. The various factors have been studied more particularly in the animal experiments, but the same classification may conveniently be employed for the observations on human patients, which are in all respects confirmatory.

A. INFLUENCE OF BODY WEIGHT.

Since the weight (broadly speaking and without considering fluctuations of water content of the body) necessarily rises and falls with the supply of available calories, a sharp differentiation of the influence of weight as distinct from the diet producing it is difficult. Three lines of evidence may be mentioned.

One of these consists in the marked benefit to the diabetes, the clearing up of all active symptoms, and the striking gain in assimilative power when the body weight is reduced. Examples are afforded in the histories of patients Nos. 12, 16, 21, 33, 35, 41, 46, 57, and 60.

The second line of evidence consists in observations of the effect of increase of weight. In the milder grades of diabetes such influence may be less obvious, though still frequently demonstrable, but in the moderate or severe grades of the disorder the influence is too plain to be missed. In anything resembling a severe type of diabetes, the present series has afforded no exception to the rule, which is believed to be general, that gain in weight means loss in tolerance. At a suitable level of weight patients or animals may remain free from diabetic symptoms for long or indefinite periods. If the diet, especially by addition of fat, is made such that the weight increases, symptoms may remain absent until some higher level of weight is reached, differing according to the severity of the diabetes. At this point active symptoms return, and continue unless checked by reduction of weight. Examples of this parallelism between body weight and diabetic symptoms are pointed out in the histories of patients Nos. 5, 16, 23, 26, 41, 57, and 66. In most of the other cases such a parallelism is more or less clearly illustrated. The entire treatment by which freedom from diabetic symptoms is maintained has for one of its constant objects the maintenance of a suitably low weight.

A third line of evidence is furnished by exercise, by which the body weight can be controlled to an important degree without variations in diet. It was concluded in the previous chapter that exercise has no apparent specific influence upon the essential diabetic disorder. This being the case, it is instructive that the sugar in blood and urine and other diabetic symptoms can to some extent be controlled by exercise without change in the diet. Examples of the checking of undue rise

of weight and corresponding control of diabetic symptoms by exercise are shown in the histories of patients Nos. 23, 37, and 42. In no instance was exercise carried out in such manner as wholly to prevent gain in weight. To this extent the studies are not decisive, and the failure of exercise here, in respect to merely delaying and not ultimately preventing the return of active diabetes, may thus receive at least a partial explanation.

B. INFLUENCE OF THE TOTAL DIET.

Inasmuch as the harm of either carbohydrate or protein in excess of the tolerance has long been recognized, this question pertains especially to the influence of fat feeding; and this is divisible into the influence upon acidosis and the influence upon glycosuria. In some of the following cases the diets were such as to increase the body weight slightly. In other cases the increase in weight was trivial or absent, so that the effects noted must be attributed directly to the changes in diet.

The production of glycosuria, and also of acidosis as indicated qualitatively by the ferric chloride reactions, was shown in Table IV of the preceding chapter. Similar injurious effects attributable predominantly to high fat rations were described in cases Nos. 1 and 17 and more particularly in case No. 5 (Chapter III). The production of acutely threatening acidosis by small quantities of fat and relief of this acidosis by diminishing the fat intake were shown in the histories of patients Nos. 54 and 60. Also reference may be made to the history of patient No. 57, where tests showing the effect of fat in diminishing carbohydrate tolerance are described.

The history and graphic chart of patient No. 24 show how the frequent traces of glycosuria were stopped, and the high blood sugar reduced to normal, by means of reduction of fat and total calories, while protein was given in larger quantity than before. Also the tolerance was markedly improved as the body weight diminished with this undernutrition.

In addition to the liberal use of fat in ordinary diabetic diets, it has been administered heretofore in large quantities on oatmeal days, vegetable days, and even fast-days, in the belief that much available

energy was thus supplied without appreciably injuring the carbohydrate tolerance or causing any important degree of acidosis. Observations early in the present series indicated the harmfulness of such use of fat. For example, in the histories of patients Nos. 2 and 4, it was pointed out how the acidosis increased and glycosuria was unduly persistent when olive oil was given in addition to green vegetables, whereas in the same and other patients periods of green vegetables alone have acted powerfully in abolishing acidosis. These results in case No. 2 are shown more clearly by Table I.

The comparison of the two fast-days, April 30 and May 7, when the patient was free from glycosuria, gives the impression that both were beneficial in diminishing acidosis, although 100 gm. olive oil were given on the former day. This result on April 30 is readily explainable by the fact that the fat and total calories were decidedly lower on that day than on the preceding and following days. It is significant that the ammonia on April 30 did not show such a fall as usually results from a plain fast-day. Though the harmful effect of this quantity of fat on a single day may seem negligible, the damage becomes more evident when a series of days is compared.

Period I in Table I was made up of vegetable days with liberal addition of fat. Glycosuria was present, and the increase of acidosis is shown by both the ammonia and acetone excretion, notwithstanding the rather high carbohydrate intake and strongly positive carbohydrate balance.

In Period II the fat allowance was sharply diminished. The glycosuria already begun continued through this period, and the carbohydrate balance was lower than on April 23 and 24, yet the fall in the ammonia and acetone output is well marked.

In Period III, continuing the same protein and carbohydrate ration, the fat (olive oil) was again increased, and on the second day of this period the increase of both ammonia and acetone was again well marked.

Period IV was characterized by a diminishing fat ration and a practically carbohydrate-free diet up to May 6. The diminution in ammonia and acetone ran parallel to the reduction of fat, and the sudden addition of 54 gm. carbohydrate on May 6 did not appreciably increase the rate of fall of the acidosis.

TABLE I.
Patient No. 2.

Date.	Diet.				Weight.	Urine.				Periods.
	Protein.	Fat.	Carbo- hydrate.	Calor- ies.		Volume.	Sugar.	NH ₃ -N	Acetone bodies (as β - oxybu- tyric).	
1914	gm.	gm.	gm.		kg.	cc.	gm.	gm.	gm.	
Apr. 21	Fast-day.				42.2	685	0.48	0.47	1.97	I
" 22	8.1	201.7	24.2	2008	41.9	1165	0	0.97	1.82	
" 23	32.6	186.0	89.3	2137	41.8	1192	+	1.06	4.21	
" 24	40.7	201.9	95.0	2432	42.2	1068	1.92	1.83	5.56	
Apr. 25	38.9	57.9	74.2	1001	42.8	735	0.74	1.06	1.54	II
" 26	25.8	5.4	74.3	459	42.4	1970	3.15	0.50	1.62	
" 27	25.8	5.4	74.3	459	42.2	2180	+	0.44	1.66	
Apr. 28	25.8	155.4	74.3	1854	41.8	745	+	0.31	0.83	III
" 29	25.8	155.4	74.3	1854	42.1	1810	0	1.18	3.01	
Apr. 30	—	100.0	—	930	42.1	1280	0	1.04	0.65	
May 1	29.5	141.5	1.0	1440	41.2	990	0	1.12	2.22	IV
" 2	30.6	142.1	1.0	1450	41.8	1510	0	1.66	2.96	
" 3	30.6	102.0	1.1	1077	41.6	930	0	1.35	0.85	
" 4	26.2	99.9	1.0	1040	42.0	1530	0	1.19	0.85	
" 5	29.2	76.4	1.0	985	41.6	1285	0	1.00	0.57	
" 6	36.8	78.0	54.0	1096	41.7	1535	0	0.80	0.61	
May 7	Fast-day.				41.6	1230	0	0.43	0.41	
May 8	32.7	67.0	83.0	1097	41.0	1830	0	0.44	0.49	V
" 9	33.1	66.4	76.4	1076	41.3	2080	0	0.24	0.33	
" 10	39.1	65.8	80.8	1062	41.2	1670	0	0.48	0.14	
" 11	Fast-day.				41.3	1820	0	0.53	0.34	
" 12	26.4	44.0	86.7	872	39.7	1140	0	0.19	0.27	
" 13	32.4	39.8	104.0	928	40.4	2080	0	0.52	0.49	
" 14	29.5	40.0	93.2	875	40.7	2157	0	0.32	0.49	
" 15	44.8	45.3	140.6	1180	40.2	2205	0	0.35	0.32	

Period V was another vegetable period with much less fat than in Period I. The ammonia and acetone excretion was consistently low, and though the protein ration was about the same and the carbohydrate somewhat higher than in Period I, glycosuria remained absent. The steady undernutrition which had reduced body weight by 2 kilograms doubtless contributed to the acquisition of this increased tolerance.

The observations on this same patient in June and July, 1914, were also instructive concerning the practical use of fat, especially for the familiar purpose of building up the weight of diabetic patients. The use of carbohydrate and the maintenance of as favorable a carbohydrate balance as possible has often been recommended as the most important means of combating the resulting acidosis. The following observations on this patient exemplify the failure of such a policy.

Here the body weight was increased by over 3 kilograms up to June 30, essentially by the addition of fat. Table II shows how acidosis ran parallel to the fat intake. The influence of the fat ration in producing glycosuria also is suggested by this study and proved by those mentioned later in this chapter. Carbohydrate was not the sole cause of glycosuria, because, for example, it was higher in Periods I and III on days without glycosuria than in Period V with marked glycosuria. Protein is not excluded as a factor in the production of the glycosuria. The particular point, however, is the manner in which the carbohydrate balance was successfully maintained and even increased during the periods of glycosuria and acidosis. It will be observed that acidosis was increased with a high positive carbohydrate balance in Period IV when the fat ration was high, and diminished with a lower carbohydrate balance in Periods III, VI, and the first part of VII, when the fat ration was low. Also a more liberal protein ration did not serve to prevent acidosis in the high fat periods. The study thus affords an example of the general rule that the acidosis resulting from the attempt to build up strength and weight by addition of fat to the diet is not prevented by an increased utilization of protein and carbohydrate, but that this acidosis falls when the fat intake is reduced. In Periods VI and VII the injury from the high fat ration was thus relieved by diminished fat. The body weight was likewise diminished. A glance at the graphic chart (Chapter III) will show that this patient then (July and August, 1914) was able to maintain herself at this reduced weight on a well balanced mixed diet with the requisite restriction of total calories.

The respective parts played by protein and fat in producing glycosuria are illustrated in Table III.

In Period I, with the protein intake constant at 40 gm., the total calories were gradually increased by addition of fat. The table shows

TABLE II.
Patient No. 2.

Date.	Diet.				Weight.	Volume.	Urine.				Remarks.
	Protein.	Fat.	Carbohydrate.	Calories.			Sugar.	NH ₃ -N.	Acetone bodies as β -oxybutyric.	Carbohydrate balance.	
	gm.	gm.	gm.		cc.	gm.	gm.	gm.	gm.		
1914											
June 5		Fast-day.			39.1	11244	2.01	0.72	0.16	-2	Period I.
" 6	68.9	53.0	106.7	1206	38.8	1859	+	0.89	0.31	+106	Low calory diet; high carbohydrate.
" 7	67.3	52.0	101.1	1173	39.4	1724	+	0.48	0.52	+101	Total calories for 5 days 5555; average per day 1111.
" 8	79.4	55.0	132.5	1379	40.1	2879	+	0.58	0.98	+132	Protein " 5 " 315.7 gm. " 63.1 gm.
" 9	75.1	64.5	115.1	1320	40.0	2428	0	0.46	0.31	+115	Fat " 5 " 243.6 " " 48.7 "
" 10	25.0	19.1	31.2		40.0	1620	0	0.31	0.21	+31	Carbohydrate " 5 " 486.6 " " 97.3 "
							0	0.31	0.21	+31	Sugar excreted " 5 " 2.0+ " " 0.4 "
											Ammonia nitrogen " 5 " 2.72 " " 0.54 "
											Acetone bodies " 5 " 2.33 " " 0.46 "
June 11	137.4	642.0	34.7	6672	39.1	510	0	0.32	1.25	+35	Period II.
											High calory; high fat; sugar, 0; NH ₃ -N, 0.32 gm.; acetone bodies, 1.25 gm.
June 12	58.6	56.5	92.7	1152	39.0	1170	+	0.83	0.14	+93	Period III.
" 13	52.3	56.4	77.0	1053	39.6	1242	+	0.78	0.19	+77	Low calory; medium carbohydrate.
" 14	58.6	58.3	81.9	1117	39.6	2928	0	0.56	0.71	+82	Total calories for 5 days 5563; average per day 1112.
" 15	58.3	60.4	82.2	1137	39.5	2759	0	0.44	0.74	+82	Protein " 5 " 285.6 gm. " 57.1 gm.
" 16	57.8	57.0	82.2	1104	39.1	12413	0	0.46	0.70	+82	Fat " 5 " 288.6 " " 57.7 "
											Carbohydrate " 5 " 416.0 " " 83.2 "
											Sugar excreted " 5 " Tr. " " Tr.
											Ammonia nitrogen " 5 " 3.07 gm. " 0.61 gm.
											Acetone bodies " 5 " 2.38 " " 0.47 "

TABLE II—Concluded.

Date.	Diet.				Weight.	Volume.	Urine.				Remarks.
	Protein.	Fat.	Carbohydrate.	Calories.			Sugar.	NH ₄ -N.	Acetone bodies as β-oxobutyric.	Carbohydrate balance.	
	gm.	gm.	gm.	kg.	cc.	gm.	gm.	gm.	gm.		
1914											
July 5	Alcohol 30 gm.			210	40.7	817	3.59	1.88	1.74	-3	Period VI.
" 6	4.2 16.0	14.4	90	40.6	727	1.02	1.24	0.23	+13	Low calory; low fat; low carbohydrate.	
" 7	4.2	1.6	14.4	230	41.4	1477	+	1.22	0.45	+14	Total calories for 6 days 806; average per day 134.
" 8	Alcohol 20 gm.			90	41.9	954	+	1.14	0.27	+14	Protein " 6 " 20.8 gm. " " " 3.9 gm.
" 9	4.2	1.6	14.4	90	43.0	1508	0	1.66	0.68	+14	Fat " 6 " 8.2 " " " " 1.4 "
" 10	5.0	1.8	16.9	106	43.0	2229	0	0.74	1.99	+17	Carbohydrate " 6 " 74.5 " " " " 12.6 "
											Sugar excreted " 6 " 4.61 " " " " 0.77 "
											Ammonia nitrogen " 6 " 7.88 " " " " 1.31 "
											Acetone bodies " 6 " 5.36 " " " " 0.89 "
July 11	13.8	2.8	45.4	268	42.3	2727	0	—	1.30	+45	Period VII.
" 12	11.0	2.9	38.8	231	42.0	1351	0	1.49	0.76	+39	Low calory; low fat; high carbohydrate.
" 13	16.3	4.8	63.2	369	42.0	2815	0	1.76	1.20	+63	Total calories for 12 days 7117; average per day 593.
" 14	24.0	8.0	81.8	507	41.2	1968	0	0.65	0.24	+82	Protein " 12 " 335.7 gm. " " " 27.9 gm.
" 15	27.8	8.1	97.9	590	41.2	2992	0	—	0.51	+98	Fat " 12 " 132.4 " " " " 11.03 "
" 16	29.3	27.6	105.5	808	40.6	1928	0	0.46	0.34	+106	Carbohydrate " 12 " 1105.3 " " " " 92.1 "
" 17	27.2	8.5	86.5	544	40.7	2027	0	0.30	0.42	+87	Sugar excreted " 12 " none; " " " none.
" 18	28.9	8.4	111.3	652	40.8	1454	0	0.42	0.34	+111	Ammonia nitrogen " 12 " 8.71 gm. " " " 0.72 gm.
" 19	36.7	9.6	100.5	651	41.3	1286	0	0.36	0.24	+101	Acetone bodies " 12 " 6.56 " " " " 0.54 "
" 20	35.4	8.0	120.3	712	41.2	2202	0	0.57	0.36	+120	
" 21	35.7	8.7	125.6	732	40.8	2591	0	0.44	0.32	+126	
" 22	49.6	35.0	128.5	1054	40.6	2761	0	0.36	0.53	+127	

the resulting glycosuria, hyperglycemia, and increase of ammonia excretion. The fast-day of October 18 diminished the ammonia output as usual. In the next two periods the ammonia and blood sugar are unfortunately deficient.

It is seen, however, that in Period II the total calories were kept constant at the low level of 800, while protein was increased by 5 gm. daily. The severity of the diabetes was such that glycosuria was thus readily produced. It is also evident that small quantities of protein produced glycosuria more promptly and strikingly than considerably larger quantities of fat, in keeping with the belief that protein is a direct sugar-former.

In Period III the protein was constant at 50 gm., *i.e.* 10 gm. higher than in Period I, and the fat was again gradually increased. With the higher protein intake it is seen that glycosuria appeared at a lower level of total calories than in Period I. Though the quantities of sugar excreted were trivial, the increased protein allowance did not prevent the development of distinct ferric chloride reactions at the close of Periods II and III.

The following three observations show the effect of changes in the fat intake, particularly upon the carbohydrate tolerance. Table IV (compare also graphic chart, Chapter III) shows how, with a constant diet of protein and carbohydrate, increase of fat through successive weeks increased the body weight, but at the same time gave rise to both sugar and ferric chloride reactions in the urine. On carbohydrate-free diet, with the same protein and greatly reduced fat, not only glycosuria but also acidosis was absent for 6 weeks thereafter. As evidences of acidosis, in addition to the ferric chloride reactions, the graphic chart shows that the ammonia was slightly lower and the plasma bicarbonate slightly higher, on the carbohydrate-free diet with reduced fat. On this diet the patient at a reduced weight was able to remain free from diabetic symptoms.

Table V (see also graphic chart, Chapter III) shows how a patient was able to tolerate a diet with 10 gm. carbohydrate in the week November 1 to 6. In the following weeks, without change in protein, the fat intake was increased, and traces of glycosuria developed accordingly. Slight sugar and ferric chloride reactions then persisted as the fat was further increased, notwithstanding the omission

TABLE III.
Patient No. 2.

Date.	Diet.				Urine.		Blood plasma.		Remarks.		
	Protein.	Fat.	Carbo- hydrate	Calories.	Sugar.	NH ₄ -N	FeCl ₃ reaction.	Sugar.		CO ₂	
	gm.	gm.	gm.			gm.		per cent.		vol. per cent.	
1916											
Oct. 1	40	47.5	—	605	0	0.99	0	—	—		
" 2	40	52.5	—	652	0	0.67	0	0.175	65.4		
" 3	40	57.5	—	698	0	0.94	0	—	—		
" 4	40	63.5	—	754	0	0.96	0	0.167	66.3		
" 5	40	68.5	—	801	0	1.01	0	—	—		
" 6	40	73.5	—	847	0	1.35	0	0.192	67.4		
" 7	40	79.5	—	903	0	0.94	0	—	—		
" 8	40	85.1	—	955	0	1.08	0	—	—		
" 9	40	89.5	—	996	0	0.89	0	0.228	63.0		
" 10	40	95.5	—	1052	0	0.86	0	—	—		
" 11	40	100.5	—	1098	0	0.74	0	0.200	68.8		
" 12	40	106.5	—	1154	0	0.94	0	—	—		
" 13	40	111.5	—	1200	0	1.02	0	0.222	65.9		
" 14	40	117.5	—	1256	+	1.18	0	—	—		
" 15	40	122.5	—	1303	+++	1.33	0	—	—		
" 16	40	122.5	—	1303	+++	1.48	0	0.238	61.2		
" 17	40	122.5	—	1303	+++	1.62	0	—	—		
Oct. 18			Fast-day.		0	0.87	0	0.231	59.8		

Period I.

Protein fat diet with increasing fat.

Total calories for 17 days 16880.

Protein " 17 " 680 gm.

Fat " 17 " 1516.1 "

Urinary sugar negative for first 13 days, moderate for last 4 days.

Ammonia nitrogen for 17 days 18.0 gm.

Ferric chloride reaction negative.

Plasma sugar rose from 0.175 to 0.238 per cent.

" CO₂ fell " 68.8 " 59.8 " "

Oct. 19	40	68.5	—	801	0	1.44	0	—	—	—	—	Period II. Protein fat diet, increasing protein, calories remaining constant. Total calories for 6 days 4804; average per day 800. Protein increasing from 40 to 65 gm. Fat for 6 days 378.4 gm., average per day 63 gm.
" 20	45	66.5	—	801	0	1.23	0	—	—	—	—	
" 21	50	64.5	—	804	+	—	0	—	—	—	64.1	
" 22	55	61.9	—	799	++	—	0	—	—	—	0.202	
" 23	60	59.3	—	797	+++	—	0	—	—	—	—	
" 24	65	57.7	—	802	+++	—	+	—	—	—	—	
Oct. 25	21.4	19.5	15	506	+	—	0	—	—	—	—	Vegetable day.
Oct. 26	50	53.5	—	877	0	—	0	—	—	—	—	Period III. Protein fat diet, protein constant, fat increasing. Total calories for 6 days 5857. Protein for 6 days 300 gm., average per day 50 gm. Fat for 6 days 385 gm., increasing from 53.5 to 69.5 gm.
" 27	50	58.5	—	924	0	—	0	—	—	—	—	
" 28	50	64.5	—	979	+	—	0	—	—	—	—	
" 29	50	69.5	—	1025	0	—	0	—	—	—	—	
" 30	50	69.5	—	1026	+	—	0	—	—	—	—	
" 31	50	69.5	—	1026	++	—	+	—	—	—	—	

TABLE IV.
Patient No. 26.

Date.	Diet.				Urine.		Blood.		Weight. kg.
	Protein.	Fat.	Carbohydrate.	Total calories.	Sugar.	FeCl ₃ reaction.	Plasma sugar.	Plasma CO ₂ .	
	gm.	gm.	gm.		gm.		per cent	vol. per cent	
1915-16									
Oct. 25							0.135	52.5	27.5
" 26							0.263	56.0	
" 25-31	304	664	85	7808	0	0			
Average per day.	43	95	12	1115					27.8
Nov. 1							0.110	46.4	27.4
" 4							0.164	54.5	
" 6							0.200	52.2	
" 1-7	330	979	90	10813	0	0			
Average per day.	47	139	13	1544					27.1
Nov. 8							0.185	50.2	27.5
" 11							—	53.2	
" 13							0.169	52.2	
" 8-14	330	979	90	10813	0	0			
Average per day.	47	139	13	1544					29.1
Nov. 15							0.100	49.2	28.2
" 18							0.167	—	
" 20							0.185	45.9	
" 15-2	330	1110	90	12022	0	+			
Average per day.	47	160	13	1717					29.5
Nov. 22							0.113	40.9	28.0
" 24							0.189	50.8	
" 27							0.232	48.5	
" 22-2	330	1236	90	13190	0	++			
Average per day.	47	176	13	1885					29.0
Nov. 29							0.154	53.2	28.7
Dec. 2							0.232	49.6	
" 4							0.294	51.9	
Nov. 29-Dec. 5	330	1346	90	14418	+++	++			
Average per day.	47	192	13	2059					29.5
Dec. 6							0.107	58.6	28.6
" 9							0.316	58.6	
" 11							0.303	53.7	
" 6-13	346	746	78	8672	+++	++			
Average per day.	43	94	9	1084					29.4

TABLE IV—*Concluded.*

Date.	Diet.				Urine.		Blood.		Weight.
	Protein.	Fat.	Carbohydrate.	Total calories.	Sugar.	FeCl ₃ reaction.	Plasma sugar.	Plasma CO ₂ .	
<i>1915-16</i>	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>		<i>gm.</i>		<i>per cent</i>	<i>vol. per cent</i>	<i>kg.</i>
Dec. 14							0.156	51.8	29.7
“ 14-19	280	472	—	5534	0	0			
Average per day.	40	67	—	790					30.2
Dec. 20-26	369	484	—	6007	0	0	—	—	29.1
Average per day.	52	69	—	858					29.5
Dec. 30							0.071	53.5	28.8
“ 27-Jan. 2	360	486	—	5988	0	0			
Average per day.	51	69	—	855					29.7
Jan. 5							0.141	53.3	28.8
“ 3-9	360	390	—	5100	0	0			
Average per day.	51	55	—	730					29.0
Jan. 15							0.123	53.2	28.9
“ 10-16	360	390	—	5100	0	0			
Average per day.	51	55	—	730					29.0
Jan. 17-23	360	390		5100	0	0	—	—	28.6
Average per day.	51	55	—	730					28.7

of all carbohydrate from the diet after November 24. With diminution of fat to make a total ration of 2000 calories, sugar and ferric chloride reactions were entirely negative in the week December 6 to 11. Exercise was carried on throughout this time, but does not detract from the conclusions of the dietary experiment.

Table VI (see also graphic chart, Chapter III) shows the record of a woman who had just completed a test with green vegetables indicating a carbohydrate tolerance of 240 gm. She was then placed on carbohydrate-free diet, on which she was free from both glycosuria and acidosis. The blood sugar, doubtless by reason of the large carbohydrate intake just preceding, remained high on November 15 to 17, and then diminished. Fat was rapidly increased while keeping protein constant. Both hyperglycemia and glycosuria resulted. Also acidosis was shown both by the marked ferric chloride reactions and by the

TABLE V.
Patient No. 2.

Date.	Diet.				Weight.	Urine.		Blood.	
	Protein.	Fat.	Carbo- hydrate.	Total calories.		Sugar.	FeCl ₃ reaction.	Plasma sugar.	Plasma CO ₂ .
1915	gm.	gm.	gm.		kg.			per cent	vol. per cent
Nov. 1	111	131	10	1710	38.6	0	0	—	—
" 2	111	131	10	1710	39.2	0	0	0.222	59.7
" 3	111	131	10	1710	39.6	0	0	—	—
" 4	108	133	10	1718	39.5	0	0	—	—
" 5	108	133	10	1718	39.8	0	0	0.270	49.9
" 6	108	133	10	1718	40.0	0	0	0.250	57.0
" 7	Fast-day.				40.2	0	0	—	—
Nov. 8	108	163	10	2000	40.0	0	0	0.356	58.6
" 9	108	163	10	2000	39.8	0	0	—	—
" 10	108	163	10	2000	40.3	0	0	0.370	44.5
" 11	108	163	10	2000	40.1	0	0	0.278	52.5
" 12	108	163	10	2000	40.2	0	0	—	—
" 13	108	163	10	2000	40.2	0	0	0.208	52.5
" 14	108	184	10	2193	40.3	+	0	—	—
Nov. 15	108	184	10	2193	39.7	0	0	0.217	56.6
" 16	108	184	10	2193	40.2	0	0	—	—
" 17	108	184	10	2193	40.4	0	0	—	51.4
" 18	108	184	10	2193	40.3	0	0	0.208	53.2
" 19	108	184	10	2193	40.3	0	0	—	—
" 20	108	184	10	2193	40.2	0	0	0.227	55.0
" 21	Fast-day.				40.2	+	0	—	—
Nov. 22	108	216	10	2495	39.0	+	0	0.294	57.9
" 23	108	216	10	2495	39.6	++	0	—	—
" 24	104	223	—	2496	39.7	++	+	0.383	48.6
" 25	104	223	—	2496	40.3	—	—	—	—
" 26	104	223	—	2496	40.0	+	+	—	—
" 27	104	223	—	2496	40.5	++	+	0.278	56.4
" 28	Fast-day.				40.6	—	—	—	—
Nov. 29	104	223	—	2501	40.3	—	—	0.213	58.9
" 30	104	223	—	2501	40.4	—	—	—	—
Dec. 1	104	223	—	2501	40.5	+	+	—	—
" 2	104	223	—	2501	40.4	+	+	0.270	48.4
" 3	104	223	—	2501	40.7	++	+	—	—
" 4	104	223	—	2501	40.7	++	+	0.244	52.8
" 5	Fast-day.				40.3	0	0	—	—
Dec. 6	104	169	—	1995	39.7	0	0	0.344	55.2
" 7	104	169	—	1995	41.3	0	0	—	—
" 8	104	169	—	1995	42.0	0	0	—	—
" 9	104	169	—	1995	41.0	0	0	0.250	58.8
" 10	104	169	—	1995	40.8	0	0	—	—
" 11	104	169	—	1995	41.4	0	0	0.227	56.6
" 12	Fast-day.				41.3	0	0	—	—

TABLE VI.
Patient No. 47.

Date.	Diet.				Weight.	Urine.		Blood plasma.	
	Protein.	Fat.	Carbo- hydrate.	Total calories.		Sugar.	FeCl ₃ reaction.	Sugar.	CO ₂
	gm.	gm.	gm.		kg.			per cent	vol. per cent
1915									
Nov. 15	100	170	—	1992	60.2	0	0	0.20	50.8
" 16	100	170	—	1992	61.1	0	0	—	—
" 17	100	224	—	2492	61.6	0	0	0.23	—
" 18	100	224	—	2492	61.9	0	0	—	—
" 19	100	278	—	2994	62.0	0	0	—	—
" 20	100	278	—	2994	62.5	0	+	0.18	55.1
" 21	Fast-day.				62.4	0	+	—	—
Total for week.	600	1344	—	18440					
Nov. 22	100	331	—	3492	61.1	0	+	—	—
" 23	100	332	—	3498	62.0	0	+	—	—
" 24	100	386	—	3995	62.6	0	++	0.22	51.9
" 25	100	385	—	3991	62.6	0	++	—	—
" 26	100	386	—	3995	62.7	0	++	—	—
" 27	100	386	—	3995	62.6	+	+++	0.20	39.0
" 28	Fast-day.				62.6	+	+++	—	—
Total for week.	600	2204	—	22966					
Dec. 6	100	167	10	2001	61.8	+	++	0.11	60.0
" 7	100	166	10	2001	62.8	+	0	—	—
" 8	100	162	20	1997	62.8	0	0	—	—
" 9	100	158	20	1961	63.2	0	0	0.18	59.4
" 10	100	163	20	2005	63.3	0	0	—	—
" 11	100	163	20	2005	63.1	0	0	—	—
" 12	Fast-day.				63.2	0	0		
Total for week.	600	978	100	11972					
Dec. 13	100	163	20	2005	62.3	0	0	0.13	66.9
" 14	100	159	30	2007	63.0	0	0	—	—
" 15	100	154	40	2002	63.7	0	0	—	—
" 16	100	148	50	1993	63.6	0	0	—	—
" 17	100	143	60	1999	63.8	0	0	—	—
" 18	100	140	70	1998	63.7	0	0	—	—
" 19	Fast-day.				64.3				
Total for week.	600	909	270	12004					
Dec. 20	100	148	50	1990	61.9	0	0	—	—
" 21	100	148	50	1990	62.7	0	0	0.11	—

decided fall in plasma bicarbonate, which evidently would have been serious except for being checked by fasting. After the injury from the fat had been corrected by an undernutrition period, December 1 to 5, the patient within 2 weeks demonstrated the ability to tolerate as much as 70 gm. carbohydrate with the same protein as before, with

TABLE VII.
Patient No. 74.

Date.	Diet.			Urine.					
	Protein.	Fat.	Calor-ies.	Vol-ume.	Nitro-gen.	NH ₃ -N	100 NH ₃ -N N	Total acetone bodies.	Sugar.
<i>1917</i>	<i>gm.</i>	<i>gm.</i>	<i>gm.</i>	<i>cc.</i>	<i>gm.</i>	<i>gm.</i>		<i>gm.</i>	
Feb. 13	50	43	600	1415	9.66	0.93	9.6	0.82	Negative.
" 14	50	43	600	1160	9.08	0.90	9.9	0.64	"
" 15	50	43	600	1470	10.14	1.00	9.9	0.43	"
" 16	50	43	600	1770	11.35	1.10	9.7	0.58	"
" 17	50	43	600	1440	9.76	0.99	10.1	0.45	"
" 18	Fast-day.			1145	6.25	0.84	13.4	0.45	"
" 19	50	150	1600	1875	8.77	1.46	16.6	4.61	"
" 20	50	43	600	1480	6.64	1.14	17.2	0.70	"

Blood Findings February 19 to 21.

Date.	Time.	Sugar.	Total acetone bodies per 100 cc.	Com- bin- ing power for CO ₂ .	Macroscopic appearance of plasma.
<i>1917</i>		<i>per cent</i>	<i>mg.</i>	<i>vol. per cent</i>	
Feb. 19	7:00 a.m. (fasting).	0.14	31.8	62	Clear.
	11:30 " (after first fat meal).	0.14	28.0	60	Slightly cloudy.
	4:30 p.m. (3 hrs. after second fat meal).	0.15	38.9	47	Milky.
	11:30 p.m.	0.17	50.0	48	Cloudy.
Feb. 20	7:00 a.m. (fasting).	0.16	35.9	57	Slightly cloudy.
" 21	7:00 " "	0.15	29.0	62	Clear.

fat diminished so as to limit the total diet to 2000 calories. Not only was the urine normal, but it is seen that the blood sugar also fell to normal. Fat was therefore clearly responsible for glycosuria, hyperglycemia, and acidosis in this case.

The immediate effect of a single large addition of fat to an otherwise fixed diet was studied in greater detail in patient No. 74. The

diet was one of undernutrition, with a negative nitrogen balance, though the deficit appears unduly large in the table because no allowance is made for the nitrogen of the soup which was taken in fixed quantities daily. On February 19, 107 gm. fat were added, divided between the morning and noon meals. Though the blood was not analyzed for fat, a tendency to pathological lipemia seemed indicated, for the plasma was unusually opaque during digestion and some cloudiness persisted in that obtained at 7 a.m. the next day. During the earliest period the total acetone in the plasma was not increased. Only at 4:30 p.m., 3 hours after the second fat meal and 9 hours after the first one, was such an increase demonstrated. At 11:30 p.m., when the lipemia had markedly diminished, the maximum ketonemia was encountered. By the following morning it had fallen to nearly the same level as before the fat addition. The plasma bicarbonate ran strikingly parallel, falling as the acetone bodies rose, and rising thereafter, as they fell. There was also a well marked increase of acetone bodies, of ammonia nitrogen, and of the ratio of ammonia to total nitrogen in the urine. Also, instead of a sparing of protein, there was an increase of nitrogen excretion on this day. No glycosuria occurred, and though the slight increase in blood sugar may be significant here as elsewhere, there is no indication that sugar was actually formed from the fat.

The effect of a smaller and more gradual addition of fat was tested as shown in Table VIII. Glycosuria being absent on an undernutrition diet of 40 gm. protein and 500 calories, the fat tolerance was tested by the addition of 5 gm. fat daily to this diet. Under the low diet it is seen that the blood sugar diminished up to October 18, whereas the fall in the acetone bodies was maintained only to October 16. Both then progressively increased, and excretion of both sugar and acetone bodies in the urine developed correspondingly. The rise of weight must be attributed chiefly to water retention, since even with the low metabolism of this emaciated condition, genuine gain in tissue is scarcely possible on the diets shown. The test indicated a very low total food tolerance in this patient and the necessity for extreme undernutrition if active symptoms were to be prevented.

A test of the sudden giving and withdrawal of a considerable quantity of fat was made upon patient No. 75, as shown in

Table IX and in the graphic chart (Chapter III). By consulting the graphic chart it can be seen that this patient had been kept in the hospital from February 21, 1917, on diets up to 60 gm. protein and 1850 calories, with urine very commonly showing the faintest detectable traces of sugar and ferric chloride reactions, but never titratable quantities of sugar in the two month period. In correspondence with the urine, the blood showed continuous hyperglycemia

TABLE VIII.
Patient No. 69.

Date.	Diet.				Weight.	Urine.			Blood.	
	Protein.	Fat.	Alcohol.	Calories.		Volume.	Sugar.	Total acetone bodies (as acetone).	Sugar.	Total acetone bodies in plasma (as acetone) per 100 cc.
	gm.	gm.	gm.		kg.	cc.	gm.	gm.	per cent	mg.
1916 Oct. 13	40	17	25	500	37.0	3850	0	0.51	0.20	26.6
" 14	40	22	25	546	37.4	2790	0	—	—	—
" 15	40	28	25	602	37.2	3170	0	0.49	—	—
" 16	40	33	25	649	37.1	2335	0	0.32	0.15	19.7
" 17	40	40	25	704	38.2	2370	0	0.36	—	—
" 18	40	45	25	750	38.0	2950	0	0.39	0.13	24.3
" 19	40	50	25	800	37.9	2515	0	0.41	—	—
" 20	40	55	25	855	38.0	2220	0	0.36	—	—
" 21	40	60	25	902	38.2	2755	0	0.61	0.14	33.4
" 22	40	65	25	958	38.9	2900	0	0.95	—	—
" 23	40	70	25	1005	38.0	3390	0	1.09	—	—
" 24	40	75	25	1051	38.0	3090	0	0.99	0.16	35.6
" 25	40	80	25	1107	38.6	2760	+	1.27	—	—
" 26	40	85	25	1153	39.0	2230	++	0.98	—	—
" 27	40	90	25	1205	40.8	6180	9.84	2.53	0.27	42.3

and a moderate increase of total acetone (31 mg. per 100 cc.) at the time the test was made. A week before this (April 30) the protein had been increased by 10 gm., and the diet at the beginning of the test consisted of 70 gm. protein and 1500 calories. In addition there was an allowance of 600 cc. clear soup and 800 gm. thrice cooked vegetables daily, which were ignored in reckoning food values. With the increase in protein, sugar reactions became slightly more pro-

TABLE IX.
Patient No. 75.

Date.	Diet.					Weight.	Urine.			Blood Plasma.			Remarks.	
	Protein.	Fat.	Carbohydrate.		Calories.		Volume.	Sugar.	Acetone bodies as acetone.	Sugar.	CO ₂	Acetone bodies as acetone per 100 cc.		
1917	gm.	gm.	gm.	cc.		kg.	cc.	gm.	gm.	per cent	vol. per cent	mg.		
May 7	70	131	—	—	1500	36.2	2615	0	+	—	—	—		
" 8	70	131	—	—	1500	37.6	2370	0	+	—	—	—		
" 9	70	131	—	—	1500	37.2	3080	0	+	—	—	—		
" 10	70	131	—	—	1500	37.1	3440	+	+	—	—	—		
" 11	70	131	—	—	1500	37.3	2860	0	0	—	—	—		
" 12	70	131	—	—	1500	36.6	2440	0	+	—	—	—		
" 13	Fast-day.					37.2	3100	0	0	—	—	—		
" 14	70	131	—	—	1500	36.2	2000	+	2.62	—	—	—		
" 15	70	131	—	—	1500	37.4	2582	0	5.73	0.208	72.0	31.0		
" 16	70	131	—	—	1500	37.5	2770	+	12.41	—	—	—		
" 17	70	131	—	—	1500	37.8	3142	++	17.58	—	—	—		
" 18	70	131	—	—	1500	38.0	3340	++	5.98	—	—	—		
" 19	70	131	—	—	1500	37.9	3152	++	3.18	—	—	—		
" 20	Fast-day.					37.2	2800	+	1.08	0.179	71.1	31.0		
" 21	70	231	—	—	2430	35.8	2413	+	5.70	0.246	—	34.7		
" 22	70	281	—	—	2895	37.4	2800	5.88	18.54	—	—	—		
" 23	70	281	—	—	2895	38.0	3480	10.26	17.32	—	—	—		
" 24	70	281	—	—	2895	37.6	3340	13.86	13.70	—	—	—		
" 25	70	281	—	—	2895	37.6	3630	16.29	18.65	—	—	—		
" 26	70	281	—	—	2895	37.2	3435	18.87	15.98	0.200	47.1	83.0	5:00 p.m.	
" 27	—	100	—	—	930	37.2	3377	18.54	7.61	0.238	57.6	63.5	10:00 a.m.	
" 28*	70	281	—	—	2895	36.4	1955	7.40	18.10	0.263	69.1	71.3	9:00 "	
										0.208	63.5	89.2	6:00 p.m.	
" 29*	70	281	—	—	2895	37.5	3483	26.13	25.01	—	—	—		
" 30*	70	281	—	—	2895	38.0	3448	22.87	49.73	0.216	57.8	108.0	5:00 "	
" 31	70	11	—	—	391	38.2	3105	21.56	17.68	0.286	59.7	57.2	9:00 a.m.	
June 1	70	11	—	—	391	37.9	2520	22.32	4.24	—	—	—		
" 2	70	11	—	—	391	38.3	2728	18.83	1.85	—	—	—		
" 3	Fast-day.					38.5	2155	8.36	0.67	0.303	69.2	12.6	10:00 "	
" 4	"					38.2	2810	+	0.90	0.204	63.6	35.8	10:00 "	
" 5	70	11	—	—	391	38.4	1760	+	0.81	—	—	—		
" 6	70	11	—	—	391	39.2	3052	+	0.81	—	—	—		
" 7	70	11	—	—	391	38.7	3030	+	0.33	—	—	—		
" 8	70	11	—	—	391	38.8	3000	+	0.18	—	—	—		
" 9	70	11	—	—	391	38.5	2790	+	0.50	—	—	—		
" 10	Fast-day.					—	38.6	3260	0	0.19	0.170	56.0	12.2	10:30 a.m.

* 20 gm. sodium bicarbonate on this day.

TABLE IX—*Concluded.*

Date.	Diet.					Weight.	Urine.				Blood plasma.			Remarks.
	Protein.	Fat.	Carbohydrate.	Alcohol.	Calories.		Volume.	Sugar.	Acetone bodies as acetone.	Sugar.	CO ₂	Acetone bodies as acetone per 100 cc.		
1917	gm.	gm.	gm.	cc.		kg.	cc.	gm.	gm.	per cent	vol. per cent	mg.		
June 11	70	11	—	—	391	38.1	2215	+	0.48	0.161	61.7	18.6	9:00 a.m.	
" 12	70	11	—	—	391	38.8	2050	+	0.18	—	—	—		
" 13	70	11	—	—	391	39.9	3640	+	0.11	—	—	—		
" 14	70	11	—	—	391	39.7	3830	0	0.11	—	—	—		
" 15	70	11	—	—	391	39.3	3470	0	0.52	—	—	—		
" 16	70	11	—	—	391	39.0	3435	0	—	0.164	—	8.3	5:00 p.m.	
" 17	Fast-day.					39.0	4110	0	—	0.182	67.3	—	11:00 a.m.	
" 18	70	11	—	70	881	38.5	1728	0	0.13	0.141	61.7	13.0	9:00 "	
" 19	70	11	—	70	881	39.9	3630	0	0.18	—	—	—		
" 20	70	11	—	70	881	39.8	3585	0	0.32	—	—	—		
" 21	70	11	—	70	881	39.4	3690	0	0.33	—	—	—		
" 22	70	11	—	70	881	39.0	2210	0	—	—	—	—		
" 23	70	11	—	70	881	38.6	3060	0	—	—	—	—		
" 24	Fast-day		—	100	700	39.0	4166	0	—	0.098	57.0	7.2	10:00 a.m.	
" 25	70	11	—	100	1091	38.4	2104	0	0.23	0.066	72.1	19.1	9:00 "	
" 26	70	11	—	100	1091	39.2	3340	0	0.23	—	—	—		
" 27	70	11	—	100	1091	38.4	3555	0	—	—	—	—		
" 28	70	11	—	100	1091	38.4	2975	0	—	—	—	—		
" 29	70	11	—	100	1091	38.6	3468	0	—	—	—	—		
" 30	70	11	—	100	1091	38.6	3685	0	—	0.12	55.1	11.1	5:00 p.m.	
July 1	111	—	3.6	100	721	39.0	4030	0	—	0.11	—	—	10:00 a.m.	
" 2	77	16.5	—	100	1170	37.6	1620	0	—	0.13	64.5	—	9:00 "	
" 3	77	16.5	—	100	1170	39.4	3535	0	—	—	—	—		
" 4	85	22	—	100	1250	39.0	3640	0	—	—	—	—		
" 5	85	22	—	100	1250	38.2	3230	0	—	—	—	—		
" 6	85	22	—	100	1250	38.2	2882	0	—	—	—	—		
" 7	85	22	—	100	1250	38.0	3990	0	—	—	—	—		
" 8	111	—	3.6	100	721	37.8	3505	0	—	—	—	—		
" 9	85	22	—	100	1250	37.4	2678	0	—	—	—	—		
" 10	85	22	—	100	1250	37.2	4807	0	—	—	—	—		
" 11	95	22	—	100	1297	36.5	4225	0	—	—	—	—		
" 12	95	22	—	100	1297	36.3	2430	0	—	—	—	—		
" 13	95	22	—	100	1297	37.8	3015	0	—	—	—	—		
" 14	95	22	—	100	1297	37.5	2998	0	—	—	—	—		
" 15	—	—	—	100	700	38.0	3350	0	—	—	—	—		

nounced in the urine, but no titratable quantity was excreted. Under these conditions 100 gm. fat were added to the diet on May 21 and another 50 gm. on May 22, so that the diet May 22 to 30 consisted of 70 gm. protein, 281 gm. fat, and 2895 calories. Also 100 gm. olive oil were given on the fast-day of May 27. The result, as seen in the table and the graphic chart, was a prompt glycosuria and ketonuria of considerable degree, also a rise of sugar and still more marked rise of acetone bodies in the blood, with a tendency to a lowering of the bicarbonate reserve. Notwithstanding the giving of 100 gm. olive oil on May 27, this fast-day accomplished part of the usual purpose. There was no reduction of blood sugar. The blood taken at 10 a.m. on May 27, before the oil had been given, showed benefit of abstinence up to that point in a lowering of total acetone and a rise in the CO₂ capacity. The 100 gm. oil were then given, and as this was so much less than the fat of the regular diet, this day of undernutrition apparently accomplished part of the benefit of a fast-day in checking the rise of acetone and fall of CO₂ capacity. The giving of 20 gm. sodium bicarbonate on May 28, 29, and 30 lowered the blood sugar only transiently if at all. It evidently safeguarded the plasma bicarbonate, but either failed to prevent the marked increase in plasma acetone, or possibly contributed directly to this increase. On May 30 the total acetone had reached the dangerous level of 108 mg. per 100 cc., and the patient's clinical condition was so unfavorable that prudence demanded a change in the diet. There was none of the dyspnea characteristic of acid poisoning, but intoxication was manifested by dizziness, malaise, weakness, and drowsiness. Beginning May 31, fat was excluded from the diet as far as convenient, keeping the protein ration unchanged. The table shows how in the remaining 3 days of that week all symptoms except the hyperglycemia strikingly improved. The clinical transformation was equally plain. Traces of glycosuria persisted up to June 13. Beginning June 18, the very low ration was augmented by first 70 gm. and then 100 gm. alcohol, but the total calories never exceeded 1300. Under this program, not only was there cessation of glycosuria and of ketonuria (aside from the trace indicated by a slight nitroprusside reaction), but also by July 1 the blood was normal in sugar, acetone, and alkali reserve. As an additional test of the relative importance of protein in produc-

ing the former glycosuria, a gradual increase of protein was then made, and it was found that with as much as 95 gm. protein and 1300 calories glycosuria was still absent on July 14.

Tests with both gradual and sudden addition of fat were performed upon patient No. 43, as shown in Tables X and XI and in the graphic chart (Chapter III). This young woman entered the hospital for her fourth admission on December 2, 1916, with heavy glycosuria and ketonuria. The condition was controlled by fasting and low carbohydrate-free diet as shown in the graphic chart. Traces of sugar at first persisted, but with continuance of undernutrition sugar and ferric chloride reactions were negative after December 17, on a diet of 50 gm. protein and 500 calories. Also 300 cc. clear soup and 300 gm. thrice boiled vegetables were given daily and not reckoned in the tables. At this point the test began with a gradual regular addition of fat to the diet through successive weeks. The diet in these earlier weeks remained one of undernutrition. Hyperglycemia was still present at the beginning of the test, but with continued low diet up to January 7 a progressive fall can be seen. Although the small additions of fat had little definite influence upon the acetone bodies in the blood, there was nevertheless a distinct increase of the excretion in the urine. In general the impression gained from this period up to January 7 is that fat gives rise directly to acetone bodies, but does not directly give rise to sugar in the body. As the diet continued to increase, the blood sugar rose after January 7, not to an excessive height at any time, but enough to make continuous hyperglycemia and thus to sacrifice the benefit of the previous undernutrition. Also traces of glycosuria appeared and became continuous. The acetone bodies reached their highest point in the blood plasma with 76 mg. per 100 cc. on January 13 and 19. The rise in the blood was not progressive, apparently because the kidneys acted efficiently in removing the excess, so that the urine showed a steady increase of acetone bodies in parallel with the increased fat ration. The ammonia nitrogen showed a corresponding gradual increase. The lowering of the plasma bicarbonate to 56 per cent on February 20 may or may not be significant. Though the diet finally reached a high level for a patient of this size at rest, weight was not gained, though there was probably a gain in body fat,

TABLE X.
Patient No. 43.

Date.	Diet.			Weight.	Urine.				Blood.		
	Protein.	Fat.	Calories.		Volume.	Sugar.	NH ₃ -N	Total acetone bodies as acetone.	Sugar.	Total acetone bodies in plasma (as acetone) per 100 cc.	Plasma CO ₂ .
	gm.	gm.		kg.	cc.	gm.	gm.	gm.	per cent	mg.	vol. per cent
1916											
Dec. 18	50	32	500	34.0	2435	0	0.55	—			
" 19	50	42	595	34.0	2249	0	0.66	—			
" 20	50	53	700	33.9	2485	0	0.95	0.49	0.27	25.2	59.0
" 21	50	64	800	33.8	3080	0	0.92	0.46			
" 22	50	64	800	33.6	2783	0	0.66	0.44			
" 23	50	64	800	33.7	3085	0	0.59	0.55			
" 24	Fast-day.			33.8	1780	0	0.46	0.39			
" 25	50	64	800	33.4	2660	0	0.59	0.72			
" 26	50	70	850	34.2	2770	0	0.65	0.80	0.21	26.2	60.0
" 27	50	70	850	34.2	3350	0	0.78	0.62			
" 28	50	70	850	34.0	2820	0	0.62	0.48			
" 29	50	70	850	34.0	3235	0	0.67	0.55			
" 30	50	75	900	34.1	3980	0	0.80	0.48			
" 31	Fast-day.			34.2	2350	0	0.61	0.31			
1917											
Jan. 1	50	75	900	33.6	2515	0	0.63	0.70	0.25	30.8	72.0
" 2	50	80	950	34.3	4855	0	0.82	1.26			
" 3	50	80	950	33.8	3750	0	0.76	0.94			
" 4	50	80	950	33.8	3790	0	0.77	0.68			
" 5	50	80	950	34.3	4690	0	0.92	0.94			
" 6	50	86	1000	34.1	3840	0	0.87	0.66			
" 7	Fast-day.			33.9	2985	0	0.62	0.97	0.19	21.3	62.0
" 8	50	86	1000	33.5	3645	0	0.75	1.09			
" 9	50	90	1050	33.5	4100	0	0.86	1.39			
" 10	50	90	1050	33.4	3795	0	0.97	1.10			
" 11	50	90	1050	33.5	3850	+	0.92	0.69			
" 12	50	90	1050	33.9	4175	+	0.95	0.75			
" 13	50	97	1100	33.2	3470	+	0.91	0.75	0.29	17.4	76.0
" 14	Fast-day.			33.3	2330	0	0.69	0.44			
" 15	50	97	1100	33.1	3275	0	0.74	1.11			
" 16	50	102	1150	33.5	4375	0	1.00	2.32			
" 17	50	102	1150	33.4	4680	+	1.09	2.06			
" 18	50	102	1150	33.1	3810	++	1.09	2.02			
" 19	50	102	1150	33.6	3810	+++	0.89	1.18	0.25	21.6	76.0
" 20	50	107	1200	33.8	4400	+++	0.90	1.10			
" 21	Fast-day.			33.8	3980	+	0.74	1.35			
" 22	50	107	1200	33.7	2950	0	0.71	1.05			

TABLE X—*Concluded.*

Date.	Diet.			Weight.	Urine.				Blood.		
	Pro-tein.	Fat.	Calo-ries.		Volume.	Su-gar.	NH ₃ -N	Total acetone bodies.	Sugar.	Total acetone bodies in plasma (as acetone) per 100 cc.	Plasma CO ₂ .
1917	gm.	gm.		kg.	cc.	gm.	gm.	gm.	per cent	mg.	vol. per cent
Jan. 23	50	112	1250	33.9	4170	0	0.97	1.00			
" 24	50	112	1250	33.8	4575	0	1.07	1.66			
" 25	50	112	1250	33.9	4390	+	1.07	0.71			
" 26	50	112	1250	34.0	4035	++	0.99	0.89	0.27	22.2	69.0
" 27	50	117	1300	34.0	4780	++	0.93	0.91			
" 28	Fast-day.			34.2	3140	+	0.49	0.53			
" 29	50	117	1300	33.4	2960	0	0.49	0.86			
" 30	50	122	1350	33.4	4425	0	0.81	1.64			
" 31	50	122	1350	34.0	5325	+	0.94	2.77			
Feb. 1	50	123	1350	34.0	3640	+	0.83	1.38			
" 2	50	123	1350	34.0	4360	+	0.99	2.44	0.29	23.4	67.0
" 3	50	128	1400	34.4	4690	+	0.99	1.59			
" 4	Fast-day.			34.3	3330	+	0.67	1.67			
" 5	50	128	1400	33.6	3175	0	0.84	1.37			
" 6	50	134	1450	34.0	3800	0	0.82	1.75	0.35	24.8	61.0
" 7	50	134	1450	34.0	4595	+	1.43	2.57			
" 8	50	134	1450	33.9	4490	+	1.21	2.83			
" 9	50	134	1450	33.9	4690	+	1.12	2.86			
" 10	50	139	1500	34.0	4380	+	1.00	3.85			
" 11	Fast-day.			34.0	1980	+	0.59	1.23			
" 12	50	139	1500	33.5	2905	+	0.72	1.60			
" 13	50	144	1550	33.6	4670	+	0.97	3.41	0.24	25.4	65.0
" 14	50	144	1550	33.0	4650	+	1.09	2.65			
" 15	50	144	1550	32.8	3955	+	1.08	2.14			
" 16	50	144	1550	32.5	3735	+	1.37	3.78			
" 17	50	150	1600	32.6	4000	+	1.16	2.88			
" 18	Fast-day.			32.8	1370	+	0.76	0.60			
" 19	50	150	1600	32.2	3420	+	0.97	3.32			
" 20	50	85	999	32.2	4820	+	1.40		0.26	29.25	56.0
" 21	50	85	999	32.4	3791	+	1.12				
" 22	50	85	999	32.7	3988	+	0.90				
" 23	50	86	1002	32.7	4645	+	0.90				
" 24	50	85	999	33.0	3750	+	0.77		0.27		52.0
" 25	Fast-day.			33.3	3190	+	0.53				
" 26	50	85	999	32.9	3228	0	0.42				
" 27	50	85	999	32.4	4040	0	0.57		0.23		
" 28	60	81	1000	33.3	4767	0	0.68				

masked by a loss of water driven out by the fat feeding. There was no improvement in strength or comfort. As a whole, the test indicated distinct injury to the patient from the laboratory standpoint by the cautious addition of fat in excess of the assimilative power, with no compensating clinical benefit.

Beginning February 20, the fat was reduced to make a total diet of 1000 calories. Glycosuria gradually cleared up and the ammonia excretion diminished.

On February 28 the protein was increased to 60 gm., keeping the total calories at 1000. Faint traces of glycosuria appeared on some days thereafter (see graphic chart). On March 14 the fat was increased to make 1100 total calories, and again on April 18 to make 1300 calories. On April 23 the fat was further increased to make 1500 calories, but then diminished on May 2 to 1300 and on May 7 to 1200 calories. During this whole period of 2 months the patient was obviously just at the edge of her tolerance, showing faint sugar and ferric chloride reactions very frequently, but never excreting a titratable quantity of sugar or developing any marked acidosis. In the first week shown in Table XI (May 14 to 20) the condition made an evident change for the worse, for on the identical diet as much as 11 gm. sugar and 2.3 gm. acetone bodies were excreted on certain days. The opportunity seemed favorable for testing whether this change represented "spontaneous downward progress" on the part of the patient, or whether it was merely the culmination of several months of diet slightly overtaxing the tolerance. A sudden addition of 100 gm. fat was made on May 21, with an additional 50 gm. on May 22, thus raising the total diet to 2600 calories. Marked and continuous glycosuria and ketonuria followed, as shown in Table XI and in the graphic chart. Also the total acetone increased in the blood plasma, and the alkali reserve fell as low as 42.3 per cent on May 26 and 27. The patient, who had welcomed the opportunity to eat more, quickly became unwell and unhappy. The daily administration of 20 gm. sodium bicarbonate on May 28, 29, and 30 seemingly lowered the blood sugar and urine on the first day, but had doubtful effect thereafter. It also raised the plasma bicarbonate temporarily, but by May 30 this was again down to 43.7 per cent in spite of the alkali dosage. It is also possible that this dosage may have been

TABLE XI.
Patient No. 43.

Date.	Diet.					Weight.	Urine.			Blood plasma.			Remarks.	
	Protein.	Fat.	Carbohydrate.	Alcohol.	Calories.		Volume.	Sugar.	Acetone bodies as acetone.	Sugar.	CO ₂	Acetone bodies as acetone per 100 cc.		
1917	gm.	gm.	gm.	cc.		kg.	cc.	gm.	gm.	per cent	vol. per cent	mg.		
May 14	60	103.0	—	—	1202	33.0	3510	0	1.49	—	—	—		
" 15	60	103.0	—	—	1202	33.4	5070	+	2.30	0.192	55.7	49.0		
" 16	60	103.0	—	—	1202	32.9	5075	5.04	1.71	—	—	—		
" 17	60	103.0	—	—	1202	33.8	5215	10.90	1.61	—	—	—		
" 18	60	103.0	—	—	1202	34.0	5200	10.40	2.24	—	—	—		
" 19	60	103.0	—	—	1202	34.3	5640	10.90	1.28	—	—	—		
" 20	Fast-day.					34.1	1895	7.22	1.03	0.213	64.5	21.8		
" 21	60	203.0	—	—	2132	34.8	3330	+	2.10	0.175	—	29.8		
" 22	60	253.0	—	—	2597	34.9	5720	+	7.01	—	—	—		
" 23	60	253.0	—	—	2597	34.6	4740	18.01	9.48	—	—	—		
" 24	60	253.0	—	—	2597	33.9	3205+	18.99	10.63	—	—	—		
" 25	60	253.0	—	—	2597	34.2	2680	18.52	9.58	—	—	—		
" 26	60	253.0	—	—	2597	34.2	2280	13.80	9.57	0.298	42.3	—	5:00 p.m.	
" 27	—	30.0	—	—	279	34.6	2035	35.60	9.80	0.233	42.3	—	10:00 a.m.	
" 28*	60	253.0	—	—	2597	33.7	1090	5.67	8.61	0.286	57.6	52.1	9:00 "	
" 29*	60	253.0	—	—	2597	35.6	2995	24.06	18.41	—	—	—	6:00 p.m.	
" 30*	60	253.0	—	—	2597	34.4	3475	24.84	17.25	0.222	43.7	99.0	5:00 "	
" 31	60	10.0	—	—	332	35.4	5115	45.72	11.18	0.216	48.3	52.1	9:00 a.m.	
June 1	60	10.0	—	—	332	34.9	5645	31.90	4.46	—	—	—		
" 2	60	10.0	—	—	332	35.0	4845	24.23	1.55	—	—	—		
" 3	Fast-day.					—	35.5	1575	8.80	1.31	0.228	57.9	40.8	
" 4	"					—	34.8	860	+	1.29	0.170	58.9	42.3	
" 5	60	4.0	—	—	282	34.4	4100	+	2.01	—	—	—		
" 6	60	4.0	—	—	282	34.6	4900	+	0.88	—	—	—		
" 7	60	3.0	—	—	275	35.4	5440	+	0.49	—	—	—		
" 8	60	3.0	—	—	275	34.9	3570	+	0.51	—	—	—		
" 9	60	3.0	—	—	275	34.5	4520	+	0.36	—	—	—		
" 10	Fast-day.					—	34.1	1855	+	0.31	0.208	64.5	43.1	10:00 a.m.
" 11	59	—	—	—	249	34.4	4005	+	0.64	0.159	59.8	20.4	9:00 "	
" 12	59	—	—	—	249	34.4	4660	0	0.42	—	—	—		
" 13	59	1.0	1.0	—	255	33.0	4610	0	0.41	—	—	—		
" 14	59	1.0	1.0	—	255	33.4	4820	0	0.29	—	—	—		
" 15	59	1.0	1.0	—	255	33.8	4605	0	0.23	—	—	—		
" 16	59	1.0	1.0	—	255	34.2	5250	0	0.47	0.128	—	13.4	5:00 p.m.	
" 17	Fast-day.					34.3	2230	0	0.54	0.200	67.3	—	11:00 a.m.	
" 18	59	1.0	1.0	40	535	33.8	3640	0	0.18	0.113	—	26.6	9:00 "	

* 20 gm. sodium bicarbonate on this day.

partly responsible for the maximum of 99 mg. total acetone per 100 cc. of blood plasma on May 30. Here also dyspnea was not present, but on account of general malaise the patient was glad to discontinue the fat ration.

Accordingly on May 31 fat was eliminated from the diet as far as convenient, keeping the protein unchanged. The first effect was seen upon acidosis, in the fall of acetone bodies in blood and urine, the spontaneous rise of the plasma bicarbonate, and the relief of the clinical symptoms. The sugar excretion rapidly diminished. The hyperglycemia was more stubborn, but there was a progressive diminution down to a normal level on June 18, following the fast-day of June 17. Thereafter it proved possible, as in the preceding patient, to increase the protein to 84 gm. daily without glycosuria. In another test, not included here, a similar return of diabetic symptoms followed an increase of the total calories of the diet. The symptoms were again abolished by diminution of calories without change in protein. It has also been possible to prolong the freedom from active symptoms up to the present, so that "spontaneous downward progress," if existent, has not as yet been manifest.

This question of downward progress has been investigated by long as well as short feeding experiments on animals, but it is seldom that circumstances permit a similar close comparison between individual human patients treated on opposed principles. It has come about that without experimental intent, treatment was carried out along opposite lines in two patients of the present series, so closely comparable as to afford the most exact comparison possible in clinical observations. These are patients Nos. 37 and 66. It will be seen from their histories that both represented juvenile diabetes of the usual type. Both cases were controlled by treatment in such manner as to restore normal conditions in both urine and blood as far as determined by the routine tests. The condition of the two appeared equally favorable from the clinical standpoint. The treatments differed in respect to the total calories of the diet. After the preliminary fasting and undernutrition which cleared up symptoms, the boy (No. 37) was treated along former orthodox lines. He was allowed a high caloric ration supposedly suitable for his age, with the idea of facilitating normal growth and development. Exercise was

employed to build up his muscles and consume surplus food. He was discharged from the hospital with nearly the same body weight as at entrance, and, with his feeling and appearance of splendid health, seemed to afford an example of the most successful treatment. He followed the diet with absolute fidelity and for a short time enjoyed a practically normal existence. 2 months after leaving the hospital, and $7\frac{1}{2}$ months from the onset of the diabetes, marked hyperglycemia was found without glycosuria or other symptoms. This plain warning was met only by diminution of carbohydrate, not of the total diet or weight. The blood sugar continued to rise, and at the second admission traces of sugar and ferric chloride reactions were present in the urine and the carbohydrate tolerance was found markedly reduced. The patient was allowed to go home after only 2 weeks in the hospital, on a diet of 40 calories per kilogram, at an increased weight, with hyperglycemia continuously present. After this discharge the progress was rather rapidly downward, and at the third admission, 11 months after the first, the patient was almost in coma. Much lower diets were then necessary, but the condition was still never adequately controlled, especially as respects hyperglycemia. After further steady downward progress, death occurred two years after the first onset of diabetes. The result of treatment was favorable only to the extent that life and comfort had been so greatly prolonged, in a patient threatened with death within a few weeks or months under other conditions.

The girl (No. 66) received such a diet in the hospital that she was dismissed weighing 5 kilograms less than at admission. The two patients were closely similar in natural size and weight. The boy had been discharged on an average ration of 2100 calories, or 43 calories per kilogram at his elevated weight. The girl was discharged on an average ration of 1630 calories, or 36 calories per kilogram at her reduced weight. This diet was slightly too high; for 5 months after discharge, or 14 months after the onset of diabetes, blood samples taken for observation purposes on 3 successive mornings before breakfast showed a slight hyperglycemia of 0.130 per cent. This warning was heeded by reducing the total calories to a little over 1300 average, by diminishing fat, while the protein was kept the same, and the carbohydrate actually increased by 5 gm. Along

with the hyperglycemia there had been a gain of 8 kilograms in weight. The reduced diet diminished the weight to 50 kilograms, which was identical with that at the first admission. Both blood and urine then remained normal. Later it happened that the girl was placed temporarily on the same treatment as the boy; that is, the fat intake was inadvertently increased, and the beginning of glycosuria was met by a reduction of 15 gm. carbohydrate in the diet. Fortunately the increase of body weight aroused suspicion. On recalling the patient to the hospital, marked hyperglycemia and strong acetone reactions were found. The mistake was corrected by reduction of fat and total calories, while the carbohydrate was again increased by 15 gm. Accordingly, in contrast to the boy's death 2 years after the onset of diabetes, the girl still has the feeling and appearance of perfect health, normal conditions in blood and urine, and full possession of her original carbohydrate tolerance. She has grown and developed normally, apart from being kept slightly but not noticeably below maximum weight. The boy on his unduly high diet developed glycosuria frequently with colds, but the girl passed through an appendix attack without showing sugar. If there is any "spontaneous downward progress" in her case, it has not yet made itself manifest.

The only objection to the comparison must be based on the assumption that the diabetes was inherently more severe and progressive in the boy, and that the girl represented one of the unusual juvenile cases with little progressive tendency. In support of this assumption is the fact that the boy was close to coma within 3 weeks from the onset of known symptoms, whereas the girl entered the hospital without alarming symptoms, 5 months after the first suspicious signs of diabetes. The justice of the comparison is supported by several considerations.

1. It has been the experience with this series of diabetic patients that the most accurate measure of severity is found in the tolerance for carbohydrate and other foods. Coma is often merely an incident depending upon the character of the diet, and is not a reliable index of the true assimilative function or progressive tendency. The girl was 1 year younger than the boy and not so robust. The actual fact is that during her several months of diabetes she had progressed

downward to such an extent that her assimilation was distinctly lower than that of the boy. In the initial test with green vegetables the limit of her tolerance was 140 gm. carbohydrate, as compared with 175 to 200 gm. for the boy. Furthermore, the capacity for improvement was far more evident in the boy, for after $4\frac{1}{2}$ months in the hospital he was able to tolerate 400 gm. carbohydrate, whereas it can be seen from the girl's graphic chart that she showed glycosuria on May 18 and 29 on a slight increase of diet which was far below the regular tolerance of the boy.

2. The progressive tendency in the girl's case was further demonstrated by the hyperglycemia and other threatening signs on two different occasions when she happened to be subjected temporarily to the same unfortunate kind of treatment as the boy. The harmfulness of an unduly high fat ration was thus proved also in her case. The development of these symptoms more quickly and on a lower diet than in the boy's case confirms the assumption that the diabetes was actually more severe in the girl.

3. The claim that the result in the boy's case was due solely to an inherent progressive tendency could be supported only on the assumption that he was somehow immune to the injurious effects of high caloric diets. Such effects have been easily and plainly demonstrable in every case tested, and the rule is believed to be without exception for all typical cases of diabetes. In the light of the plain evidence of all the preceding experiments, it can only be concluded that the excessive caloric ration was one important cause of the downward progress in the case of this boy. Downward progress has thus far been avoided in the girl's case by avoiding such overstrain of the metabolic power. It is strongly suggested that a similar result might have been obtained by similar methods in the boy's case, and that his death within 2 years was not due to any inherent and inevitable process in himself, but directly to the lack of proper treatment.

Though experimental results place the principle of total caloric restriction for diabetes on a basis not affected by the many variables which determine clinical success or failure, yet the general results of treatment under this method, in comparison with the results obtained with such fat diets as have heretofore been employed in the management of diabetes, constitute the most important body of evidence

in support of the practical usefulness of this plan. A number of case histories in this series show the disasters which have occurred whenever the principle of total caloric regulation has been violated. On the other hand, as far as the treatment has been properly carried out, it is believed that the method of restricting fat and total calories in the same manner as carbohydrate and protein has proved valid in its conception and beneficial in its application.

CHAPTER VII.

RESULTS—PROGNOSIS.

Severity of the Cases.

A standard of severity of diabetes is difficult to define. In an attempt to classify cases according to the actual degree of the diabetic disturbance and the problems offered in treatment, the judgment of severity has been formed from three factors, (1) carbohydrate tolerance, (2) age, and (3) clinical course.

1. Accepted criteria in the past have been the assimilation of carbohydrate added to a protein-fat diet, the intensity of glycosuria on a given diet, acidosis, and (with a few authors) changes in protein metabolism and the degree of difficulty in bringing the urinary nitrogen quantitatively and qualitatively to normal. If diabetes is a disorder of the total metabolism, these indices based upon carbohydrate, fat, and protein metabolism are equally valid and yield equivalent information. The essential thing is the power of assimilating food. Diabetes is severe in proportion as this power is deficient. The choice of a test comes down to a question of convenience of performance, ease and reliability of interpretation, and safety for the patient. In some severe cases, the injury from excess of protein or fat is promptly evident. Generally, however, the manifestation is slower, and the injury is correspondingly more lasting. Carbohydrate acts most rapidly in producing glycosuria. Standard conditions for comparison are provided by testing with carbohydrate alone with exclusion of other foods. Glycosuria and hyperglycemia produced by pure carbohydrate subside promptly on its withdrawal, in contrast to the slower rise and fall when they result from protein-fat excess. Such a carbohydrate period, with its attendant undernutrition, acts favorably upon acidosis and upon the diabetes itself, so that with intelligent management a therapeutic as well as a diagnostic purpose may be served. Diet and other accidental factors in-

roduce many elements of confusion in the untreated case. When the rush of symptoms is checked by fasting and perhaps a subsequent undernutrition period, until the acute condition is well controlled, a carbohydrate test has always proved a reliable index of the general food tolerance. Other conditions, such as noted below, being equal, the food tolerance has afforded the best basis of judgment concerning the existing grade of severity of the diabetes, comparisons between patients, and the degree of difficulty to be anticipated in treatment. A patient received in or near coma may have far milder diabetes and be much easier to keep in good condition subsequently than one received with slight or no active symptoms but with a minimal assimilative power. Later tests give indications of the progress when modifying influences are properly considered. For example, with therapeutic reduction of weight there may be an apparent gain of assimilation, and with increase of weight there may be an apparent loss of assimilation, while the actual functional capacity is unchanged. Increased tolerance at the same or higher body weight shows genuine improvement.

2. Age is no absolute guide, for mild diabetes in children and severe diabetes in the aged are known. In general, however, it is recognized that the danger from diabetes is in inverse proportion to the age. Two reasons may be assigned for the difference: first, the higher metabolism in children especially imposes a heavier burden upon a weakened assimilative function; second, the more severe type of diabetes, occurring generally in the young, is a specific disorder of the islands of Langerhans, seemingly partly functional in most cases, but subject to rapid aggravation and organic degeneration of islands due directly to overfeeding. The milder diabetes of later life seems often or generally different in origin, perhaps from chronic rather than acute pancreatitis; at any rate, it generally is less rapidly and seriously affected by excesses of diet. The inherently milder form sometimes occurs in children, and there is a possible hope that recovery from both the pancreatitis and the diabetes may then be more complete than in adults. It is useful to distinguish diabetes which is in a mild incipient stage but is inherently and potentially severe. For this reason every case of diabetes in a child calls for the most careful treatment from the earliest possible moment, preferably under a

specialist; and such juvenile diabetes, even in the early stage with high tolerance, may be classified among severe cases, unless later experience proves it clearly to be of the rarer mild form. On the other hand, no patient is so old that diabetes is harmless to him. No senile diabetes is so free from progressive tendency as not to be aggravated by prolonged diet keeping up active symptoms, or so mild as not to carry the threat of gangrene, blindness, or other form of death or disability at any time. When, after experience with severe cases in young persons in this series, some older patients with long standing diabetes were taken, the supposition that treatment would be quick and easy proved to be a mistake. Not only are an appreciable proportion of such patients subject to the danger of acidosis on fasting, but their glycosuria may be very stubborn and hyperglycemia and acidosis still more so, the apparent food tolerance may be almost nothing, and months of rigorous undernutrition may be required if the condition is to be controlled. The patient and friends may feel that a relatively harmless glycosuria has been exchanged for a state of weakness and discomfort, for a merely theoretical benefit expressed in the laboratory findings; but with perseverance in right management, the reward is obtained in an evident improvement of health, as well as in relief from lurking dangers. Notwithstanding the necessity and the frequent difficulty of rational treatment, the influence of age can generally be trusted to assist; laxness of methods can often be tolerated to an extent which would be fatal in the young. For example, when glycosuria is effectually controlled, the stubborn hyperglycemia and slight ketonuria generally do not demand the infliction of further acute privations upon the old person, but will gradually diminish and disappear in the course of months, provided always that the plan of diet is fundamentally correct. The ultimate results as respects preservation of life and the recovery of strength and ability to take a satisfying diet are also, other things being equal, generally more favorable in the old.

3. The clinical course of diabetes has always been an important criterion of its severity. Until recently, the very acute cases in young persons, terminating fatally within a few weeks, have stood as the extreme type of severity defying all treatment. Fasting has proved surprisingly successful in checking the progress of such cases, and it is

established that they are often not the most severe as measured by the food tolerance, and do not necessarily run the most rapid or unfavorable course. Nevertheless, the rapidity and degree of the breakdown of fat, carbohydrate, and protein metabolism, as shown by acidosis, carbohydrate intolerance, high or "total" dextrose-nitrogen ratios, and exaggerated protein catabolism and aminosuria, must be regarded as important evidence of the inherently dangerous and progressive character of the case. Some allowance is necessary for dietary, infectious, and other modifying influences. For example, an unwise protein-fat diet may bring on early coma. Likewise, in cases Nos. 37 and 66, previously compared, the cold which marked the onset of acute symptoms in the former, and the larger appetite of an athletic boy as compared with a delicate girl, might well be responsible for different rates of initial progress, without relation to any differences in the specific diabetic condition. Sufficiently long subsequent observation may prove that an occasional case, alarming because of intensity of symptoms or its occurrence in a child or young person, is actually mild or transitory in character. Diabetes discovered with an acute infection is notably subject to this rule. For example, among the pneumonia cases in the present series, No. 6 was presumably a mild diabetes rendered temporarily more severe by the infection and resuming its chronic course thereafter; in No. 40, either transitory diabetes was produced by the infection, or latent diabetes was made active and afterward became again latent. In all cases, the results of treatment are instructive. Patient No. 24 was at an age when diabetes is generally more moderate in grade; his case appeared severe, and the difficulty and slightness of improvement with treatment gave the demonstration that it was actually severe. A greater number of the elderly patients, as Nos. 12, 21, 33, and 35, had diabetes which was severe from the standpoint of food tolerance at the outset, but undernutrition finally revealed its essentially mild or moderate nature. Obviously cases may progress from one stage to another. If all the juvenile cases had been counted as severe at the outset because of their youth, there would have been no place to classify them after they had actually reached a worse stage. The readiness with which progress occurs upward or downward may be one index of severity. In the four cases last mentioned, it cannot be

claimed that a change of type has been effected, at least up to the present time, for if they regained their former weight they would probably lose most of their apparent increase of assimilative power. Examples of downward and upward progress are mentioned in the review of cases below. The latter is notoriously more uncommon and uncertain. Genuine changes of the grade of diabetes may be considered as, representing, on the one hand functional deterioration or anatomic degeneration, on the other hand functional recuperation or organic regeneration of the islands of Langerhans. The abyss of severity is found where the assimilative power is not only minimal, but also rises little or not at all with the most thorough and prolonged treatment.

Other occasional features carry some prognostic weight. One of these is obesity. As noticed especially by the French clinicians, *diabète gras* is generally mild.¹ But there is no sound basis for setting this apart as a distinct type, and plenty of cases of "fat" diabetes carry a very bad prognosis unless the patients are relieved of their fat. The obesity in itself is always harmful, never beneficial or protective as so often supposed. The retention of an ordinary good state of nutrition after years of diabetes is strong testimony for the essential mildness of the case, though rigorous and prolonged therapeutic reduction of weight may prove necessary, and there is also the possibility that the case may have turned rather rapidly severe toward the close. The existence of or special susceptibility to any acute or chronic infection is rightly classed among the gravest features in prognosis, and the habitual immunity to infection displayed by many diabetic patients, even on extreme undernutrition, is a strong point in their favor. Such factors, however, properly belong among complications, all of which have important influence upon the patient's fate, but are scarcely elements of the diabetes itself.

Cases and Results by Decades.

Some statistical data are presented in the General Summary Table of Chapter III. In the following survey, it has seemed useful to adopt the well known plan of dividing the cases according to the dec-

¹ The still better prognosis for fat diabetes with careful treatment is indicated by the statistics of Hornor and Joslin, *Am. J. Med. Sc.*, 1918, clv, 47-56.

ades of life. An estimate of the severity is also given, on the composite basis above outlined, chiefly upon the food tolerances, without any absolute standard, since some arbitrary element is necessarily involved in any such judgment.

The actual number of diabetic patients treated in this hospital to date is 100, the total deaths 33, so that it would be possible, if desired, to claim a mortality of approximately 30 per cent instead of the 43 per cent in the above table. A further reduction could be made by subtracting five deaths (Nos. 11, 25, 34, 38, 46) not due to diabetes. No. 48 was counted as dead because of the practical certainty of the outcome under the circumstances. On the other hand, Nos. 7 and 47 were counted among the living patients, though one was lost track of and the other is near death from diabetes. The list of deaths will probably be increased by Nos. 22, 58, and 61, from causes not chiefly referable to diabetes.

The series was limited first to the cases received up to June, 1916, so as to insure at least 16 months observation in every published case. It was enlarged to include five fatal cases and three others (the severe case No. 75 as the subject of special study, cases Nos. 73 and 76, as examples of juvenile diabetes) from the number admitted since that time. The omissions represent only a few mild cases and a larger number of severe ones. These patients are known to be alive and sugar-free, but have been observed for less than the specified time. The selection of the list for publication was governed by the following considerations. First, some adequate period of observation is necessary for judging results in a chronic disease. Second, the more recent cases present nothing different from the early stages of the reported cases. Third, some of the cases were taken particularly for the study of acute acidosis. Some of them may be referred elsewhere for further treatment, and, if so, should be omitted from our permanent statistics. Fourth, the purpose is merely to present the most valuable 76 of the total 100 histories. Had a record of high success been sought, it could easily have been obtained by slight precautions in the selection of cases for treatment. For medical purposes, failures are among the most instructive experiences; therefore the published list was chosen to include all deaths, failures, and bad results in the whole series, including those from discontinuance of treatment, complications, or any other causes.

TABLE I.
Cases in First Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Degree of diabetes.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
68	11 $\frac{1}{12}$ yrs.	10 $\frac{10}{12}$ yrs.	1 mo.	None.	Impending coma.	Moderate.	Superficial initial success; downward progress on excessive diet.	Severe diabetes; kept alive on low diet; weak and emaciated.	1 $\frac{4}{12}$ yrs.	1 $\frac{6}{12}$ yrs.
55	2 $\frac{2}{12}$ yrs.	1 $\frac{10}{12}$ yrs.	3 wks.	"	"	"	Superficial initial success; treatment later abandoned.	Dead.	1 $\frac{2}{12}$ yrs.	1 $\frac{2}{12}$ yrs.
73	2 yrs.	1 yr.	1 yr.	Immediate, in incipient mild stage; subsequent high diet.	Temporary success; subsequent downward progress.	Severe.	Diets too close to verge of tolerance; little further change in condition.	Weak and emaciated.	1 $\frac{10}{12}$ yrs.	1 $\frac{10}{12}$ yrs.
76	4 yrs.	3 wks.	3 wks.	Carbohydrate restriction for 2 days.	Glycosuria almost stopped.	Mild incipient.	Stationary or slowly improving.	Good.	7 $\frac{1}{12}$ yrs.	8 $\frac{1}{12}$ yrs.
45	6 yrs.	9 mos.	9 mos.	Early, but variable; mostly orthodox dietetic method.	Downward progress, extreme weakness, impending coma.	Severe.	Acidosis overcome, but weakness and complications caused death after 10 days.	Dead.	10 days.	1 $\frac{10}{12}$ yrs.

517	6	1 yr.	In coma within 1 wk. from first symptoms without treatment; then 1 yr. on fasting and under-nutrition.	Symptoms more or less controlled; downward progress greatly slowed.	Moderate.	Temporary success; diet later violated.	Dead.	1	2
539	7	2 yrs.	Conventional diet well carried out from the beginning.	Downward progress, without acutely threatening symptoms.	Severe.	Temporary success; later relapse and neglect of treatment.	"	1 ^a 1 ^b	3 ^a 1 ^b
719	7	2 "	Early and efficient.	Successful until diet was broken; then rapid progress to coma.	"	Lived 9 days; too weak to endure extent of fasting necessary for acidosis.	"	9 days.	2

TABLE II.
Cases in the Second Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Degree of diabetes.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).
	At admission.	At onset.		Time and character.	Result.				
13	11 yrs.	10	8 mos.	Moderate carbohydrate restriction from beginning.	Marked downward progress.	Severe.	Downward progress on diets too close to verge of tolerance.	Dead.	From admission. 2 1/2 yrs. 3 7/12
28	11	11	2 wks.	Moderate carbohydrate restriction for 2 wks.	Not evident.	Moderate.	Improvement in spite of imprudent diet.	Good.	2 9/12 2 10/12
42	11	11	3 "	Slight, brief carbohydrate restriction.	" "	Mild.	Marked improvement on undernutrition; marked downward progress on overfeeding; terminal tuberculosis.	Dead.	1 10/12 1 11/12
4	12	5	7 yrs.	Conventional treatment under best auspices from outset.	Slow downward progress; emaciation and threatened coma.	Severe.	Improvement; then aggravation from transgressions of diet.	"	4 7/12 7 1/2
64	12	12	3 wks.	Very slight.	Impending coma 3 wks. after onset.	Mild.	Initial success; downward progress on overfeeding.	Moderate diabetes and emaciation; life maintained on reduced diet.	1 9/12 1 9/12

72	12	1 yr.	Starch-poor, fat-rich diet from outset.	Impending coma.	Severe.	Imperfect treatment; transgression of diet; rapid aggravation.	Dead.	$\frac{4}{12}$ $\frac{1}{12}$
63	13	1 "	Various.	Coma.	"	Downward progress on diets overtaxing tolerance and some transgressions.	"	$\frac{8}{12}$ $\frac{1}{12}$
26	14	9 mos.	Orthodox restrictions from outset.	Loss of weight and tolerance.	"	Practically stationary on diets close to tolerance.	Moderate emaciation; fair strength and comfort.	$\frac{2^{10}}{12}$ $\frac{4}{12}$
66	15	5 "	None, during 4 mos.	Diminished tolerance.	Moderate.	Improvement on total caloric restriction.	Good.	$\frac{1}{12}$ 2
18	16	3 wks.	Carbohydrate restriction during 3 wks.	Not evident.	Mild.	Initial improvement; rapid aggravation on violation of diet.	Dead.	1 $\frac{1}{12}$
37	16	3 "	None during 3 wks.	Impending coma.	Moderate.	Initial benefit; downward progress on overfeeding.	"	2 $\frac{1}{12}$
2	17	$1\frac{5}{12}$ yrs.	Partial carbohydrate restriction.	Gradual downward progress.	"	Improvement, even on diets sometimes unsuitable; downward progress on repeated transgressions.	"	3 5
10	17	10 mos.	Partial carbohydrate restriction.	Emaciation; threatened coma.	Severe.	Initial benefit; rapid aggravation on violation of diet.	"	$\frac{4}{12}$ $\frac{1}{12}$
62	19	5 yrs.	Orthodox carbohydrate restriction.	Gradual loss of tolerance, weight, and strength.	"	Almost stationary on diets too close to tolerance.	Persistent emaciation; fair comfort.	$\frac{1}{12}$ $\frac{6}{12}$

TABLE III.
Cases in Third Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Degree of diabetes.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
48	20 yrs.	19 yrs.	1 yr.	Carbohydrate restriction; habitual transgressions. None.	Loss of strength, weight, and tolerance. Impending coma.	Severe.	Initial success spoiled by later transgressions. Initial success; downward progress on overfeeding.	Dead (?).	1(?) yrs.	2(?) yrs.
32	21 yrs.	20 yrs.	8 mos.			Moderate.	Initial benefit; later tuberculosis.	Severe diabetes; fair strength and comfort. Dead.	2½ yrs.	3½ yrs.
74	23 yrs.	22 yrs.	1 yr.	Slight carbohydrate restriction after first mo. Carbohydrate-free diet from outset. None.	Emaciation; severe acidosis. Moderate emaciation and acidosis. Serious acidosis.	Severe.	Initial benefit; diet later abandoned. Benefit from under-nutrition; gradual downward progress from unintentional dietary errors.	"	½ yrs.	1½ yrs.
9	24 yrs.	23 yrs.	1 "			"	Initial benefit; comfortable at discharge, Apr., 1915. Initial benefit; death from appendicitis.	"	½ yrs.	1½ yrs.
3	26 yrs.	26 yrs.	4 mos.			Mild.	Initial benefit; comfortable at discharge, Apr., 1915. Initial benefit; death from appendicitis.	Tolerance diminished; strength and comfort retained.	3½ yrs.	3½ yrs.
29	26 yrs.	26 yrs.	1 mo.	Partial carbohydrate restriction.	Not perceptible.	Moderate.		Dead.	1½ yrs.	3½ yrs.
34	26 yrs.	23 yrs.	2½ yrs.	Conventional diet, faithfully followed throughout.	Slow downward progress; increasing acidosis.	"				

39	27	22	4½ yrs.	Partial carbohydrate restriction first 2 yrs.; fasting treatment thereafter; frequent violations due to psychic weakness.	Gradual downward progress.	Moderate.	Benefit as far as diet was followed; downward progress from repeated transgressions.	Dead.	2½	6½
43	27	27	5 mos.	Brief hospital treatment, followed by relapse.	Rapid downward progress.	"	Initial benefit; downward progress on prolonged violations of diet.	Severe diabetes. Emaciated. Kept alive on low diet.	2½	2½
52	27	23	4 yrs.	None for nearly 4 yrs.; then partial use of fasting method.	Downward progress slow at first, rapid toward close.	Severe.	Initial benefit; downward progress on diets too near tolerance, and transgressions.	Dead.	1½	5½
1	28	27	1 yr.	Careful dietary restriction most of time.	Emaciation; serious acidosis.	"	Slow downward progress on inadequate treatment.	"	1½	2½
8	29	28	1 "	Carbohydrate restriction faithfully followed from outset.	Emaciation; impending coma.	"	Initial benefit; later tuberculosis.	"	½	1½
40	29	29	Onset with pneumonia.	None.	—	Moderate.	Apparently complete recovery at discharge July, 1915.	No report since discharge.		
54	29	29	4 mos.	Carbohydrate restriction for 3 mos.	Impending coma.	Severe.	Continuously downward in spite of extreme undernutrition.	Dead.	½	1½

TABLE IV.
Cases in Fourth Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Degree of diabetes.	Progress of treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	To Oct. 1917.
36	30	29	1½ yrs.	Conventional dietary restriction from outset.	Emaciation; septic infections; acidosis.	Severe.	Temporary control of symptoms on diets too close to verge of tolerance; aggravation on violations of treatment.	Dead.	1½ yrs.	3½ yrs.
49	30	29	10 mos., probably more.	Orthodox diet not faithfully followed.	Loss of weight and strength; acidosis.	"	Improvement on undemutrition; death within 1 mo. after breaking diet.	"	1½ yrs.	1½ yrs.
56	30	27	2½ yrs.	Carbohydrate restriction from outset.	Loss of weight and strength; acidosis.	"	Temporary benefit; downward progress on diets slightly overtaxing tolerance; infections and dietary errors contributory.	Weak and emaciated.	1½ yrs.	4½ yrs.

NO.	AGE	DURATION	DIETARY RESTRICTION	CONTINUOUS GLYCO- SURIA.	SEVERE.	GLYCOBURIA EASY TO CONTROL ON INDIFFER- ENT TREATMENT; CHIEF TROUBLE CARDIO- RENAL.	IMPROVED.	AGE	AGE
47	31	27	4 yrs. Partial carbohy- drate restriction for 3 yrs.	Loss of weight; acidosis; im- paired health.	Moderate.	Improvement on un- dernutrition, and endurance of subse- quent high diets; downward progress on breaking diet.	Near death.	3	7
44	33	32	1 yr. Carbohydrate re- striction for 5 mos.	Loss of weight; acidosis.	Mild.	Improvement on mod- erate undernutri- tion; patient later passed through pneumonia without glycosuria or acido- sis.	Good.	2½	3½
75	33	31	2½ yrs. Fasting treatment.	Extreme emacia- tion.	Severe.	Symptoms controlled by low diets.	Emaciated and hungry.	9 1½	3½
5	34	33	1 yr. Partial carbohy- drate restriction for 3 yrs.	Loss of weight and strength.	Moderate.	Slow progress down- ward on undue lax- ity of treatment.	Severe diabetes; barely able to continue regu- lar work on re- duced diet.	3½	4½
70	34	32	2 yrs. Conventional car- bohydrate re- striction from onset.	Loss of weight and strength; acido- sis.	Severe.	Improvement; death from influenza.	Dead.	4 1½	2½
31	35	32	3 " Conventional car- bohydrate re- striction from onset.	Loss of weight and strength; super- ficial infection of foot.	"	Favorable progress; dismissed because of untruthfulness and infractions of diet.	Fair.	2½	5½

TABLE IV—Concluded.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Degree of diabetes.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	To Oct.
7	36 yrs.	36	7 mos.	Carbohydrate restriction for 4 mos.	Loss of weight and strength.	Moderate.	Initial benefit; patient dismissed for irregular conduct.	Unknown.	yrs.	yrs.
57	37	19	18 yrs.	None for first 10 yrs.; various diets for last 8 yrs.; frequent irregularities and transgressions.	Gradual impairment of health; at last incapacity for work.	Mild.	Improvement on reduction of obesity.	Good.	1½	19½
20	38	37	1 yr.	Moderate carbohydrate restriction throughout.	Loss of weight and strength.	Moderate.	Improvement on moderate undernutrition.	"	2½	3½
19	39	38	1½ yrs.	Carbohydrate-free diet for 1 mo. past; none before.	Loss of weight and strength.	"	Improvement on undernutrition.	"	2½	4½
38	39		Unknown.	None.	Coma developed with acute infection.	Probably mild.	Relief of coma; death from infection.	Dead.	11 days.	
73	39	38	8 mos.	Partial carbohydrate restriction for 7 mos.	Loss of weight and strength; acidosis.	Severe.	Initial benefit; later abandonment of diet.	"	½	1½

TABLE V.
Cases in Fifth Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Severity at admission.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
15	42 yrs.	40 yrs.	2 yrs.	None.	Coma.	Probably moderate.	Coma not relieved; bicarbonate infusion perhaps partially responsible for death.	Dead.	2½ hrs.	2 yrs.
27	42	34	8 "	Moderate carbohydrate restriction from onset.	Loss of weight and strength; frequent infections; carbuncle.	Moderate.	Recovery from infection; gain in tolerance.	Good.	2½	10½
60	43	42	9 mos.	Moderate dietary restriction 4 mos.; rigorous undernutrition 5 mos.	Loss of weight and strength; acidosis prevented.	Severe.	Symptoms controlled by extreme and prolonged under-nutrition.	Emaciated; kept alive on low diet.	1½	2½
23	44	35	9 yrs.	Moderate carbohydrate restriction.	Retained weight and strength, masking serious downward progress.	Moderate.	Improvement on radical under-nutrition.	Good.	2½	11½

TABLE V—*Concluded.*

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Severity at admission.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
24	44 yrs.	37 yrs.	7 yrs.	Careful dietary restriction, especially for last 6 yrs.	Dangerous weakness and emaciation.	Severe.	Symptoms controlled by stringent undernutrition.	Emaciated but comfortable.	2 $\frac{11}{18}$ yrs.	9 $\frac{11}{18}$ yrs.
30	45	45	7 mos.	None for 4 mos.; carbohydrate restriction for 3 mos.	Loss of weight; moderate acidosis.	Probably moderate.	Fatal acidosis produced by fasting.	Dead.	10 days.	7 $\frac{1}{12}$
21	46	46	6 "	None.	Loss of weight.	Mild.	Improvement on reduction of obesity.	Good.	2 $\frac{11}{18}$	3 $\frac{5}{18}$
59	46	Between 31 and 41.	Certainly 5, possibly 25 yrs.	Spasmodic for 3 yrs.; undernutrition method part of time for 2 yrs.	Gradual loss of weight and strength.	Severe.	Condition imperfectly controlled by diets too close to verge of tolerance.	Emaciated. Able to perform only a little work.	1 $\frac{11}{18}$	At least 7.
67	46	43	3 $\frac{4}{18}$ yrs.	Various diets from outset.	Gradual loss of weight and strength.	Moderate.	Condition imperfectly controlled by diets too close to verge of tolerance; no apparent benefit from treatment of syphilis.	Fairly comfortable, but with glycosuria.	1 $\frac{9}{18}$	4 $\frac{10}{18}$

16	47	42	5 yrs.	Irregular dieting.	Loss of weight and strength.	Moderate.	Improvement on undernutrition; no perceptible difference before and after treatment of latent syphilis.	Good.	$2\frac{11}{13}$	$7\frac{11}{13}$
6	48		Unknown.	None.	No symptoms noticed.	Probably mild diabetes suddenly aggravated by pneumonia.	Initial control of acidosis and glycosuria; return of mild diabetes on abandoning treatment.	No complaint.	$3\frac{2}{13}$	—
46	48	47	1 yr.	Carbohydrate restriction from onset.	Loss of weight and strength.	Moderate.	Diabetic symptoms controlled by undernutrition; later pulmonary gangrene.	Dead.	$\frac{6}{13}$	$1\frac{6}{13}$
12	49	46	3 yrs.	Partial carbohydrate restriction from outset.	Loss of weight and strength; superficial ulcers on feet.	"	Steady improvement on undernutrition.	Good.	$2\frac{11}{13}$	$5\frac{11}{13}$

TABLE VI.
Cases in Sixth Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Severity at admission.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or to Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
25	50 yrs.	47 yrs.	3 yrs.	Slight carbohydrate restriction from onset; carbohydrate-free diet for 1 wk.	Incipient coma.	Moderate.	Favorable as to diabetes; principal trouble and cause of death cardio-renal.	Dead.	3 yrs. $\frac{6}{13}$	3 yrs. $\frac{6}{13}$
14	51 yrs.	44 yrs.	7 "	Diets always violated.	Slow loss of weight and strength.	"	Temporary benefit; treatment later abandoned.	Continues business, but with glycosuria.	2 yrs. $\frac{11}{13}$	9 yrs. $\frac{11}{13}$
33	51 yrs.	49 yrs.	2 "	Continuous partial carbohydrate restriction.	Loss of weight and strength; much discomfort.	"	Improvement on reduction of obesity.	Good.	2 yrs. $\frac{9}{13}$	4 yrs. $\frac{9}{13}$
22	52 yrs.	50 yrs.	2 "	Slight carbohydrate restriction.	Emaciation and weakness.	Severe.	Improvement on undernutrition; relapses on breaking diet; principal trouble nephritis.	Nearly dead from nephritis and apoplexy.	2 yrs. $\frac{11}{13}$	4 yrs. $\frac{11}{13}$

41	52	48	4 yrs.	Slight carbohydrate restriction.	Slight loss of weight; deterioration of general health.	Mild.	Improvement on slight undernutrition; no perceptible change on treatment of latent syphilis.	Good.	$2\frac{6}{12}$	$4\frac{6}{12}$
65	53		Less than 2 yrs.	Practically none.	Slight loss of weight.	"	Improvement on slight undernutrition.	"	$1\frac{7}{12}$	$2\frac{7}{12}$ (?)
50	54	51	3 yrs.	Moderate carbohydrate restriction.	Moderate loss of weight; nervous breakdown.	Moderate.	On reduced nutrition, marked improvement in both diabetes and myxedema.	"	2	5
11	55	48	7 "	Conventional carbohydrate restriction for 7 yrs.	Continuous glycosuria, serious acidosis.	Probably moderate.	Death from cardiac failure or embolism.	Dead.	5 days.	7

TABLE VII.
Cases in Seventh Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Severity at admission.	Progress on treatment after admission.	Condition Oct., 1917.	Duration (to death or Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
35	61	50	11 yrs.	Careful orthodox treatment from outset.	Steady aggravation; impaired health; acidosis.	Mild.	Decided improvement on undernutrition.	Good.	From admission. 2½ yrs.	From onset. 13½ yrs.
17	69		Probably 7 yrs.	Partial carbohydrate restriction for last 6 wks.; none previously.	Incipient gangrene of foot.	Severe.	Gangrene and other symptoms controlled by undernutrition; subsequently relapse of diabetes on less rigid diets elsewhere.	Poor.	2½	10(?)

TABLE VIII.
Cases in Eighth Decade.

Case No.	Age.		Duration of diabetes before admission.	Treatment before admission.		Severity at admission.	Progress on treatment after admission.	Condition Oct. 1917.	Duration (to death or Oct., 1917).	
	At admission.	At onset.		Time and character.	Result.				From admission.	From onset.
58	72	72	More than 4½ yrs.	Slight carbohydrate restriction for 4½ yrs.; none previously.	Retinitis; cataract.	Mild.	Improvement on under-nutrition; successful cataract operation; later departures from diet.	Fair.	1½	—

TABLE IX.
Mortality.

Decade of life.	Total number of patients.	Dead.				Living.			
		No.	Per cent.	Average duration.		No.	Per cent.	Average duration.	
				Under treatment.	From first symptoms.			Under treatment.	From first symptoms.
				<i>mos.</i>	<i>mos.</i>			<i>mos.</i>	<i>mos.</i>
1	8	5	62.5	8	22	3	37.5	11	16
2	14	9	64.3	16.5	30.9	5	35.7	31.2	41.2
3	14	9	64.3	13*	35*	5	35.7	33†	39†
4	16	5	31.2	10‡	24‡	11	69	28§	81§
5	13	3	23.0	2	9	10	77	31	86
6	8	2	25.0	3	63	6	75	27	63¶
7	2	—	—	—	—	2	100	27	142
8	1	—	—	—	—	1	100	20	Above 74.
Total or average.....	76	33	43.4	10.2	30.8	43	56.6	27.3	67.8

* Case No. 48 estimated.

† Cases Nos. 29 and 40 omitted.

‡ Case No. 38 omitted.

§ Case No. 7 omitted.

|| Case No. 6 omitted.

¶ Case No. 65 estimated.

At the same time, no hesitation is felt in discussing the results from the therapeutic standpoint, even on the basis of the 43 per cent mortality of the table.

First, if any defense of the principle of treatment is called for, it suffices to mention that the harmful effect of an increase of fat and total calories has been proved upon a fair number of the cases and is capable of proof in all the rest. None of these patients could be treated successfully by former methods, and if 56 per cent have been kept alive for the period in question, the figure represents almost clear gain. Many of them would not even drag along for months if overfed, but would die very quickly, as indicated by some observations in the preceding chapter.

Second, a critic may claim that this record at any rate justifies the traditional pessimistic attitude toward diabetes, irrespective of tem-

porary benefit by improvement in dietetic treatment. It may be recalled that in the above tables, some cases formerly considered to represent the extreme limit of severity have been ranked as mild or moderate, and those classed as severe not only possess an actually low assimilative power, but have also reached the stage of hopeless inability to recover the lost power. A few milder, senile, obese, or other cases had to be included as examples of their type. Otherwise, broadly speaking (apart from rare cases with extraordinary sugar and nitrogen excretion and acidosis, not always proving excessively severe in the long run) the present series of cases is believed to be representative of the most severe diabetes that exists. The proportion of examples of acutely threatening acidosis or complications, as tabulated below, should also be borne in mind. The critic of the mortality is invited to make comparison with the results in similarly selected cases of any acute or chronic disease with any therapeutic method whatsoever. It may be contended that in these other diseases the patient who does not die is cured. But if sufficiently bad cases be chosen for comparison, there are paralyses and other troubles after diphtheria; there are recrudescences of syphilis, especially if the choice includes a proper proportion of syphilitics too ignorant or too careless to pursue treatment faithfully; and the worst cases of hyper- and hypothyroidism are by no means all cured. The general medical attitude toward these other diseases is not pessimistic, and a pessimistic position toward diabetes cannot be founded upon the results in the most severe cases.

Third, a glance at the mortality table shows that the majority of the patients below 30 years die and the majority of those above 30 live. It may therefore be claimed that these figures at least confirm the inevitably bad prognosis of the severe form of diabetes in young persons. The question to what extent there is such an inherently hopeless severity in youthful diabetes, and to what extent merely a greater sensitiveness to injurious influences, is discussed later in this chapter.

In Table X, "under treatment" includes patients in the hospital or following diet faithfully at home; "without treatment" designates those who have broken diet and died without returning to the hospital. All the deaths can be classified under coma, complications, and inanition.

Under inanition are placed patient No. 1, who abandoned treatment at home and gradually wasted away on a carbohydrate-rich diet which apparently prevented coma; No. 4, a boy who was unduly undernourished by mistake arising from his stealing food; No. 13, a child who gradually progressed downward under inadequate treatment; No. 45, a child received with incipient coma and extreme weakness and impossible to save on the latter account; and No. 54, a woman showing continuous downward progress not checked by prolonged undernutrition. This last case was atypical, as was also case No. 8, in which the necessity of gradual starvation was due to tuberculosis. Under the usual conditions of treatment, even in the severest cases, a necessary choice between death from diabetes and death from starvation has not yet been encountered in this series, though it may later have to be faced in a patient such as No. 73 and probably ultimately in some others.

Among the deaths from complications, those of patients Nos. 11 and 25 were clearly independent of the diabetes. The infectious complications are discussed in connection with Table XII below.

The patients of this series are mostly such as typically die in coma. With the single exception of patient No. 1, who starved to death on starches and candy, every patient who broke diet died in coma, some very quickly. Where question marks are placed after the numbers in the table, the positive diagnosis was not obtained, but the circumstances made coma reasonably certain. No patient has gone into coma while under the dietetic treatment. Since the principle of treatment is to keep acidosis entirely absent, this statement means only that the application has been feasible and successful. The only exceptions to the general statement are patient No. 42, whose diet was relaxed because of tuberculosis, and five others (Table X, first column) whose treatment was incomplete, either because of initial acidosis uncontrollable by fasting, or subsequent departures from diet. These results indicate a genuine advance in the control or prevention of acidosis; and that this is not confined to the present series of patients but has become fairly general, at least in hospitals, is indicated by the fact that a supply of levorotatory β -oxybutyric acid for experimental purposes is now decidedly more difficult to obtain than formerly. Better success in the treatment of actual or threatened coma is also indicated by Table XI.

TABLE X.
Causes of Death.

Case Nos. of patients dying of.					
Coma.		Complication.		Inanition.	
Under treatment.	Without treatment.		Character of complication.	Under treatment.	Without treatment.
					1
	2			4	
		8	Tuberculosis.		
	9				
	10				
		11	Cardiac failure; perhaps embolism.		
				13	
15					
	18				
		25	Nephritis. Apoplexy (?).		
30					
		34	Appendicitis.		
	36				
	37				
		38	Pregnancy. Pneumonia.		
39					
42			Tuberculosis probable.		
				45	
		46	Pulmonary gangrene.		
	48 (?)				
	49				
	51 (?)				
	52 (?)				
	53				
			Some complication possible.	54	
	55 (?)				
	63 (?)				
	69 (?)				
		70	Influenza.		
71					
72					
		74	Tuberculosis.		
Total					
20		8			5

TABLE XI.
Treatment of Coma.

Case No.	Stage of coma.	Coma brought on by.	Lowest CO ₂ of plasma. vol. per cent	Nature of treatment.	Result.
1	Incipient.	Conventional diabetic treatment.	—	Fasting and alkali.	Recovery.
8	"	Conventional diabetic treatment.	—	" "	"
10	"	Neglected diabetes.	—	Fasting.	"
15	Full.	"	—	Bicarbonate intravenously.	Death, perhaps from bicarbonate.
25	" atypical.	Sudden change to carbohydrate-free diet.	—	Fasting, alkali, purgation.	Recovery.
30	Atypical.	Fasting.	—	Purgation, stimulation; food and levulose when too late.	Death.
32	Incipient.	Neglected diabetes.	26.4	Fasting, purgation, alkali.	Recovery.
37	Incipient (1st admission).	"	25.0	Fasting and alkali.	"
37	Incipient (3rd admission).	Relapse under treatment.	24.2	Alternation of fasting and protein feeding, without alkali.	"
38	Full.	Infection, probably in mild diabetes.	30.4	Fasting and alkali.	Came out of coma, died of infection.
39	Incipient.	Violation of diet.	20.7	" "	Deep coma and death in spite of treatment.

	Incipient.	Infection, with latent or transitory diabetes. Progress of diabetes under excessive bicarbonate dosage.	—	Fasting and alkali.	Recovery.
40	Incipient.	Infection, with latent or transitory diabetes.	—	Fasting and alkali.	Recovery.
45	"	Progress of diabetes under excessive bicarbonate dosage.	46.9	Fasting.	Acidosis cleared up; death from inanition.
50	"	Diabetes with myxedema.	53.2	"	Recovery.
63	Full (1st admission).	Mistreated diabetes.	12.3	" and alkali.	"
63	Incipient (3rd admission).	Transgression of diet.	26.0	Plain fasting.	"
64	Incipient.	Neglected diabetes.	16.6	Fasting; bicarbonate on one day.	"
68	"	Untreated	20.2	Fasting and alkali.	"
71	"	Violation of diet.	22.1	" "	Full coma developed, partially cleared on fasting, returned when failure of strength required feeding; death.
72	" (1st admission).	Conventional dietetic treatment.	30.5	Fasting.	Recovery.
72	Full (2nd admission).	Inadequate treatment and violation of diet.	14.0	" and alkali.	Death.

The majority of all the patients had marked acidosis when received. There is no fixed boundary for the beginning of coma, or between threatened or incipient and complete coma. Patients exhibiting merely slight hyperpnea, malaise, drowsiness, or other prodromes have been excluded from the above list. Only those have been included who presented these symptoms in a degree sufficient to make it evident to any observer that coma was actually beginning. The standard of complete coma was not deep unconsciousness with absent reflexes, since in some patients dying of acidosis such a stage is absent or very brief; but when the patient was unable to comprehend where he was or answer questions intelligently, the condition was classed as full coma.

The total number of such cases treated was 21, the deaths 7, or $33\frac{1}{3}$ per cent, the recoveries 14, or $66\frac{2}{3}$ per cent. It would be possible to improve these figures by considering the fact that patient No. 38 came out of deep coma and died of complicating infections which would have sufficed to cause death in a non-diabetic. There were two deaths due to weakness; *i.e.*, patient No. 45 recovered from incipient coma on fasting, went into full coma when fed on account of weakness, then came out of coma on fasting and died free from acidosis; patient No. 71 entered in incipient coma, went on into deep coma before fasting could take effect, partially woke up on continued fasting, lived 9 days without fully regaining consciousness, and died in coma when feeding was compelled by failure of strength. A number of patients have entered with extreme weakness and emaciation, and these features have not prevented treatment of the acidosis in any adults of this series, for strength has usually been gained rather than lost by such patients on fasting. Patients Nos. 45 and 71 above mentioned were small children, and the excessive weakness was the more dangerous on this account. Fasting was risked because it offered a chance, whereas without it death from acidosis seemed inevitable.

Complete Coma.—The chances must be considered to be strongly against a patient in full coma under any treatment, and the results in this series were more favorable than can be claimed as a rule. Mention was just made of the two children (Nos. 45 and 71) who came out of complete coma temporarily, also of patient No. 38, who revived temporarily even in the presence of severe infection. Of the

five examples of full coma at the time of admission, No. 25 was atypical and probably less grave in character. Patients Nos. 15 and 72 died after respectively $2\frac{1}{3}$ and $7\frac{1}{2}$ hours in the hospital. Patient No. 63 showed the lowest plasma bicarbonate and the most extreme collapse of the series, and lived. It is possible that children go into and come out from coma more readily than adults. In cases Nos. 38 and 71 with temporary recovery, and in case No. 63, the coma was complete in the sense of absolute unconsciousness and loss of corneal reflex. In the fatal case No. 15 there was no such stage. Patient No. 30 was clearly conscious almost to the end, as frequently happens in fasting acidosis.

Incipient Coma.—Excluding the two cases (Nos. 45 and 71) with excessive weakness and the one (No. 38) with fatal infection, there were twelve instances of patients received with incipient coma, with one death. The recoveries include case No. 40, with coma impending in the presence of lobar pneumonia. The fatality was patient No. 39, who violated diet and was readmitted with extreme dyspnea but perfectly clear intelligence. There was abundant time for treatment, but the methods were vacillating and uncertain, and the patient went on into deep coma and died. This single death was of a sort which will probably be avoidable when the treatment under these circumstances is worked out better in certain details.

Alternate Feeding and Fasting.—The last mentioned case was one which apparently did not respond well to fasting. An example of relief of fasting acidosis by protein diet was afforded by patient No. 37 at his third admission. The result of failing to recognize the condition in time was shown by the death of patient No. 30. Protein-carbohydrate diet is used for this purpose under the well known plan of Joslin. Even protein-fat diet may sometimes serve, as illustrated by case No. 35 (not in Table XI).

Alkali.—Patient No. 10 received 10 gm. sodium bicarbonate on one day. Patient No. 64 received 25 gm. on one day only. Patient No. 72 (first admission) was an example of treatment of threatening acidosis without alkali. The high dosage of alkali given to patient No. 1 was unnecessary in her case and in most cases. In certain instances (Nos. 38, 40, 63) high bicarbonate dosage by mouth (40 to 125 gm. daily) has seemed both necessary and life-saving. In the majority of the cases it appeared that fasting was the essential treat-

ment and would have sufficed by itself, but that sodium bicarbonate in moderate dosage (15 to 30 gm. daily, in doses of 5 gm. each) hastened the restoration of blood alkalinity and the clearing of clinical symptoms. Joslin has rendered service in emphasizing the harm and possible danger in the prevalent abuse of soda, and has demonstrated the successful routine treatment of acidosis cases without alkali. Patient No. 45 illustrated such injury from bicarbonate by mouth; even with all the other factors against him, he might possibly have recovered if he had not been thus dosed with alkali. Sodium bicarbonate intravenously failed to save any patients in this series (e.g. No. 30). There was suspicion that a liter of 4 per cent solution intravenously was responsible for the death of patient No. 15, who otherwise might have had a chance for recovery. It also seemed likely that a somewhat smaller injection hastened death in patient No. 39, who would have died anyway, and in whom the infusion was tried only as a last resort. It is plain from the literature that some patients have survived such measures in the past, but the danger of large intravenous doses of alkali should be more generally recognized. There is also some evidence in recent literature that when not enough alkali can be absorbed from the intestine because of nausea, diarrhea, or other difficulty, smaller doses, perhaps 200 cc. 4 per cent sodium bicarbonate, may be given intravenously with benefit and repeated at intervals of several hours. Most of the truth about the real effect of alkali in treatment is yet to be learned. It is certain that its wholesale use is pernicious. Also, it is probably bad policy to try to force a low blood alkalinity suddenly up to or above normal by large alkali dosage, especially intravenously. Progress is favorable if the level of the plasma bicarbonate tends distinctly even though gradually upward. A basic element of success in the newer treatment of acidosis consists in allowing the organism time and opportunity to adjust its disordered relations under the metabolic relief afforded by abstinence from food.

Infections.

One of the fears expressed concerning the undernutrition treatment has been that the traditionally low resistance of these patients would be reduced still lower, and that the favorable initial results

respecting diabetes would in prolonged experience give way to a high mortality from infections. The reverse has proved true. Table XII includes all the important infectious complications encountered in the entire series of 100 patients, except the 3 cases (Nos. 16, 41, 67) of latent syphilis. The list includes 27 infections with 7 deaths and 20 recoveries. Noteworthy among the recoveries are 4 cases (Nos. 6, 40, 44, 62) of typical lobar pneumonia. Among the deaths, it may be noted that normal persons sometimes develop conditions like those in Nos. 34 and 38, and die from them, so that these results are not necessarily attributable to diabetes. Patient No. 46 seemed to be an individual of naturally low resistance, who might have succumbed to pulmonary gangrene independently of diabetes. Also tuberculosis is a leading cause of death among the general population, and it must not be expected that diabetics shall be immune. Patients Nos. 9 and 12 were taken because of the suspicion of incipient tuberculosis, which could not be definitely confirmed. It was possible by undernutrition treatment of their diabetes, together with fresh air and light exercise, to bring them into good physical condition, and pulmonary signs and symptoms cleared up completely. The weak and emaciated condition may be held chiefly responsible for 4 deaths, those of patients Nos. 8, 42, and 74 from tuberculosis, and of No. 70 from influenza, but this condition had resulted from the severity of the diabetes and was not attributable to the therapeutic undernutrition.

The general experience may be summarized as follows:

First, efficient treatment of the diabetes, even though this involved the most radical undernutrition, has seemed in every instance the best treatment for the infectious complications. The results of absolute fasting with carbuncle in case No. 27, with incipient gangrene in case No. 17, with influenza in case No. 41, and with some of the pneumonia cases, are examples in point.²

Second, the susceptibility to either major or minor infections has in no way run parallel to the degree of therapeutic undernutrition. The great majority of the complications included in Table XII have been present at admission or have developed on rather liberal diets. The most radically undernourished patients of the series are not represented in this table. Also it might be shown by similar analysis of the

² Benefit in cutaneous lesions has been reported by Grau, R., *Cronica Medico-Quirurgica de la Habana*, January, 1918.

TABLE XII.
Infectious Complications.

Case No.	Present on beginning treatment.		Developed under treatment.		Result.
	Character.	Character.	Character.	Dietetic status at onset.	
6	Pneumonia.	Tuberculosis.			Recovery.
8				Low diet, but slightly overtaxing tolerance.	Death.
9	Bronchitis; tuberculosis suspected.				Recovery.
12	Bronchitis; hemoptysis.				"
16		Otitis media.		Undernutrition 3 mos. after discharge.	Uneventful paracentesis.
17	Incipient gangrene.				Recovery.
27	Carbuncle.				"
28		German measles.		High diet at home.	Uneventful recovery.
31	Superficial infection of foot.				Recovery.
32		Frequent tonsillitis.		Diets slightly overtaxing tolerance.	Partial relief after tonsillectomy.
34		Appendicitis.		43 calories per kg. at home.	Perforation; death.
38	Pneumonia; otitis media; empyema or pericarditis.				Death.

40	Pneumonia.			Recovery.
41	Influenza.			Prompt recovery.
42		Tuberculosis.	Low diet, slightly overtaxing tolerance.	Death.
44	Symptoms suggesting tuberculosis.			Recovery.
44		Influenza.	43 calories per kg.	Recovery
44		Pneumonia.	34 " "	"
46		Pulmonary gangrene.	36 " "	Death.
47	Superficial genital infection, result of pruritus.			Recovery.
49	Cold and fever.			"
57	Furunculosis.			"
58	Superficial infection of foot.			"
62		Pneumonia.	Undernutrition.	"
66		Appendicitis.	Liberal diet.	"
70		Influenza.	32 calories per kg.	Death.
74		Tuberculosis.	37 " "	"

cases that common colds and other minor troubles have been most numerous in the overfed patients. Presumably resistance is best in the mildest diabetes permitting assimilation of a fairly liberal diet. The patients who are worst off in susceptibility to and injury from infections are those with severe diabetes on low diets which nevertheless slightly overtax their assimilative power. The experience indicates that the resistance of these patients is increased by reducing their nutrition within the limits of their assimilation. Also both glycosuria and acidosis, which are the common accompaniments of infection in inadequately treated cases, are frequently avoided when the dietetic management has been thorough, as exemplified by various cases in this series. The vicious circle of aggravation of infection by diabetes and of diabetes by infection is important to avoid. Patient No. 42 might never have acquired tuberculosis had not tolerance and resistance been broken down by unduly high diets, and the infection in turn made the diabetes hopeless. Similar illustrations might be pointed out in regard to less serious infections. The benefit of thorough dietetic treatment consists not only in raising the existing tolerance and resistance, but in preventing them from falling lower.

Third, apart from the one case of pulmonary gangrene and three cases of tuberculosis, none of the traditional complications of diabetes has occurred in any of the 100 cases under treatment. The freedom from pruritus may be mentioned as affording prophylaxis against infection from scratching. Wounds have healed normally, and slight accidents have never had serious consequences. It will probably be conceded that under inadequate treatment the numerous troubles listed in older text-books are constantly overhanging every patient. The relief from them is one of the greatest advantages of the present treatment for both comfort and safety.

In conclusion it may be said that patients undernourished so as thoroughly to control diabetic symptoms may be expected to display a lowering of resistance corresponding to that of equally undernourished normal persons. The large proportion of extremely undernourished patients enjoying complete freedom from infection, or recovering from occasional colds and other accidents like normal persons, proves the safety and benefit of the undernutrition treatment from this standpoint. Food in excess of the assimilation apparently lowers resistance by poisoning the organism. Resistance is raised by

increasing the assimilative power rather than the food supply. The widespread contrary practice based on preconceived ideas is erroneous.

Reasons for Failure in Treatment.

At the outset of the present work, it was proposed³ to take patients solely on the basis of their diabetes, without regard to intelligence, social position, or reliability of character. It was understood that the statistics would suffer thereby, but it was deemed of interest to learn what might be accomplished with the average run of severely diabetic patients. This policy has not been followed throughout, for especially in view of the large number of applicants, there was an inevitable drift toward choosing those who were most dependable and deserving. The character qualification has been given a high place during the last year or more. On the whole, however, the group has been fairly representative; the patients have ranged from the ignorant shiftless poor to the pampered willful rich; and some judgment is afforded concerning the two influences discussed in the preliminary communication mentioned; *viz.*, the "human factor," representing all the weaknesses of human nature, and the "scientific factor," representing all the faults of treatment.

Table XIII classifies the failures of the present series, to the number of 52. On this basis, only 24 of the 76 cases rank as successes. The failures may be divided into total and partial. The former are reckoned at 40, *viz.* the 33 deaths, and cases Nos. 6, 7, 14, 17, 22, 47, and 56, in which abandonment of treatment makes a bad prognosis. Partial failure is understood as downward progress or failure to maintain the initial improvement. There are twelve examples. The classification under fault of treatment does not always mean that the treatment was mistaken. For example, a number of patients died of coma or complications when no known methods could have saved them, and in some instances diabetic treatment was not blame-worthy because death was not caused by diabetes. But it is not possible to distinguish sharply between deaths due to diabetes and deaths independent of diabetes; also, when there is failure with no fault on the part of the patient, it can only be said that the treatment

³ Allen, F. M., *Boston Med. and Surg. J.*, 1915, clxxii, 241-247.

TABLE XIII.
Responsibility for Failures.

Direct cause.		Contributing cause.		Result.
Disobedience of patient.	Reason.	Disobedience of patient.	Reason.	
1	Lack of self control; Christian Science.	1	Badly planned and irregular diets; lack of blood analyses.	Death.
2	Poverty.	2	Unduly high diets.	"
4	Too lax dietary regulations; lack of blood analyses in early period.	4	Inadequate watching.	Downward progress.
6	Neurotic character.			Death.
7	Too lax dietary regulations; lack of blood analyses in early period.			Downward progress.
9	Ignorance.			Relapse; bad prognosis.
10	Untrustworthiness; perhaps drug habit.			Dismissed; bad prognosis.
	Tuberculosis.			Death.
	Deficient will and judgment.			"
	Ignorance.			"
	Cardiac disease.			"
14	Unduly high diets; inadequate control of hyperglycemia.			Relapse; bad ultimate prognosis.
	Unreliable character.			Death.
	Failure to relieve coma; unwise use of bicarbonate.			

17	Poverty; bad environment.			Relapse; constant pain.
18	Carelessness; lack of parental control.			Death.
22	Self indulgence.			Relapse; dying of nephritis.
25	Nephritis.			Death.
29	Ignorance; removal to distant country.			Probable bad prognosis.
30	Mistaken use of fasting.			Death.
31	Carelessness and unreliability.			Relapse; dismissed.
32	Recurrent grippe and tonsillitis; unduly high diets; failure to control hyperglycemia.			Downward progress.
34	Appendicitis.			
36	Neurotic nature; faith cures.	36		Death.
37	Unduly high diets; failure to heed warning of hyperglycemia.	37		"
38	Pneumonia and other infections; pregnancy.			"
39	Neurotic nature; unfavorable environment.	39		"
42	Unduly high diets; failure to note early signs of downward progress.			"
43	Lack of self control; unfavorable environment.	43		Downward progress.
45	Dilemma of coma and weakness.			Death.
				Unduly high diets; failure to control hyperglycemia.
				Abandonment of treatment toward end because of discouragement.
				Unduly high diets; failure to relieve final coma.
				Unduly high diets; failure to control hyperglycemia.

TABLE XIII—*Concluded.*

Direct cause.		Contributing cause.			Result.	
Disobedience of patient.	Failure of treatment.	Reason.	Disobedience of patient.	Failure of treatment.		Reason.
47	46	Pulmonary gangrene. Carelessness.		47	Unduly high diets.	Death Downward progress; dying.
48		Unreliable character.				Dismissed; death (supposed). Death.
49		Carelessness.				"
51	52	Childish indiscretion; unfavorable environment. Unduly high diets; lack of thoroughness.	52			"
53		Failure to return to hospital.		53	Carelessness; repeated minor transgressions; treatment abandoned later. Unduly high diets; inadequate control.	"
	54	Inability to check progressive diabetes.				"
	55	Excessive diet.	55			"
	56	Unduly high diet; failure to control hyperglycemia.	56		Abandonment of treatment in later stage due to discouragement. Abandonment of treatment in later stage due to discouragement.	Downward progress; bad prognosis.
58	59	Senile carelessness. Unduly high diet; lack of thoroughness.	59		Impatience and overactivity.	Relapse; loss of benefit. Indifferent progress.

62	Unduly high diets; failure to control hyperglycemia.				Slight downward progress.
63	Unduly high diets; lack of thoroughness.	63			Death.
64	Excessive diet; too long period without blood analyses after discharge.				"
67	Unduly high diet; lack of thoroughness.	67			Relapse.
68	Excessive diet; lack of blood analyses after discharge.				Downward progress.
69	Neurotic nature.		69		Death.
70	Influenza.				"
71	Dilemma of weakness and intense acidosis.	68			"
72	Lack of thoroughness; failure to control hyperglycemia; inability to relieve final coma.				"
74	Tuberculosis.				"
29		9	9		
Total number 23					

was ineffectual to save him. The classification also does not mean that treatment was perfect in the cases ranked as successful, or in those where the patient is held solely responsible for failure. Also on the patients' side it does not signify that those held guiltless never took a piece of forbidden food, though some in the series can truthfully boast such a record. The serial numbers of the patients are set down in columns according to the sole or primary fault on their part or on the part of the treatment. When contributing factors are present they are set down similarly. The reason for the difficulty is also epitomized as accurately as possible in the parallel columns.

Diabetes has been and is now probably the worst treated of all diseases. The statement does not express so much the genuine difficulty and mystery which have overhung the subject, as the failure to acquire and apply existing and readily available knowledge. Space does not permit enumerating all the faults on the part of the profession at large. Mainly they are gross errors and carelessness in the kind and quantity of diets prescribed, due largely to ignorance of the underlying principles of metabolism and nutrition, and ignorance and neglect of laboratory methods for early diagnosis and for control of treatment. This history of the urine tests will doubtless be more or less repeated with the newer blood analyses. Specialists cannot be criticized for high caloric diets when these were considered proper. But there is experimental proof that dogs cannot live on the extremely low protein, high fat diets such as specialists have considered ideal in severe cases; yet they blamed patients for breaking these diets. Also, how many specialists of the highest standing have subjected patients to an intolerable régime in hospital and been thankful to dismiss them as soon as glycosuria was absent or minimal, knowing perfectly the immediate relapse that must follow, yet recording these cases as "improved" and shifting responsibility for the subsequent fate always upon the patient under one of two headings, either transgression of the (impossible) diet, or "spontaneous downward progress"? The patient cannot begin to be blamed until he has been made thoroughly symptom-free, on a diet which maintains him in equilibrium in this condition and is otherwise feasible to follow, and has been instructed adequately in the management of this diet and in the routine urine tests. Such a program involves hardships in

proportion to the severity of the diabetes, and a patient must have the courage and will power to endure these hardships if he is to live. He can be blamed if he breaks a diet which a fair proportion of other patients have proved able and willing to follow.

Table XIII assigns the responsibility for accessory causes of failure to patients and to the treatment in 9 cases each. The direct or exclusive source of trouble is blamed upon the patients in 23 cases, while in 29 cases the treatment was unable to avert disaster or there were faults in its application. The commonest blunder was feeding beyond the true tolerance and lack of thoroughness in controlling hyperglycemia and other symptoms. In less carefully treated cases, it must hold in still greater degree that diabetics are more sinned against than sinning.

One of the possible fears regarding an undernutrition treatment is that patients will not consent to follow it. The actual experience here and elsewhere has been that they adhere to these diets more faithfully than to the former high caloric diets. Some temporary or long continued (*e.g.* No. 57) successes have been achieved with individuals who had persistently broken orthodox diets. No patient has been forced by hunger to transgress. The great majority of those listed in the above table as disobedient have been on fairly liberal or often high and varied diets, and were the sort of persons who would not abide by any restrictions no matter how slight. On the other hand, the most rigorously undernourished patients, like the majority of the others in the whole series, have for the most part been faithful and trustworthy; so that for every one who has transgressed it is possible to mention one or more who have cheerfully followed equal or lower diets. Doubtless only a minority will bear permanently the extreme restrictions requisite in the cases of maximal severity.

There is greater difficulty with half treated than with thoroughly treated patients. The reasons are physical and psychical. The first consists in the avoidance of true diabetic polyphagia, and of the inordinate carbohydrate craving which comes from an overbalance of fat in the ration. Simple hunger is much more easily and rationally endured than either of these. Psychically there is the encouragement and confidence of continuous sugar-freedom, along with absence or diminution of the neurotic irresponsibility which belongs more often

to the active symptoms of diabetes than to the constitution of the patient. One weak point of the dietetic treatment necessarily is its dependence upon human nature. In general, diabetic patients have proved agreeable and satisfactory to deal with. They have their state of health in their own hands to a greater degree than any others. Since diabetes affects the higher more than the lower grades of humanity, wholesale charges against diabetics are the more improbable. Many of them apply to their treatment the intelligence and resolution that have brought them success in important fields of work. An unexpectedly high proportion of poor and uneducated patients have shown the ability and willingness to carry out their diet efficiently. The fidelity and cooperation on the part of a majority of children with diabetes is remarkable. On the physician's side, success lies in relieving patients of abnormal cravings and nervous states as far as may be done by rational diet, and in establishing the necessary relations of personal confidence.

No hesitation is felt in acknowledging mistakes of treatment as the cause of failure in a high proportion of cases. If anyone treating such a condition as diabetes is not able in looking back over several years' experience to see mistakes in his methods, it is a sign of lack of progress. The errors in this series of cases have been chiefly of three sorts. First, in the early cases, there were some mistakes carried over from the older methods of treatment, and the uncertainty inevitable in beginning a new method. In particular, it was hoped that the tolerance would rise if freedom from glycosuria and acidosis were maintained for a prolonged period, and experience was required to prove that in the genuinely severest cases such a rise is negligible. At this time, when both the clinical and animal investigations, and especially the whole of the laboratory work, were carried by one person without assistance, the necessary completeness of study was impossible. Second, there was some hope that exercise might permit a higher level of diet and strength, especially if the blood sugar were kept normal; and some injury was done before it was learned that burning up calories by exercise is not fully equivalent to subtracting them from the diet. Third, the independent basis of association of the collaborators has given free scope to divergence of opinions and methods. It has thus happened that the practice of feeding to the

verge of tolerance, and the familiar attempt to "build up" patients, especially children, have received a full and fair trial in a high proportion of the cases, with consequences not profitable unless for their instructiveness as experimental controls of the primary principle of treatment. Readers looking for model histories will therefore find few if any, but may profit like the authors from the record of blunders and mismanagement, especially as most persons who have tried to carry out the treatment have doubtless committed the same sort of mistakes. Acknowledgment is always to be made of the shortcomings of the treatment itself, inherent in its negative nature as a mere rest for a weak function, without any positive element of cure. The feeling is that the method has accomplished more benefit than could be achieved by any former plan of treating diabetes, but that much better results than those obtained in this series of cases are possible in the future.

Severity of the Treatment.

The prompt effectiveness of fasting and undernutrition in controlling diabetic symptoms has recommended the treatment in most quarters, but has excited some misgivings in others. A requirement not always fulfilled is that a critic should be able to furnish evidence that he has carried out the treatment correctly in at least a few cases. Two fears may be worth mentioning.

The first is the apprehension as to the suffering involved. This may pertain to the initial fast or to the subsequent diet. The experience in this hospital has received abundant confirmation from numerous physicians and patients elsewhere, that the initial fast as a rule is easily borne. In the severest cases the fast is an absolute necessity, because less radical measures fail to control the symptoms. In all other cases, dietary restrictions in proportion to the severity are always necessary. Under former methods, weeks or even months have been required to abolish symptoms in cases at all severe. Besides the waste of time and money and the injury to the diabetic condition by such prolongation of metabolic overstrain, there is ample testimony that the long program is actually a greater tax on the patient's endurance than is the brief fast. With regard to the subsequent diet, it should be understood that the ideal is the best

possible nutrition compatible with freedom from active symptoms. Opponents must then support one of two theses: either that they can bring about a higher assimilation without active symptoms by some other method than by this method; or that patients will live either longer or more comfortably when allowed to suffer the usual symptoms of glycosuria, acidosis, and complications either in full force or in some mitigated degree. It is believed that facts contradict both these propositions. The latter is the one more likely to be defended by those who seek to justify lax or careless methods; but it may be pointed out that in this case they stand opposed to the best authorities on diabetes from Naunyn to the present, who have held that glycosuria and acidosis should be kept absent if possible.

A second question pertains to the possible danger or harm of reducing the weight and nutrition of diabetic patients. The observed facts have already been stated concerning subjective health and comfort, longevity, and the chance of infection when the patient is faithful to diet. With regard to breaking diet, the conclusion was drawn that this is less rather than more frequent under the new treatment. The remaining question then is what is the effect of the treatment when it is begun and later not followed out properly. A physician clearly should not impose fasting if he is not competent to maintain the benefit subsequently. When glycosuria is abolished by fasting, then brought back by improper diet, then stopped by fasting again, and so forth, the nutrition is lowered with no corresponding gain in assimilation, and this harmful process may be continued even to death from starvation. This is wrong management. When a patient abandons treatment, there is a risk of arbitrary judgment without tangible support. If he dies quickly, it may be claimed either that the treatment injured him, or that it was the means of prolonging life in a case demonstrated as severe by the outcome. If he lives long, this result may be regarded as an after-benefit from the treatment, or as proof that the stringent measures were unnecessary and that a longer and happier life was made possible by discarding them. Confusion is largely obviated by considering facts as follows. Numerous patients in the present series have been received in critical condition, have been kept alive for long periods under treatment, and have died in coma soon after breaking treatment, thus

demonstrating the severity of the diabetes. When they have escaped early coma, they have lived surprisingly long for patients of such a type; *e.g.*, patients Nos. 1 and 60. As already mentioned, the vast majority of deaths are due to acidosis and not to undernutrition. To show an injury from the treatment, it would be necessary to prove that patients are made more susceptible to coma by having their acidosis completely cleared up. It is believed, therefore, that careful treatment represents clear gain, even if it is later abandoned.

Prognosis.

The expression, by word or act, of opinion concerning the probable course and termination in diabetes is more than prognosis; it is a part of the therapy. It is important that patients should be told the actual truth, without favorable or unfavorable bias or concealment. Great harm is frequently done by careless judgment of the earliest and mildest cases and by an unwarrantably gloomy forecast in the severe ones.

According to Naunyn,⁴ “*der Verlauf der Krankheit ist so verschieden wie denkbar.*” The statement is correct in the sense intended by that author, signifying the wide extremes of mild and severe, acute and chronic forms. It is not true in the sense of any bizarre heterogeneity of the disease, indicative of multiple organic origins or forbidding prognosis in individual cases. With allowance for the rare exceptions encountered with every ailment, with consideration of the principal factors of severity previously mentioned, and with cognizance of the influence of all three classes of foods, it is possible to outline fairly definitely the prospects in the great majority of diabetic cases. Predictions can be hazarded to some extent at the outset, but are more certain after a period of observation under treatment. The prognosis of possible accomplishment under the present method pertains to comfort and longevity.

If a patient can be kept alive, it is generally desired to know at what level of comfort, strength, and efficiency this is possible. As no cure exists, it should be stated plainly that this level is lowered in proportion to the severity of the case. Tables I to VIII show the

⁴ Naunyn, B., *Der Diabetes melitus*, Vienna, 2nd edition, 1906.

existing condition of the patients of this series, which in the majority of those living is decidedly, and in many of them extremely below normal. A point not to be overlooked is that, except for some bad results due to transgressions by the patients or mistakes in treatment, this state of invalidism had been present before and was benefited by treatment, and the way to avoid such a state is to adopt the most efficient treatment possible at the earliest possible stage. To generalize the actual results, it may be said that the patients as a whole have been relieved of the tormenting complications of diabetes. Therapeutic reduction of weight has ordinarily been attended by increase, not by diminution of strength. The notions of "starved" patients entertained by those having no experience with the method are widely erroneous. Of 18 living patients above the age of 30 who have been faithful to diet (excluding the cardiorenal case No. 61), all but 2 are carrying on their regular duties more or less satisfactorily, and 13 of these are almost or entirely free from impairment of strength, working power, appearance, or subjective health referable to diabetes. The most extremely undernourished man (No. 24) has carried on his business continuously. The most radically undernourished woman (No. 60) has continued light household tasks and supervised the bringing up of her daughter. There is frequently a tendency to progressive gain in health in this older group. Of the 5 in the third decade counted as living, one was an exceptional case resulting in apparent cure, one is emaciated by reason of transgressions of diet, one looked and felt well at departure to Finland, and two are leading their usual lives in such condition that a stranger would notice nothing wrong, over 3 years from the onset of their diabetes. The younger patients are discussed more in detail below. The best accomplished in them has been to preserve such strength and well-being as they possessed at the time of beginning treatment.

A familiar defense of overfeeding is that the patient must die anyway and should be kept as comfortable as possible in the meantime. Very often this is a mere excuse for mismanagement, and it is not justified by the present experience. No patient of this series has broken diet with impunity. The penalty of eating much or little in excess of the tolerance has been corresponding reduction not only

of length of life but also of strength and comfort. Cases mild enough to drag along for months or years on improper diet are also mild enough for a reasonably satisfactory diet and bodily condition under proper treatment. The more severe cases face a correspondingly worse dilemma. Moderate overeating does not satisfy; diabetic polyphagia is harder to endure than simple hunger, and the malaise of chronic acidosis and the troubles of various complications are super-added. Excessive overeating of carbohydrate increases polyphagia and emaciation; excessive overeating of fat brings quick coma. The only argument against thorough treatment must therefore be that it is cruel to prolong the state of impaired health. But euthanasia is no more justified in diabetes than in numerous other conditions. The strongest reason for the earliest and most efficient treatment possible is not the relief of the immediately threatening or troublesome symptoms, but is rather the fact that such treatment acts to preserve strength, comfort, and assimilative power, and either saves from the condition of extreme privation altogether or holds it off to the farthest possible time. Diabetics who overeat for the deliberate purpose of killing themselves are uncommon. In this respect the experience shown in Table XIII probably holds for diabetics in general. The patients who died from breaking diet were not driven to desperation by hunger or suffering. They were generally not the ones who had to endure the greatest privations. They were rather the ignorant, the careless, the weak-willed, the neuropathic, and others who would not have been faithful to any restrictions no matter how mild. Under such circumstances it is the physician's duty to strengthen, encourage, and aid. The condition of the living patients of the present group, young and old, ranges from perfect subjective health to very serious privation, according to the severity of their diabetes. The lesson from the standpoint of comfort is wholly in favor of efficient treatment at the earliest possible stage, not in favor of bad treatment at any stage. The only apology for reciting these obvious facts is the frequency with which the fallacy in question is encountered.

As to the prognosis for preservation of life, Tables I to IX show the high mortality of 43.4 per cent as what the physician may expect if he limits his practice to cases like these. For dia-

betic patients themselves, it is instructive to extend the inspection to Table X. Two or three elderly patients have paid for breaking diet only in loss of health and not by loss of life. Otherwise, the record stands that the patients who abandoned treatment died, all but one of them in coma. This statement is unjust in a few instances where patients only gave up because of discouragement after downward progress; but it can still be answered that none of them had been called upon to endure lower diets than others have successfully endured. If the list be limited strictly to those who have faithfully followed treatment throughout (and they are the majority) then only fourteen deaths remain to be explained. Of these, three (Nos. 15, 30, 45) were acute deaths, due to coma immediately following admission to the hospital for commencing treatment. Nine were due to complications (tuberculosis in Nos. 8, 52, 74; heart disease in No. 11; nephritis in No. 25; appendicitis, pneumococcus infection, pulmonary gangrene, and influenza in Nos. 34, 38, 46, and 70). No. 13 was complicated with urinary calculi and the diabetic treatment also was not thorough. No. 54 was an unusual case, with fatal course suspected as due to some complication. If all these cases were set aside, it would make an absolutely clean record without deaths in the entire experience of $3\frac{1}{2}$ years. Of course it is not permissible to wipe the slate clean in this manner. For example, the tuberculosis in case No. 52 was clearly the result of bad progress of the diabetes under wrong treatment; the influenza in case No. 70 was probably fatal chiefly because the patient was weak from diabetes. On the other hand, some deaths from complications were, as stated, apparently independent of diabetes. The fact may further be noticed that diabetic statistics are perhaps the only ones in which patients who do not follow the treatment are included among the failures of the treatment, even when, as with most of the disobedient ones here, the fault was solely their own. This exception with respect to diabetes is just, because one important test of the practical worth of a treatment is its feasibility, not for some specially selected patients, but for the general average of human nature. Nowhere more easily than in diabetes is it possible to obtain that familiar form of therapeutic data which in themselves are not false, but are so selected as to lead to erroneous conclusions. It can be repeated that in the choice of

these cases, all pains were taken to invite the highest mortality possible. It is fair to claim that disobedience, coma, and complications do represent special difficulties. From the medical standpoint all the deaths and failures from all causes belong strictly in the series, and they were given full weight in the foregoing account. From the patient's standpoint, however, it is justifiable to point out that if he is constantly faithful in treatment, if he has not died in coma at the outset, and if he is not one of the small proportion (9 or 10 in 100 cases in this series) to succumb to complications, his chance of survival according to the above statistics to date would be close to 100 per cent. These figures apply to a group of cases of high average severity, in which coma, complications, weakness, and other dangers are most common; also it was noted that there was considerable injury from mistakes in treatment. It is believed that the record offers a hopeful outlook for the average diabetic patient under efficient care. It will not be possible to keep patients with the severest diabetes alive indefinitely by this or any other dietetic treatment, but the great prolongation of life in them shows how much may be hoped when such treatment is applied in the earliest and mildest stages, as it properly should be.

“Spontaneous Downward Progress.”

The belief in an inherent progressive tendency in at least a large proportion of diabetic cases is universal. The evidence in the literature is valueless. The belief rests largely upon the rapidly fatal course of many severe, especially youthful, cases. Other instances cited, as by Naunyn, are merely those in which glycosuria was suppressed by carbohydrate restriction and returned on the usual high caloric diet. This question of spontaneous downward progress may rank as the most important one in the entire subject of diabetes, from two viewpoints. The first is clinical. It is the question of the possible prolongation of life; whether, with adequate regulation of all classes of food and abolition of all symptoms, the diabetic process is brought to a standstill, or is merely slowed so that the fatal end comes somewhat later but just as surely. The second pertains to the pathology and etiology of diabetes; whether the cause producing the diabetes is a transitory or a continuous and progressive process.

Knowledge on this point would decide the clinical prognosis. Conversely, observations of the progress of patients with relief from food injury will throw much light on the nature of the diabetic process.

From one aspect, it might seem natural to anticipate that, since diabetes is not actually caused by diet, the essential process should not be halted by change of diet. This point could not be settled except by an anatomic investigation, as described in the following chapter. This pathologic study has shown that the downward progress due to food injury is an additional and separate process, independent of the original cause of the diabetes. A standard object of comparison is the partially depancreatized dog. Here a surgical resection produces a definite degree of pancreatic deficiency, and the absence of any inherent progressive tendency has been established by prolonged experiments. More or less gain in assimilation may be observable, dependent in at least some cases on hypertrophy of the pancreatic remnant. But when a fairly fixed limit of tolerance has been determined for some time, this shows little further spontaneous change in experiments extending over years. The behavior in this respect is like that of many human diabetics. The most important point is that in suitably prepared animals with rather severe diabetes, the prevention of active symptoms and fatal result requires restriction not only of carbohydrate and protein but also of total calories and body weight. By addition of fat to a diet on which the condition is demonstrably stationary, the "spontaneous downward progress" of clinical cases can be precisely imitated. Even with milder diabetes, it is possible to prove the same relation between weight and tolerance as exhibited by human patients. There are dogs now living whose tolerance can be varied at any time by manipulating their body weight.

The pathologic evidence needs to be supplemented by clinical observation. It is obvious from the former that pancreatitis is sometimes chronic and progressive; also, even an acute inflammation starts up changes which continue to a variable time and degree. Such a process is necessarily beyond the power of dietetic treatment. Clinical experience must therefore decide what proportion of human patients show indications of such an advancing lesion, or any other progressive factor not present in dogs and independent of food injury.

The present series of cases should have answered this question, and the greatest disappointment of the clinical research has been the inability to carry out the original plan to this end. The existing observations are presented for the partial information which they afford. As mentioned before, the aggravation resulting from infection was exhibited by patient No. 8 with tuberculosis, and by other patients with various acute infections. Similarly, patient No. 54 was a typical example of downward progress according to the idea which has been so prevalent. When freed from symptoms by radical undernutrition, it was impossible for her to remain so on any living diet; the symptoms kept recurring in spite of progressive reduction of weight and metabolism; there seemed to be nothing but a continuous choice between inanition and coma, and the patient finally died after a steadily losing fight of 9 months. This is the conception which has existed in some quarters concerning the undernutrition treatment of severe diabetes. It is possible that some progressive process was at work in this case. It is certain that the other cases of the series have not been of this sort. The experience with the others can best be considered in the groups above the age of 30 and in the decades below that.

In the patients above 30 years, it may not appear surprising that no progressive downward tendency has as yet been observed. Yet the older patients are the ones in whom the pathologic studies in the literature have shown chronic pancreatitis most frequently. If there were a progressive decline clinically, it might be readily explained by progress of the pancreatic lesion, and some cases must certainly show such a decline ultimately. In view of the known pathologic findings, the accepted favorable prognosis of diabetes in the elderly is rather remarkable. Patient No. 24 is a man aged 44 years, with the most severe diabetes of any man of this group, and with the typical history of the disease beginning in mild form 7 years previously, and gradually progressing to the extreme stage present on entering this hospital. There was a history of indigestion, pale feces, and jaundice in the year prior to the diagnosis of diabetes. The skin is yellowish, there is a dyspeptic tendency, and especially fat easily upsets the digestion. The prediction can be made that if autopsy is obtained it will reveal chronic pancreatitis. The case has actually

shown the stationary tolerance characteristic of severe diabetes, and has done well under the circumstances during almost 3 years of observation. The woman No. 60 had the severest diabetes represented in this group. The type was more like that of younger persons. Within less than a year after onset, the condition had attained such severity that only the most radical undernutrition was able to control it. Even though her hyperglycemia was not thoroughly controlled, the downward progress was apparently halted, and there was no perceptible further loss of tolerance during nearly 2 years of observation. The improvement manifested by other patients when their weight was reduced has persisted with continuous regulation of diet and weight. Particularly important are the observations with patients such as Nos. 23 and 41, showing how assimilation rises and falls inversely with the weight, just as in dogs. Though such cases belong among the milder ones of the series, it is plain that "spontaneous downward progress" can be produced in them at any time by the familiar "building up" in diet and weight. With relief from such an overload, they have shown generally an upward tendency as far as the period of observation extends.

In the third decade (cf. Table III) a number of cases are of service only as examples of the rapid downward progress resulting from dietary errors. The cases with complications are excluded; none showed downward progress prior to the fatal infection. Patient No. 40 apparently illustrated complete recovery from acute diabetes accompanying pneumonia. Patient No. 29 was lost from observation. No. 54 was the atypical case above mentioned. This leaves Nos. 1, 3, 32, and 52 as suitable for the present discussion. All showed more or less downward progress. No. 3, for example, had been a very rapidly progressive case, with active glycosuria and acidosis under the previous treatment and with the prognosis of only a few months of life. A consistent reduction of diet and weight was maintained during the $3\frac{1}{2}$ years since. With the mistakes in diet known to have occurred in hotel life, causing slight glycosuria at times, it is not surprising that some decline of tolerance has occurred in such a case; but this has been slow in proportion as the dietetic errors have been slight. The other three patients illustrate the effects of continually feeding to the verge of tolerance, keeping up continuous hyperglycemia

and occasional glycosuria. In dogs, one of two things occurs under these circumstances. One possibility is that the pancreas remnant increases in size or function and hyperglycemia diminishes and disappears. This is the result which is noticed frequently in the more elderly patients, and which originally was hoped for in others. The other possible outcome in dogs is a gradual breakdown of function under the overstrain when the pancreas is unable to rally in this manner. This breakdown is much slower than on a higher diet, but the susceptibility to this injury is in proportion to the real severity of the diabetes. Accordingly the youngest patients are generally the most susceptible. There is nothing perceptible in this group of cases that cannot be exactly imitated in dogs.

In the second decade (Table II), case No. 4 illustrates the fact that not all patients can be classified together in prognosis merely because of youthful age. This diabetes began at 5 years; the diet was the conventional sort on which children ordinarily die quickly, and there were frequent transgressions; yet the boy lived to the age of 12. There is natural interest as to what might have been the result with this child if all active symptoms had been kept absent by efficient dietary regulation from the outset. Several of the other cases illustrate the rapid downward progress caused at this age by disregard of diet. One of these, No. 10,⁵ showed "total" diabetes, as demonstrated by the D:N ratio and the respiratory quotient at the time of his admission. The gradual marked gain in food tolerance represents upward not downward progress, in contrast to what quickly happened when he abandoned restraint. In the history of case No. 2 (Chapter III) it was pointed out how rapidly aggravation was produced by each departure from diet, while in the long intervening periods in the hospital the absence of any perceptible downward tendency was demonstrated, even though the treatment was far from ideal. The patients of this group who were fairly faithful to diet can be divided into those received in the final severe stage of diabetes, and those received in an earlier, mild or moderate stage.

The former group consists of cases Nos. 13, 26, 62, and 63. The faults in their treatment are pointed out in the histories. In par-

⁵ Gerald S. in the paper of Allen and DuBois.

ticular, hyperglycemia was kept up almost continuously by diets too close to the verge of tolerance. The important feature is that they had already reached the stage where improvement to the extent of tolerating a high diet was not possible even temporarily. Therefore, to avoid glycosuria and acidosis, all were limited to low diets. Two are alive, and two have recently died, after periods of 8 months to nearly 3 years under this treatment, and 20 months to 6 years of total duration of diabetes. More or less rapid downward progress was evident in all before beginning this treatment. It has since been not perceptible in two, and has been slow in the other two, due to obvious mistakes and accidents. The result is the more remarkable because dogs with similarly severe diabetes would have been dead long ago if treated in this fashion. An inherent downward tendency is therefore not revealed.

The cases in the mild or moderate stage comprise Nos. 28, 37, 42, 64, and 66. Patient No. 28 improved decidedly during hospital treatment with undernutrition which reduced her weight by 1 kilogram. She was allowed high diets after discharge, and has grown and developed normally and gained markedly in assimilative power. Experience here and elsewhere has proved that the result of such high rations in diabetic children is almost always disastrous; and it is a fair inference that this case was somewhat unusual in type, probably the result of an acute infection, and more or less comparable with the adult case No. 40, where there was apparently complete recovery from diabetes accompanying pneumonia. The prognosis for this child was almost certainly unfavorable if active symptoms had been allowed to continue. With the aid of temporary undernutrition the expected downward progress was changed into upward progress, and the result is a thoroughly comfortable and normal appearing child, whose improvement may perhaps continue further to an unknown extent. On the other hand, trouble may yet result from her heavy diet, occasional transgressions, and hyperglycemia;⁶ and there is further the question how much more rapid and complete her recovery might have been to date if the diets had been more prudent.

⁶ As noted in the history, this patient on excessive diet has suffered relapse, as feared.

Of the four others, patient No. 64 was a boy of 11 years, with the most acute form of juvenile diabetes, threatening coma within 3 weeks of the first observed symptoms. His history shows the rapid improvement with undernutrition, the ability to tolerate 50 gm. carbohydrate and 1750 calories at discharge proving that the actually severe stage had not yet been reached. The tendency of the blood sugar to fall to normal was reversed by the unwise increase in diet. The initial improvement was therefore not maintained. In consequence of a relapse, the diet was reduced to 1250 calories, still with 50 gm. carbohydrate. This ration might have been tolerated at first, but is now too high, as shown by the persistent hyperglycemia, and further relapse will occur unless the treatment is changed. Patient No. 42 was a girl, also aged 11, and with diabetes of 3 weeks duration. The glycosuria and acidosis were controlled by undernutrition as usual, and the blood sugar also was brought to normal. She was 232 days in the hospital, and the great and genuine improvement during this time was beyond question. She was then overnourished so that the original weight was regained, and was allowed a diet of 1500 calories, averaging 48 calories per kilogram, at discharge. The warning of the subsequent hyperglycemia was not properly heeded, and the inevitable relapse followed. The diet then had to be cut to 800 calories; *i.e.*, as usual, both food and body weight were made lower than would have been required for proper treatment at the outset. Even so, the measures were not rigorous enough to control hyperglycemia, and the characteristic downward progress continued, until terminal tuberculosis closed the failure. The story of patient No. 37 is similar. He also had diabetes of 3 weeks duration, which had already brought him to the verge of coma. With him also the symptoms were abolished by undernutrition and the blood sugar was reduced to normal. The inherent power of recovery was so great that a tolerance for over 400 gm. carbohydrate was regained in hospital. Here also undernutrition was abandoned, an average ration of 43 calories per kilogram was prescribed at discharge, and at his second admission he showed a gain of 6.2 kilograms weight and a corresponding hyperglycemia. The diet was then somewhat reduced, but not enough to stop the downward progress. The subsequent history and fatal termination were the familiar results of a "building up" policy. The fact is

noteworthy that these patients, taken in the relatively mild stage of their diabetes, with demonstrated capacity for improvement in assimilation, are dead, while patients of the former group, taken in the stage of severe diabetes after practically all power of regaining tolerance had been lost, have survived after a corresponding interval of time. The evident difference is that those with severe diabetes were kept on low diets perforce, for fear of glycosuria and acidosis, whereas in the milder cases the manifest tendency toward recovery was abused by overloading with diets such as could only be justified on the assumption that a short period of undernutrition had practically cured the diabetes. The difference is plainly not one of the inherent progressive nature of the cases; for some of those showing the most alarming initial tendencies have displayed the most marked power of recovery under treatment. The truth is that full recovery is very rare, and the method of undernutrition, by which the initial success is gained, must be followed in the later treatment in proportion to the requirements of each case, if success is to be achieved. Additional support is given to this principle by comparison of the remaining case No. 66 with those just described. The parallelism and contrast are particularly strong between this and No. 37, as detailed in the previous chapter. Greater severity of the diabetes in the girl No. 66 was seemingly indicated not only by the lower carbohydrate and total food tolerance, but also by the practical absence of the power of improvement. Precautions with respect to total diet and body weight were observed with this patient. The boy No. 37 died at the end of 2 years of diabetes, while the girl No. 66 after 2 years suffered not the slightest diminution in health or tolerance. Further evidence is afforded by the fact that unduly high diet or body weight has in each instance given rise to hyperglycemia in the girl, whereas by limiting these her blood sugar is kept normal. It is evident that diets much lower than those imposed upon the boy would in her case even more quickly produce the "spontaneous" downward progress. It is certain that by the difference in treatment in her case, the aggravation to which she is clearly susceptible has either been prevented absolutely, or reduced to such a minimum that it is not perceptible within 2 years.

The cases in the first decade (Table I) in which treatment was followed sufficiently to permit judgment on this point, are also divisible into those received in the severe and those received in the mild or moderate stage. The only representative of the former is case No. 73. The history of this 3 year old girl is that 1 year before admission she received treatment for her diabetes in its incipiency. She was then allowed the high diet which she could apparently tolerate, and within 10 months marked downward progress was manifest. Stringent reduction of diet was necessary in the severe stage, and though the treatment has been imperfect, no further downward progress has been perceptible in the subsequent 10 months.

Patients Nos. 55 and 68 were babies aged respectively 26 and 23 months, with early but intense diabetes. The symptoms were controlled as usual, and then undernutrition relaxed, the diets at dismissal averaging respectively 3.8 gm. protein and 48 calories, and 5 gm. protein and 68 calories per kilogram. In the light of experience, nothing but downward progress could have been expected, since children generally show no greater power of recovery than older patients. Both children finally died after the parents had given up the diet from discouragement. It can only be claimed that by this inadequate treatment the downward progress was slowed. Patient No. 76 is a boy aged 4 years, likewise with diabetes of about 3 weeks duration. His diet has been such as to prevent him from gaining weight unduly. He has been comfortable, active, and of healthy appearance, his blood sugar has been kept normal, and he has certainly not lost and apparently gained considerably in assimilative power during 8 months. This case seems unquestionably to be of the type which ordinarily progresses very rapidly to a fatal end, but there has as yet been no perceptible sign of any "spontaneous" tendency, unless it be upward.⁷

Accordingly in the first and second decades of life, when the prognosis is supposed to be worst, there have been altogether 13 patients in this series who have followed diet to a reasonable extent. The deaths have been five in number, or 38.5 per cent. The living ones number eight, or 61.5 per cent. The average duration of the five fatal cases under treatment (to October, 1917) was 20 months, the

⁷The favorable condition is still maintained (June, 1919).

average duration from the first diabetic symptoms 25 months. The average duration under treatment in the eight living patients has been 20 months, from the first known symptoms 69 months. Mention was made of the part played by mistaken management in all the fatal cases and some of the living ones. Nevertheless the figures are better than any reported for cases of this type under any former method of treatment, and contradict the time limits heretofore set for juvenile diabetes. An outstanding feature is that even the childish patients have displayed actually greater resistance to the injury of overfeeding than dogs with correspondingly severe diabetes. It must therefore be concluded that as yet no spontaneously progressive tendency has been demonstrable in any of these cases.

Such a conclusion, if confirmed in the future, will possess scientific importance in relation to the etiology and pathology of diabetes. It will not necessarily assure therapeutic success. Transgressions of diet, infections, and the demands of growth are among the difficulties to be thought of, independent of any specific progressive process in the pancreas or elsewhere. It can only be repeated (1) that children as a rule make good patients; (2) that infections are most frequent and work greatest havoc when the diet is wrong, and are fewest and least harmful, often leaving no lasting injury to the diabetes, when the dietetic management is right.

There is always the possibility that sufficiently prolonged observation will yet reveal an inherent progressive tendency in some or most cases of diabetes, especially in youth. It has also been freely conceded from the first that no known dietetic treatment can enable children with the severest diabetes to grow and develop normally. It is a gratifying surprise that the weakened function can bear the strain of the high metabolism of childhood as well as it does. It is not feasible to fix any theoretical standard as to what ration a diabetic child must take. The safe level of diet and weight necessarily varies with the severity in different cases. Maintenance at reduced weight is possible on rations far below current text-book stipulations, because undernutrition acts powerfully to reduce metabolism even in children. The rule followed at present is, after controlling glycosuria and acidosis by fasting, to work up to 1.5 to 2 gm. protein per kilogram, enough carbohydrate if possible to keep acetone reactions

negative in the urine, and finally such fat and total calories as can be borne without either acidosis or hyperglycemia. Possibly the metabolism may sometimes have to be brought as low as that of normal adults or lower. The observations do not yet permit generalization as to what happens with the growth of such children, or whether undernutrition is the sole retarding influence or whether a specific diabetic defect plays a part. The unfavorable prognosis for development in the extreme cases should not be too rashly extended to juvenile diabetes in general. Apart from the very mild or transitory examples occasionally described in the literature, it may be noted that out of eight early but intense cases in this series (Nos. 55, 68, 76, 28, 37, 42, 64, and 66), three (Nos. 28, 66, and 76) are indistinguishable from the normal in appearance, and the high capacity for improvement exhibited at first by Nos. 37, 42, and 64 suggests the possibility of really satisfactory results, had they been granted a fair chance in their later treatment. Under any interpretation, these figures to date offer a prospect of growth and development in a higher proportion of cases of juvenile diabetes than admitted heretofore.

It will probably prove erroneous to group all cases of youthful diabetes together in a common prognosis. Rare cases as mentioned in the literature are transitory in spite of unregulated diet. A few others have recovered completely after prolonged conventional treatment. It is reasonable to believe that still others will recover more slowly and incompletely, and the ease and extent of such recovery may be governed by the treatment. As suggested above, patient No. 28 might have died under former treatment, and the actual result might have been better had the treatment been better. Others may possess little or no power of improvement in assimilation, and growth and development may have to suffer in proportion to the actual deficiency of metabolic function, and downward progress may even occur in spite of any dietetic treatment. The outstanding feature of present observations in this connection is that this unfortunate condition of minimal food tolerance and absent recuperative ability, with the accompanying dark outlook for growth and development, was practically always the consequence of improper feeding in the earlier stage. It ought to be self-evident that not food, but the power of normally assimilating food, is the essential thing which

diabetic children lack; and the best growth and development are obtained by the method which best conserves and strengthens their assimilative capacity. Success does not lie in trying to force them with any kind or quantity of food in excess of the true tolerance. Universal experience has proved that on such an overfeeding plan, what develops is the diabetes and not the child. The same principle applies to the nutrition of adult patients. It is the more important since there is now evidence that excessive diet can produce actual anatomic destruction of islands of Langerhans.

Whatever the truth may prove to be concerning spontaneous tendencies in diabetes as revealed by sufficiently extensive study, it has been urgently necessary that this question be raised and investigated. "Spontaneous downward progress" has been the excuse for every kind of mismanagement, blunder, and failure of diabetic treatment in the past. The present work, though not competent to exclude such a process, does prove decisively that it is generally no more than a minor factor, even in cases of the worst type. The traditionally rapid course of diabetes in infants and children indicates not an inevitably acute process in them, but rather a high degree of susceptibility to breakdown of their islands and their assimilation by overstrain. The danger is increased by their naturally high metabolism, which would fatally injure the tolerance in any adult with severe diabetes.

The most important therapeutic lesson is the need of limitation of the total diet and metabolism with care proportioned to the potential severity of the case. For this reason it is important that children and all others subject to severe diabetes should come under the care of a competent specialist at the earliest possible moment. Practitioners at large may do well to limit themselves to the care of the milder diabetes of older persons, always with the understanding that this also requires no small study and attention. For the young patients their greatest service will consist in the earliest possible diagnosis, and, if a specialist is not close at hand, the initial control of symptoms by fasting and low diet. This stage is generally comparatively simple; the real difficulty comes in planning a diet which shall be practicable to support life while guarding as effectively as possible against downward progress. A tremendous amount of damage is commonly done

to these patients at the time when the therapeutic results are imagined to be most brilliant. It is extremely important to realize that such injury is absolutely irreparable according to present knowledge. The high tolerance, the capacity for improvement, the chance for growth and development, which may be present at the time of the first diagnostic symptoms, have been lost when the young patient, after a period of unskilled handling, is finally sent to the specialist to save him from imminent death. Notwithstanding the suggested limitation of the rôle of the family physician, it is evident that some country doctors are treating diabetes better than some specialists. There can be no possible restriction against anyone willing to equip himself with the necessary technique and training. But the fact is that the best diabetic treatment does require laboratory equipment and the ability to use it, together with rather exceptional knowledge of metabolism and a fair experience with diabetes itself.

Three desirable aids to the success of practical dietetic treatment of diabetes may be named in order of importance as follows: (1) Early diagnosis and prompt use of the necessary measures on the part of the general medical profession. (2) Competent specialists and consultants, with properly equipped hospitals, clinics, and dispensaries, for the treatment and instruction of both rich and poor patients. The diabetic classes in connection with clinics in some cities are an important advance. (3) Institutions where diabetics may live or at least board continuously when they need and are willing to follow careful diets but have not the facilities or means to obtain them. The opportunity to support themselves by work within their ability would be a great assistance. Only a small proportion require as long hospital treatment as the very severe cases of the present series, but nevertheless hospital care should be longer than is the general rule. The process of discharging as soon as symptoms are relieved and readmitting for successive relapses is fatal. Improved treatment merely prolongs the misery when continuous after-care is prevented by ignorance or poverty. Patients could sometimes support their families if they could have the right work in the right environment, when without it the outcome is disastrous for them and their families. The need is real, but it is difficult to formulate concrete suggestions for relief.

General Summary.

The preceding chapters show that the acutely threatening symptoms of diabetes have been controlled by the present treatment in a successful and radical manner which bears comparison with the most powerful therapeutic measures for any acute or chronic disease; but the diabetes is not cured, and downward progress occurs in practically all potentially severe cases unless the same principle of limitation of the total metabolism and body weight is adequately observed at all times. Exercise and some approach to a normal existence have been found possible and beneficial generally even in the severe stage. The most potent cause of aggravation of the condition is overfeeding; and since carbohydrate and protein have long been limited, by far the greatest harm in recent times has been due to the customary excesses in fat and total calories. The unwise use of fat can give rise to glycosuria as well as acidosis, though none of the observations indicates any formation of sugar directly from the fat. Spontaneous or inevitable downward progress has generally been either absent or not demonstrable in typical cases of diabetes of even the worst type. The power of recovering a rather high degree of assimilation at least temporarily has been clearly evident in even the gravest sort of cases in their incipiency, but never in the extreme stage after prolonged overfeeding. Success has naturally been easiest with patients above the age of 30; but with properly applied treatment, several cases also of juvenile diabetes have been kept demonstrably free from downward progress for periods up to 2 years. The defect in this experience for absolute disproof of the existence of an inherently or inevitably advancing process in average cases lies not only in the limited interval of time, but also in the fact that unduly numerous examples of downward progress have occurred in the present series. These were attributed to blunders and mismanagement in the application of the principle of treatment, which are believed to be plainly evident in these instances. The hope of continuing this study under efficient dietetic care has been blocked by war conditions. Therefore at present a final conclusion is withheld, aside from classing the "spontaneous" element as at most no more than a minor factor.

Final attention must again be called to the limitations inherent in every dietetic treatment. It affords only rest of a weakened function, when a stimulus is often needed. Essential progress must take the direction of supplementing the negative and passive therapy with a positive and active force. The knowledge of diabetes is advancing rapidly enough that even the patient whose outlook seems darkest should take courage to remain alive in the hope of treatment that can be called curative.

CHAPTER VIII.

ETIOLOGY AND PATHOLOGY.¹

The table of general summary at the opening of Chapter III includes the etiologic features as far as known. The ratio of 40 males to 36 females agrees with the accepted view that sex is probably an indifferent factor. The statistical value of the series depends chiefly upon the care employed in the study, and is limited by the comparative fewness of the cases and the special standard of selection. Thus the age incidence shown is worthless, since the choice of severe cases involved an unnaturally high proportion of young patients. Reference may be made to the more extensive data of Joslin, Williamson,² and the older text-books.

The general subject will be considered in the divisions of I, etiology, II, pathology, and III, clinical application.

I. Etiology.

1. *Carbohydrate or Dietary Excess.*—This ancient explanation, dating at least from the Hindu Vedas, is not now seriously considered as an original cause of diabetes. Even Cantani, the strongest modern champion of this hypothesis, recognized that some other predisposing cause must be assumed, because large numbers of normal persons are guilty of fully as great excesses as those who develop diabetes. This factor is noted in only a small minority of cases in the above table. No exact line can be drawn between excess and moderation, but the conviction has been reached that the previous eating habits of diabetics are not noticeably different from those of the general population. A few of the patients in this series developed diabetes notwithstanding an unusually abstemious prior life. Comparisons be-

¹ The pathological investigation by one of the authors, outlined here in preliminary form, will be published in detail elsewhere.

² Williamson, R. T., *Brit. Med. J.*, 1918, i, 139-141.

tween races or classes of society are inconclusive because other influences than diet undoubtedly enter in. The most tangible evidence is afforded by experimental animals. No animal is made diabetic by carbohydrate or other diet unless it was potentially diabetic before. Tests with excess of glucose and starch, as also of protein and fat, for as long as 17 months, have established this fact not only for normal animals but also for those depancreatized just short of the point of diabetes. The large margin of safety still present when three-fourths of the pancreas has been removed shows the impossibility of damage from carbohydrate with a normal pancreas. This fact is made still plainer by the observation that the lowering of assimilation from dietary excess in diabetic animals is due to loss of Langerhans cells through hydropic degeneration, while the most prolonged hyperglycemia and glycosuria fail to produce this effect upon the pancreas of non-diabetic animals.

On the other hand, inasmuch as the aggravating influence of dietary excess upon diabetes at any stage is well established for both animals and patients, its rôle as a possible exciting cause must be recognized. Le Goff³ has shown strikingly the parallelism between the increase of sugar consumption and of diabetes in the modern civilized world. Even though the latter increase be chiefly apparent, due merely to better diagnosis, the raising of the general standard of nutrition and the development of sedentary life and luxurious habits may well be expected to make active a certain proportion of diabetic cases which with lower nutrition and a harder struggle for existence would have remained latent. Such a conclusion is in line with the universal belief that dietary restriction is an important prophylaxis for those suspected of predisposition to diabetes by heredity or otherwise. From the standpoint of prophylaxis, it is to be remembered that sugar most readily gives rise to glycosuria, and its rapid absorption may impose a particularly dangerous load upon a weakened assimilative function, but it is undoubtedly most dangerous in combination with gluttony; and a regulated mixed diet, rather than carbohydrate abstinence, is to be recommended for prophylaxis on the same principle as for treatment.

³ Le Goff, *Gaz. hôp.*, 1911, lxxxi, 556-558.

2. *Obesity*.—Neither the fatness naturally resulting from excessive eating, nor pathologic obesity can constitute a primary cause of diabetes (unless possibly through local fat deposit disturbing the function of the pancreas). The supposition that diabetes may for a time be masked by obesity, through formation of fat from the excess of circulating sugar, is now plainly absurd. The tendency to pathologic obesity is known to be an internal secretory disorder. Even with a pituitary or other demonstrated basis for the obesity, it is possible that changes in the pancreas may at least partly account for the diabetes, and more careful pathologic investigations are demanded rather than speculations. Notice must be taken of the peculiar clinical course of diabetes with hypophyseal disease, in that glycosuria may give way to a high carbohydrate tolerance. It is necessary to keep clear the definition of diabetes as a deficiency of the internal secretion of the islands of Langerhans. It is undecided whether other glands influence the function of the islands, or whether changes in appetite, food absorption and sugar excretion, and the altered metabolism of cachexia, merely suppress glycosuria and other usual symptoms without fundamentally changing the diabetes, the usual mildness of which is evidenced by the rarity of coma and is apparently confirmed by the pancreatic findings. Broadly speaking, fibrous and fatty changes in the pancreas may be considered the organic basis of the obese form of diabetes. Granted this predisposition, the simple increase of body mass in either physiologic or pathologic obesity may bring on active diabetic symptoms. The proof is furnished by experiments in which the fattening of animals predisposed by operation exactly reproduces the development of such diabetes, and also by the disappearance of symptoms and the striking gain in assimilation when animals and patients alike are reduced in weight. Since such a high proportion of abnormally obese persons develop diabetes, the fatty tendency should in itself be taken as a warning. The dietary control of obesity is the most important prophylaxis against diabetes in such persons. Also physicians should determine the glucose tolerance of any noticeably obese patient, by blood as well as urine analyses, in order to begin treatment in the stage of hyperglycemia if possible, before glycosuria has ever appeared.

3. *Pluriglandular Disorders*.—There is no diabetes with a normal pancreas. This dictum is now accepted even by the von Noorden school. As previously pointed out,⁴ diabetes may exist with either hyper- or hypofunction of other glands. The present series affords one example (case No. 50) of diabetes with myxedema. Persons with disorder of one internal secretory organ are doubtless more liable than normal persons to disturbance in some other organ. Granted a pancreatic deficiency, it is conceivable that the increased metabolism of exophthalmic goitre, and possibly other endocrine intoxications, may bring on diabetes, though examples are rare. There is at present no proof that deranged action of other organs can produce either functional or structural abnormalities in the pancreas, and thus serve as a primary cause of diabetes. The negative results of thyroid feeding of dogs predisposed by partial pancreatectomy stand against such an assumption; but longer experiments and more efficient methods will be necessary before the problem of glandular interactions can be satisfactorily solved. The self-evident probability that any organ of the body is more or less influenced by other organs was grossly distorted and perverted in the polyglandular craze started by Eppinger, Falta, and Rudinger. These speculations, based largely upon confusion between diabetes and other forms of glycosuria, were promulgated with such lack of evidence and have been so completely discredited that only the least informed writers are still guilty of glib statements concerning antagonism between pancreas, thyroid, adrenals, and other glands. Clearer understanding of pancreatic pathology will remove much unnecessary confusion. The existence of other endocrinopathies should never be allowed to confuse the fact that diabetes is synonymous with pancreatic disease. The therapeutic conditions correspond. Hyperthyroidism, for example, as a possible exciting or aggravating factor in diabetes, should be relieved by surgical or other means, and benefit to an associated diabetes should be anticipated. But there is no record of an actual cure of diabetes by such treatment of a coexisting disorder. Also, pluriglandular disease with diabetes is the rare exception and not the rule. Not only the overthrow of the polyglandular doctrine, but also direct experimental

⁴ Allen, F. M., *Glycosuria and Diabetes*, Chapter XIX.

evidence, forbids the extirpation of healthy glands or other mutilations in the attempt to treat diabetes.

4. *Constitutional Defects.*—This vague notion is mentioned midway between pluriglandular and hereditary abnormalities, as being more or less related to both. Minkowski⁵ vigorously denounced this superstition. In addition to being too intangible for any use, the concept of diabetes as a “diathesis” lacks any real support. Defectives of any sort may naturally show more than the average liability to some other particular defect. But the majority of diabetics do not appear constitutionally defective or abnormal. They rather give the impression of an average, often a high type of humanity. Unless there is some evidence to the contrary, they should be regarded as normal persons who unfortunately have become afflicted with a definite organic disease, instead of being branded unjustly with the stigma of constitutional taint.

5. *Heredity.*—This holds a traditionally high place in the etiology of diabetes; but before intelligent judgment is possible, competent investigators of heredity will have to classify the cases in a fashion which has not yet been done. Clinically, four provisional groups suggest themselves, as follows:

(a) *Cases of Clear-Cut Accidental Pancreatitis, Due Perhaps to Gall Stones or Any Chance Infection.*—Such diabetes might well arise in the absence of any hereditary history, and—a point of practical importance—such patients should be capable of producing children free from any special diabetic tendency.

(b) *Familial Diabetes Not Due to True Heredity but to Infection.*—Syphilis is a good example, which has been most strongly emphasized by Warthin.⁶ The occurrence in successive generations might conceivably be congenital or the result of independent infections, associated perhaps with the environment. Three patients of the present series (Nos. 16, 41, 67) had syphilis, and it is a question whether this may be viewed as a sufficient cause of their diabetes, without reference to the family history of diabetes in two of the cases and psychic disorders in the third; and whether, consequently, there is any danger

⁵ Minkowski, O., *Med. Klin.*, 1911, vii, 1031–1036.

⁶ Warthin, A. S., and Wilson, U. F., *Am. J. Med. Sc.*, 1916, clii, 157–164; Warthin, A. S., *The Harvey Lectures*, 1917–18, xiii.

to the children of such patients other than the danger of syphilis. Most investigators⁷ do not attribute so high an etiologic position to syphilis as Warthin, but in view of the known pancreatic lesions of both congenital and acquired syphilis, it could scarcely fail to be sometimes a cause of diabetes. On the one hand, searching clinical examinations, Wassermann tests of the spinal fluid as well as of the blood in suspicious cases, and careful pathologic studies, are necessary to fix the true etiologic position of syphilis. (In one case recently seen in military practice, with negative history and negative Wassermann reaction in the blood, a strongly positive Wassermann test of the ascitic fluid decided the diagnosis.) On the other hand, the fact should be recognized that most pancreatitis is not due to syphilis, and this agrees with other evidence that most diabetes is not due to syphilis.

(c) *Numerous Cases of Diabetes without Known Heredity.*—It may be that these are the majority of all cases, just as they constitute the majority of the present series. There is always the possibility that an existing diabetic tendency has merely skipped several generations. Any wide investigation is made almost impossible by two factors, one the lack of accurate knowledge of even their recent medical family history on the part of most patients, the other the high proportion of failures to diagnose diabetes on the part of physicians, introducing an element of uncertainty into the anamnesis of even the best informed patient. An occasional patient can establish an apparently perfect record back to his grandparents, showing a rugged old age in the majority of his near relatives, and convincing causes of death in the others. Patient No. 35, for example, came of unusually sound country stock. The question is made much more prominent by the occasional instances of diabetes in all or several children of a family, with parents and ancestors normal as far as known. Foster⁸ gives an example. A recent patient in this hospital was a 12 year old country boy, free from diabetic, luetic, or other taint as far as ascertainable. The family history was not very complete, but contained nothing suspicious except that the mother's father supposedly

⁷ Williams, J. R., *J. Am. Med. Assn.*, 1918, lxx, 365-367.

⁸ Foster, N. B., *Bull. Johns Hopkins Hosp.*, 1912, xxiii, 54-55.

died of tuberculosis (diabetes undiagnosed?). Both parents are alive and well, but the record of their children has been as follows: first, a boy, diabetes discovered at 16, resulted in death at 23; second, a girl, married, always in perfect health; third, a girl, died of diabetes at 3; fourth, a boy, died of spinal meningitis at 4 or 5; fifth, a boy, aged 19, always healthy, now in army; sixth, a girl, died of diabetes at 15; seventh, the diabetic boy mentioned. Such remarkable occurrences raise the question for a large group of diabetics without hereditary history, as to the possible rôle of innate and of environmental or acquired factors in the causation of their disease.

(d) *Cases of Unmistakable Hereditary Character.*—In the most pronounced type, there is a high prevalence of diabetes through generation after generation. Frequently, associated disorders accent the hereditary taint. Although obesity is the best established of these, Williams,⁹ selecting only cases with fairly complete family history, compared 100 diabetics with 100 non-diabetics, and found that arteriosclerosis, nephritis, apoplexy, and nervous and mental disorders were also more common in the ancestors or relatives of the former. If such associations, on careful examination, prove fundamental, they will throw valuable light upon the nature of the condition. Racial tendencies also belong here. Not only are savages generally less disposed to diabetes than civilized peoples, but it seems also true that under similar environmental conditions certain races, as the Jews and portions of the population of India, are more subject to diabetes than are other races, as the Japanese. One fact now seems evident, which is so important for this question that surprise must be felt that it has never been pointed out before. This is that even the most typical hereditary diabetes arises, like other diabetes, on the basis of pancreatitis. True congenital pancreatic hypoplasia, as described for example by Ghon and Roman,¹⁰ is so rare as to be a curiosity. Findings of subnormal size or weight of the pancreas should be judged with reference to general emaciation and inflammatory atrophy. Scarcity of islands has never been established as con-

⁹ Williams, J. R., *Am. J. Med. Sc.*, 1917, cliv, 396-406.

¹⁰ Ghon, A., and Roman, B., *Prag. med. Woch.*, 1913, xxxviii, 245. A congenital deficiency is also mentioned by Hornor, A. A., and Joslin, E. P., *Am. J. Med. Sc.*, 1918, clv, 47-56.

genital in any case, and as far as known is always the result of degeneration due either to the cause producing the diabetes or to the diabetes itself. If this be true, the problem of hereditary diabetes becomes simply the question why certain families or races are specially subject to pancreatitis or to a particular form or consequence of it. Of various possibilities, three at least have suggestive interest. First, a purely hereditary explanation might be that the islands are inherently defective in function or vitality, so that they either undergo early senility or break down under the ordinary strain of life, or suffer unduly from slight injuries. Arteriosclerosis is one factor to be considered. The second possibility is a structural peculiarity predisposing to secondary changes. A clear example might be a duct which by reason of its form or course is easily blocked. The pancreatitis and atrophy caused by stasis of secretion is well known in both dogs and human beings. With reference to Opie's demonstration that obstruction by a gall stone may result in pancreatitis due to forcing of bile into the pancreatic ducts, Bunting¹¹ pointed out that this is possible only with a special shape of the ampulla of Vater. It is conceivable that trivial appearing malformations of the duct, head of the pancreas, or duodenum may conduce to stasis of secretion or circulation, or facilitate the entrance of microorganisms.¹² It may be remarked in passing that a pseudohereditary diabetes might be imaginable in families or races where occupation or mode of life might be responsible for malposition, stasis, abnormal intestinal flora, or other causes of inflammation. A third possibility is a specific lack of resistance to infection or intoxication. This may be conceived as general or local. The latter would mean that the pancreas is abnormally susceptible to invasion by bacteria, or that the islands are unusually sensitive to circulating toxins. Certain existing evidence is suggestive for decision among these three possibilities. It would appear, first, that simple senility never produces the anatomic picture of diabetes; second, that when islands go to pieces from functional overstrain, they are not invaded or replaced by fibrous tissue; third, that the form of pancreatitis in hereditary diabetes typically is not that

¹¹ Bunting, C. H., *Bull. Johns Hopkins Hosp.*, 1906, xvii, 265-266.

¹² Winternitz, M. C., *Ibid.*, 1908, xix, 237-241.

which arises from stasis or infection of the ducts. Likewise, jaundice is uncommon in diabetics (Joslin). This leaves the special susceptibility of the pancreatic tissue or islands to infectious or toxic injury as a leading possibility; but the evidence is far from sufficient to warrant anything more than suggestion, and the causes may be found different in different cases.

The present series includes only 19 known hereditary cases (counting as hereditary all where diabetes occurred in any blood relative), against 57 without known heredity; *i.e.*, exactly one-fourth were hereditary to the patients' knowledge. The proportion of Jews was almost the same; *i.e.*, 18 Jews against 58 of all other races (chiefly Americans with ancestry too mixed to distinguish). Of the hereditary cases, there were 6 Jewish against 13 non-Jewish; *i.e.*, about one-third were Jews. There was no intentional racial selection in admitting patients. Also, the knowledge of their family history certainly averaged no higher among the Jews than among the others, but it is noticeable that Jews seem generally better acquainted with diabetes. In general, the high proportion of Jews and their family histories support the current view of the racial and hereditary element in etiology.

If the material can be properly sifted, students of heredity may perhaps be able to determine to what extent the incidence of diabetes is governed by Mendelian or other known laws. Aside from its theoretical interest, the question touches matters of the greatest practical importance. One of these is prevention, in finding which persons need prophylaxis, and, if the nature of the heritable abnormality be discovered, in guiding to a more effective means of prevention than diet. Again, if scientific medicine is to achieve constantly better treatment and perhaps ultimate cure of all diseases, it must be recognized that a mere cure of heritable diseases like diabetes by no means removes the heredity, but on the contrary preserves a numerous class, who formerly died, to transmit their characteristics to a greater extent than ever before. If such hereditary disease is an indication of degeneracy in even a single organ, a cure may not prove an unmixed blessing sociologically. It can only be repeated that diabetics seem often to be persons of high type in their general characteristics.

6. *Nervous Causes*.—A nervous etiology of some cases of diabetes, regarded as a certainty by Naunyn, is supported by the following seven considerations. (a) Diabetes sometimes runs in the same families with nervous and mental disorders. (b) Neuropathic individuals and nervous races are frequently subject to diabetes. Civilization is accused of increasing diabetes by reason of mental and nervous strain. (c) The majority of patients with severe diabetes are more or less neurotic. (d) Pain, excitement, and any emotional or psychic disturbances are apt to cause slight glycosuria in normal persons, and there are numerous reports of the onset of diabetes following such occurrences. Similarly, certain railway statistics are said to show the highest incidence of diabetes among those employees whose work involves greatest danger and strain. (e) Fractures of the skull and spine, and other nerve injuries, often give rise to glycosuria of variable, generally slight, degree and duration, and true diabetes has been reported by a number of authors following such trauma. (f) Existing diabetes is notoriously aggravated by nerve injury, shock, or strain. Glycosuria occasionally follows operations upon potentially diabetic dogs, but attempts to imitate clinical conditions adequately in them and in similarly predisposed cats, by tying and the other usual gentle measures, were unsatisfactory, until a cat under observation for another purpose by accident escaped from its cage and was badly mauled by a bulldog, with a resulting aggravation of the existing diabetes demonstrable for some 2 weeks. (g) Claude Bernard's puncture of the medulla produces a well known experimental nervous glycosuria; and though Bernard's conception of it as a transitory diabetes is erroneous, yet in one dog predisposed by removal of three-fourths to four-fifths of the pancreas, it was demonstrated¹³ that diabetes was absent before the *pigûre* and present in permanent and fatal form after it. This experiment, though isolated, seems to be positive. Attempts to repeat it have resulted in glycosuria for no more than a few days, the nervous injuries being either fatal or else insufficient for permanent diabetes. It is expected that more effective methods will further demonstrate the potency of nervous irritation, but it is doubtful if diabetes can ever be produced by nervous

¹³ Allen, *Glycosuria and Diabetes*, p. 775.

agency in an animal with an intact pancreas. Paralytic causes seem to be excluded by the fact that severing the pancreatic nerves or transplanting the pancreas remnant to some other part of the body has no perceptible effect upon the assimilative power. The remarkably dilated capillaries of islands occasionally seen in a diabetic pancreas might suggest a possible vasomotor abnormality, but in partially depancreatized animals the pancreatic function has appeared widely independent of the blood supply, unless ligation of vessels were carried to a point resulting in atrophy, thus imitating the possible effects of arteriosclerosis in a few human cases.

It will be noticed that, notwithstanding the multitude of *piqûres* and other nerve lesions inflicted upon animals, diabetes has never resulted unless they were already predisposed. It seems probable that a similar rule will apply to mankind. Though it is conceivable that nervous agencies alone may cause diabetes, they probably seldom are sufficiently powerful or selective to cause it if the pancreas is normal. Accordingly, they may for the most part be excluded as primary causes of diabetes and reduced to the rank of secondary or exciting causes. All the older evidence is susceptible to criticism in this direction. A causal relationship between diabetes and neuroses is no more established by their occurrence in the same families and individuals than a causal relationship between diabetes and gout or nephritis. The Japanese furnish an example of a nervously tense people with an ancient civilization and relative freedom from diabetes. Many or most diabetics were not neurotic before the beginning of their diabetes; and so far as causal connection exists, the nervousness is generally the result of the diabetes and the expression of a badly nourished nervous system, together with anxiety. The traditional effects of nervous disturbances upon an existing diabetes are avoided or reduced to a minimum under properly thorough dietetic treatment. Real evidence in favor of neurosis or psychic shock or stress as a cause of diabetes is surprisingly scanty in the present series of cases. The principal new light on this problem is afforded by the world war, in which it appears that nervous strain, shock, and injuries in unparalleled number and variety have occasioned no striking increase of diabetes. Some cases must necessarily arise, as in civil life. The question of the importance of the nervous factor is

at present answerable only from the older statistics, which seem to indicate that it somewhat increases the incidence of diabetes; in other words, that this exciting cause perhaps suffices to develop some cases which otherwise would have remained latent.

7. *Trauma*.—This topic necessarily overlaps and is partly synonymous with the preceding. The strict criterion of traumatic diabetes heretofore has been absence of glycosuria before the injury and its presence within a reasonably short time thereafter. This is incomplete clinical evidence, for doubtless in many such cases hyperglycemia already existed. Scientifically conclusive proof could be furnished only by pathologic examination. It is a justified prediction that the pancreas in almost any case of traumatic diabetes is the seat of abnormalities antedating the trauma. Experiments with direct and indirect injuries of the pancreas in animals, and the clinical knowledge concerning acute pancreatitis, practically exclude the possibility of any immediate production of diabetes by direct pancreatic trauma; either the damage will fall short of this, or it will cause death rather promptly. It is conceivable, however, that acute injury of a previously normal pancreas may inaugurate a process which will later result in diabetes. Such cases have never yet been demonstrated and must necessarily be rare. No clear-cut example of traumatic diabetes has been seen at this hospital. The recent war has given the death blow to trauma as an important cause of diabetes. For practical purposes, the best founded view-point is that trauma, shock, nervous injuries, etc., bring on diabetes only when the pancreas is already diseased. Autopsies upon all possible cases of traumatic diabetes, especially if death occurred shortly after injury, are highly important in this connection. Medicolegally and otherwise, the status of trauma is like that of other exciting causes, in that it seemingly gives rise to some cases which otherwise might not have become active. Whether diabetes might have been anticipated without such an exciting cause could be judged to some extent by a qualified pathologist, but not infallibly. Compensation to the injured individual is not thus invalidated, since there is no doubt that any exciting cause may at least hasten the onset of an impending diabetes or aggravate an existing diabetes.

8. *Infection and Inflammation.*—The most advanced views of the infectious etiology of diabetes were expressed recently by Woodyatt¹⁴ as follows:

“Diabetes mellitus, a name now given by clinicians to any case in which as the chief incident—or as one of several incidents—there occurs from natural causes a diminution of the endocrine function of the pancreas sufficient to cause the symptom diabetes. The factors which determine such diminutions are infections of the pancreas, the term implying an interaction between a susceptible tissue and a suitable pathogenic germ. So called *diabetic predispositions* consist in inherited susceptibilities to certain types of infection. Well known *variations in the clinical course of diabetes* in the same case at different times and in different cases are not wholly ascribable to variations in diet, etc., but often to infectious moments. *Concurrence of other diseases* as Basedow’s, dyspituitarism, myocarditis, arteriosclerosis, etc., with diabetes, are not due to ‘correlation of ductless glands,’ nor to metabolic disturbances secondary to diabetes, but to simultaneous infections in different tissues.” Prophylaxis is held to consist in preventing diabetogenous infections (tonsillitis, sinusitis, pyorrhea, parotitis, cholecystitis, ulcer, prostatitis) rather than in dietary restrictions. “These views are based on the literature, an analysis of 100 clinical cases with aid of D. E. Abbott, the character and frequency of pancreas lesions in 538 animal inoculations with different strains of streptococcus group by E. C. Rosenow, clinical improvements following treatment of foci of infection in certain cases, previous views of Rumpf, Lépine and others, general development of knowledge concerning relation of foci of infection to visceral diseases (Billings, Rosenow, Irons, and others), knowledge of the selective affinity of certain strains for certain tissues (Rosenow).” Woodyatt has also placed strong emphasis upon the occasional cases of acute diabetes accompanying acute infectious disease, in which apparently normal carbohydrate assimilation is regained after recovery from the infection.

The above may stand as the clearest expression of the Rosenow school concerning diabetes, related to their corresponding doctrines concerning other diseases. Notwithstanding an active following, this contention in general is not at present regarded as established by the majority of the medical profession. For diabetes in particular, importance is assigned to focal and other infections by J. R. Williams, while Joslin in his wide experience, and Greeley¹⁵ in an analysis

¹⁴ Woodyatt, R. T., Abstract of Proceedings of Seventh Annual Meeting of the American Society for the Advancement of Clinical Investigation, 1915, 25–28.

¹⁵ Greeley, H. P., *Wisconsin Med. J.*, 1915–16, xiv, 464–468.

of the large material of Hodgson's sanitarium, were unable to find evidence that such infections are more prevalent among diabetics than among other hospital patients, or that they are a determining factor in the clinical course. The interpretation of transitory diabetes accompanying an acute infection is necessarily ambiguous, since the latter might be a primary or merely an exciting cause, and the assimilation might subsequently appear normal even though the pancreas were reduced considerably in mass or function. Proof of the frequency of pancreatic lesions in experimental septicemia will be a valuable contribution, but such experiments cannot in themselves be decisive unless they produce either diabetes or a marked and permanent lowering of sugar tolerance. The above writers have courageously recognized that the hypothesis of an infectious etiology of all cases of diabetes must be extended to various other metabolic disorders. The particularly close relation of diabetes and obesity must hold also here. While it is not impossible that obesity may yet be numbered among the infectious diseases, such a bold conception must appear today as prophecy rather than proof. The uncertainties in the whole subject of diabetes are such that tangible evidence is the chief need.

The one tangible and outstanding fact is the frequency with which pancreatitis has been described by all authors of all shades of opinion who have made accurate microscopic observations in diabetes. The present pathologic study has given an unexpectedly sweeping corroboration of this lesson from the earlier work. It is possible to set up a general dictum, "without pancreatitis, no diabetes," and challenge pathologists to produce exceptions. A diabetic pancreas in which careful search fails to reveal more or less evidence of present or past inflammation is at least a great rarity, and, if ever found, will merely illustrate the remarkable completeness of organic recovery sometimes possible after acute inflammation even of a degree sufficient to produce diabetes. The principal stumbling-block has been the apparent discrepancy between structure and function, as found in the presence of diabetes with seemingly insufficient anatomic alterations, and the absence of diabetes with more extreme visible change; and this disagreement persists even with distinctions between interlobular and interacinar forms of pancreatitis, and with comparisons

limited to destruction of islands rather than of total parenchyma. Discussion must partly be deferred to the subsequent section on pathology; but much of the uncertainty necessarily connected with clinical conditions is cleared away by consideration of animal experiments, divisible into the following four groups.

(a) When the duct and perhaps part of the blood supply of a pancreatic remnant are occluded, gradual atrophy brings on the well known Sandmeyer diabetes, as late as 13 months after operation in one of that author's cases. Such diabetes has never been produced with the whole pancreas *in situ*, even when the ducts have been injected with paraffin by Claude Bernard and others, or recently with alcohol by Auer and Kleiner.¹⁶ The extreme degeneration and sclerosis finally resulting were shown in the pathologic examinations of Sandmeyer, J. H. Pratt, and Auer and Kleiner. Nevertheless, diabetes has not been observed unless two-thirds or more of the gland has first been removed (or, rarely, destroyed by gangrene). The reason evidently is that indigestion, emaciation, and cachexia are in progress at the same time, and prevent the familiar diabetic symptoms even when the destruction of islands has reached a point at which the animal must be classed as potentially diabetic. With the entire pancreas present, these other disturbances will cause death before frank diabetes develops; but removal of most of the gland causes the internal secretory deficiency to become manifest earlier in proportion as the pancreatic remnant is smaller.

(b) After simple partial pancreatectomy leaving the remnant with natural duct drainage, the tissue generally remains soft, lobulated, and normal, except for a narrow zone of fibrosis adjoining the area of amputation. More or less hypertrophy occurs sometimes; otherwise conditions are found unchanged even after several years. The nutrition and assimilative power are correspondingly maintained unless the remnant is so small that the animal is potentially diabetic, in which case dietary and metabolic influences may cause functional and structural decay of the islands, without inflammation or fibrosis and without alterations in the acinar tissue.

¹⁶ Auer, J., and Kleiner, I. S., *Proc. Soc. Exp. Biol. and Med.*, 1916-17, xiv, 151-153.

(c) Sometimes more or less fibrosis takes place in a pancreas remnant, presumably as the result of undue trauma in the operation. Upon this hint, it was found possible to produce diabetes with considerably larger remnants than usual, by setting up inflammation by crushing between the fingers. The course of the fibrosis following acute injury varies. Sometimes the process apparently halts, so that no further impairment of structure or function is evident in rather extended observations. In other cases the sclerosis continues, so that diabetes develops after several weeks or months, and the pancreas remnant is found atrophic, sometimes almost as extremely as after occlusion of the duct.

(d) As a better means of inducing aseptic inflammation, rubber-covered clamps were applied to cut off the blood supply for 20 minutes to 2 hours continuously. Diabetes results more easily in proportion as the pancreas remnant is smaller, but has been produced with fully a third of the pancreas present. Part or the whole of the uncinata process is the most convenient remnant for this purpose. Shorter periods of clamping are used at first; if diabetes does not result, gradually longer stasis can be applied in later operations without death from fat necrosis. Apparently only technical obstacles prevent producing diabetes with the entire pancreas present. This would have much theoretical interest, but the success actually achieved is sufficient to establish the principle. Incidentally, the pancreatic ganglia withstand anemia for as long as 2 hours, so that the hope of observing the effects of the loss of the intrinsic nerve supply has been disappointed. The after-effect of this acute experimental inflammation reproduces strikingly the pancreatic pictures seen with clinical diabetes. Various grades of chronic fibrosis are found; but the most interesting result is a pancreas which is soft, lobulated, and normal appearing in gross, and which microscopically is characterized by scarcity of island tissue, without corresponding destruction of acini, and with visible evidences of pancreatitis apparently altogether too slight to account for the condition. Either the islands are injured more easily and profoundly than the acini, or their power of recovery is less. The trivial clinical disturbance in the dogs even during the early period of most intense pancreatitis is also remarkable, but it could not be safely inferred that human patients would

be equally little affected. It is therefore of interest that Whipple¹⁷ found acute inflammation of the pancreas precisely similar to the experimental form in 6 out of 230 unselected autopsies, most often with pneumonia and a smaller proportion with other infections, and stated: "These cases were all under careful observation in the wards of the Johns Hopkins Hospital, and gave no symptoms of pancreatic disease."

Though the two columns of infections in the General Summary table (beginning of Chapter III) may at first glance seem imposing, a classification of the 76 cases of this series will show something like the following four groups:

(a) 23 cases characterized by more or less numerous infections, the causal relationship of which to the diabetes must be purely speculative, without any definite indications. These are cases Nos. 1, 4, 6, 8, 9, 11, 13, 14, 15, 19, 20, 21, 29, 31, 32, 38, 42, 44, 48, 49, 53, 63, 72.

(b) 29 cases not only lacking any suggestive infectious etiology of the diabetes, but rather exceptionally free from infections in general. These are cases Nos. 2, 7, 10, 12, 18, 22, 25, 34, 35, 39, 45, 46, 47, 50, 51, 52, 54, 55, 57, 58, 64, 65, 66, 68, 70, 71, 73, 74, 75.

(c) 9 cases in which an infection stands in suggestive relation with the outbreak of diabetes. Patient No. 3 not only had "colitis" 5 years before admission, but, just before the first diabetic symptoms, suffered appendicitis and appendectomy, followed by phlebitis apparently indicating septicemia. Patient No. 5 at the beginning of his diabetes had symptoms which may have represented acute pancreatitis. No. 24 gave a clear-cut history of obstructive jaundice, without evidence of gall stones or biliary infection, followed within a year by the gradual onset of diabetes. The child No. 26 had some unknown disturbance which caused vomiting, followed immediately by diabetes. The suspicious condition in another child, No. 28, was merely fever of unknown origin; the subsequent slight choreiform movements do not prove that it was poliomyelitis, and it might have been pancreatitis. In No. 36, the beginning of diabetes is significantly related with general sepsis. No. 37 had nothing but an alveolar abscess, then an ordinary cold; diabetes promptly followed.

¹⁷ Whipple, G. H., *Bull. Johns Hopkins Hosp.*, 1907, xviii, 391-396.

No. 40 was admitted for pneumonia; he had apparently been a well man before, and his apparently complete recovery from the diabetes suggests pneumococcus pancreatitis as the probable cause. The young boy No. 76 had only otitis media, indicated by earache and fever. Diabetes quickly followed, and the only further evidence of pancreatic involvement is that digestive upsets have since occurred from slight causes.

(*d*) 15 cases in which at least a possibility of connection exists between diabetes and pancreatic injury produced by some infection acquired many years previously. Three of these (Nos. 16, 41, 67) are cases of syphilis. No. 17 had a serious combination of pneumonia and empyema 20 years before admission, and a later history of indigestion. No. 23 had suffered from "bloody dysentery" 14 years previously. No. 27 had had mumps with orchitis at the age of 18, a pancreatic involvement being imaginable; there was also "jaundice" at the age of 20. No. 30 had passed through some ordinary infections, and gave a significant history of "nervous indigestion" and pale feces for years past. No. 33 twice suffered from acute nephritis following colds. The pancreas is certainly as susceptible to infection as the kidney, and there was a history of indigestion. In No. 43, this combination of sepsis and nephritis, with subsequent diabetes, is especially striking. No. 56 had inflamed cervical glands in childhood, and was also subject to gastrointestinal attacks with fever of unknown origin. No. 59 gave a history of biliousness, nausea, and vomiting throughout childhood. No. 60 had had "gastric fever" in 1896. No. 61 in childhood had suffered from intractable diarrhea; subsequently he had typical rheumatism; and as the infectious origin of his cardio-renal disease is not doubted, the same may be assumed as the cause of pancreatitis. No. 62 gave an unintelligible description of some childhood trouble possibly related to her diabetes. In No. 69, sepsis may be thought of as a possible cause.

The elements of personal judgment and clinical uncertainty are illustrated here as necessarily in all such inquiries. It is to be recognized that groups (*a*) and (*b*) comprise 52 cases, or over 68 per cent of the series. That is, this large majority shows no perceptible relation between known infections and diabetes. The relations suggested in groups (*c*) and (*d*) are purely a matter of interpretation and

carry no demonstration in any instance. The connection supposed in group (*d*) between events so many years apart might easily and sometimes doubtless rightly be considered imaginary.

The most definite group, (*c*), is open to quite different interpretations, by reason of the well known facts that diabetics are specially liable to infections and that existing or latent diabetes is aggravated by infection. Thus, patient No. 40 might have had some preexisting diabetic tendency; the latent diabetes may have been awakened by the pneumonic infection and subsided again with the subsidence of the latter. Zealous advocates of infection might choose to change cases Nos. 6 and 38 from group (*a*) to (*c*). But there is here no evidence of anything but pneumonia in persons already mildly diabetic; thus, patient No. 6 considered herself well before the pneumonia, when there was no knowledge of diabetes; she continues to consider herself well now, when it is known that glycosuria is constantly present. Patient No. 57 was included in group (*b*), because measles at the age of 8 was the only illness known before his diabetes. The accidental fact that he studied medicine afforded the sole information that glycosuria was present then, 8 years before the supposed onset of diabetes. Except for this, it would have appeared that repeated tonsillitis and then furunculosis were followed by diabetes, and the case might have been placed in group (*c*) on suspicion of staphylococcus pancreatitis. In patient No. 41, diabetes was first discovered in connection with a cold and sore throat, as in some of the cases in group (*c*); but in him the more probable cause of diabetes is syphilis. It is probable that minor abnormalities, as of the teeth and lymph glands (see again General Summary, Chapter III) are no more common in diabetics than in others, unless as the result of the diabetes; and an etiologic position has never been demonstrated for them in any case. In the absence of other infections, some might lay stress upon caries and pyorrhea in such a case as No. 67; but here syphilis is known to exist. All the clinical conditions are therefore confusing, and the only trustworthy guide is the pathology. This compels recognition of the fact that, unless these diabetics are different from the large series covered by the present microscopic study and from the many others in the literature, the basis of the disease in all of them is pancreatitis. The existence of pancreatic

inflammation, and the search for its cause, is thus extended to all four groups alike. The cause ordinarily to be supposed is bacterial; but a connection with any other general or focal infection is clinically discoverable at best in only a minority of cases, and even in them is subject to many doubts and mistakes.

The basis of belief in the inflammatory origin of diabetes is therefore essentially a generalization from the classical studies of diabetic pathology, with experiments and deductions to clear away some apparent inconsistencies and confusion. The view of Woodyatt and others of the Rosenow school, concerning the status of focal infections, specific relations of bacteria to organs, etc., is a distinctly new suggestion, concerning which the above observations do not decide. This contention in diabetes is on the same basis as in a variety of other diseases, and must stand or fall as the general evidence may determine.

II. Pathology.

Since the former review of this subject,¹⁸ papers have appeared by Koch,¹⁹ supporting the archaic notion that the islands are merely degenerate and functionless portions of the parenchyma, and by Major,²⁰ dealing with a comparative study of the pancreas in 35 non-diabetic and 13 diabetic necropsies.

The pathologic changes of the pancreas in diabetes are divisible into those causing the diabetes and those resulting from the diabetes.

A. CHANGES CAUSING DIABETES.

For general purposes, details of fibrous, fatty, hyaline, and other alterations may be ignored, and all cases grouped roughly in three classes, as follows.

1. Cases of extensive loss of parenchyma, involving islands and acini alike, and in the most extreme instances comparable to the Sandmeyer diabetes of dogs. The earliest pancreatic lesions described by Cawley and others were naturally of this class.

¹⁸ Allen, *Glycosuria and Diabetes*, Chapter XXI.

¹⁹ Koch, K., *Virchows Arch. path. Anat.*, 1913, ccxi, 321-330.

²⁰ Major, R. H., *J. Med. Research*, 1914, xxxi, 313-330.

2. Cases of selective injury of islands. There is never much destruction of islands without some involvement of the acinar tissue, and all gradations between this and the first group are met, but the best instances, notably of fibrous and hyaline change, well justify Opie's use of them as the basis of the insular hypothesis.

Under this same heading may be mentioned also certain peculiar pictures, described early by Weichselbaum and Stangl²¹ and recently by Williams and Dresbach,²² but not heretofore correlated as stages of a special process. They may in fact not represent a distinct and progressive sequence, but comparison between different cases and between different portions of the same pancreas frequently reveals the following graded examples. In the seemingly incipient form, the island appears sometimes congested, frequently hypertrophic, and perhaps irregular in structure, but the essential feature is the striking pyknosis of certain nuclei, with the cytoplasm about them often only a narrow band. Even at this stage, slight fibrosis or at least a few round cells are present. Through successive degrees, this condition seems to pass over into what Weichselbaum and Stangl called atrophy of the islands, in which condition they are small, more or less fibrous, and characterized predominantly by the shrivelled cells with pyknotic nuclei and scanty cytoplasm. These pictures, though common, are doubtful in interpretation. The change is distinguishable from typical hydropic degeneration; for though pyknosis of nuclei is a feature of the latter, it is plainly subsequent to the vacuolation of the cytoplasm. Shrunken cells may be present in the same island with hydropic cells, but apparently never become hydropic themselves, perhaps because they are no longer functional. Weichselbaum and Stangl considered the atrophic islands not diagnostic of diabetes, because found in some non-diabetic cases. In 1911, Weichselbaum again mentioned this atrophy, in which the island cells resemble lymphocytes, and this time considered it probably a result of hydropic degeneration, therefore diabetic. This picture is very rare in experimental diabetes, but what is probably a true reproduction of it has finally been observed in a few diabetic animals. Here also the

²¹ Weichselbaum and Stangl, Bibliography of Chapter 1.

²² Williams, J. R., and Dresbach, M., *Am. J. Med. Sc.*, 1917, cliii, 65-78.

shrinkage of island cells is accompanied by round-cell infiltration, and the change is probably inflammatory in origin.

Its presence raises a suspicion of diabetes; and even if the latter be absent, the reason might be only that the change is not yet sufficiently advanced or general. Widespread "atrophy" of islands is diagnostic of diabetes, generally of the severest form. Islands showing this change in advanced degree are certainly functionless, because they are often present in large numbers in cases with scarcely any food tolerance. The finding of such "atrophy" after widely different dietetic management, *i. e.* in flagrant diabetes with no food restriction whatever, and after the traditional protein-fat diet as in Weichselbaum and Stangl's cases, and also in cases kept symptom-free by prolonged rigid undernutrition, furnishes partial proof, first, that it is not of dietary origin, and second, that it is permanent and irremediable under any form of treatment now known.

3. Cases in which the visible abnormalities in both islands and acini seem too slight for a rational explanation of the diabetes. Some of these have given rise to the belief that diabetes may exist with a histologically normal pancreas. Some examples have been cases of very rapid course in young persons, formerly supposed to represent the extreme of severity, and therefore responsible for considerable confusion in the past. Autopsies of such cases in their incipiency are rare and therefore will be specially valuable whenever obtainable. From some examples of early death in coma, however, it is possible to infer that diabetes may begin with a pancreas showing only slight fibrous or round cell invasion and containing an apparent abundance of normal looking islands. One difficulty in forming quantitative judgments is that the amount of pancreatic or island tissue necessary to prevent diabetes in man is not known. Comparison with animals is unreliable, since these vary widely and irregularly, from the cat at one extreme, which becomes diabetic with about a fifth of the pancreas remaining, to the pig, in which a tiny fragment of pancreas prevents both diabetes and cachexia. The monkey approximately resembles the dog in requiring removal of seven-eighths to nine-tenths of the pancreas for diabetes. Man is probably to be reckoned among the most highly susceptible species, but the few reports of resection of the human pancreas do not suffice for decision, partly because of

inexact estimation of the portion removed or left, and partly because the pancreas in such cases is diseased. Careful surgical, medical, and pathologic studies of such patients in the future will possess obvious importance. The best information at present seems to be afforded by the case of Ghon and Roman,¹⁰ of a boy dying at the age of 14, with idiocy, status lymphaticus, and other abnormalities, including a congenital pancreatic deficiency, apparently the result of failure of development of the dorsal pancreatic anlage, so that only the portion formed by the ventral anlage was present. This roughly rectangular plate of tissue adjoining the duodenum measured in its greatest dimensions 7.4 cm. in length, 4.5 cm. in width, and 2 cm. in thickness.

Microscopically, "the changes consisted on the one hand in a focally occurring increase of the interstitial tissue, in which here and there also small round cell infiltrations were observable, and on the other hand in an everywhere observable injury of the Langerhans cell islands. In comparison with the pancreas of a boy of the same age dead of scarlet fever, studied for a control, the Langerhans cell groups of our case showed not only increase of the intransular connective tissue, but also the change which Weichselbaum has described as hydropic degeneration. The hydropic degeneration change was mostly demonstrated only in its incipient stages, but we saw also many islands, which following Weichselbaum we could designate as atrophic."

The boy was physically well developed, and the existing diabetes therefore probably of recent origin. The authors are doubtless justified in attributing its onset to the slight pancreatitis rather than to the simple metabolic strain of growth and puberty. There is a further possible question whether the abnormalities in the body elsewhere had any influence, and even whether the inherent functional capacity of the islands was normal. On the whole, however, it appears that this considerable piece of pancreas was barely sufficient for metabolism, and that diabetes ensued when it was only slightly injured by inflammation. This interpretation agrees with other scanty evidence that man is rather highly susceptible to diabetes, and that the "margin of safety" in the human pancreas is not so wide as in most experimental animals.

In addition to anatomic destruction, the existence of a functional incapacity of the island cells must be assumed, and is demonstrated, even without excessive labor of counting and measuring islands, by

the following five facts: (a) Autopsy comparisons show that diabetes often exists in cases where island tissue is widely and unmistakably more abundant than in other cases without diabetes. (b) The anatomic deficiency of islands is generally demonstrated only at death from diabetes, after a course of months or years, during which pancreatitis or hydropic degeneration or both have been in progress; and it must be assumed therefore that islands were more plentiful at the beginning of the diabetes. (c) As illustrated by certain cases in the present series and others,²³ the most intense, even "total" diabetes may exist, as demonstrated by the dextrose-nitrogen ratio and the respiratory quotient, and yet fasting may bring the condition under control and a tolerance amounting sometimes to hundreds of grams of carbohydrate may rapidly be recovered. Such patients formerly met early death in coma, supposedly because of the hopeless severity of their disease, and perplexity concerning the pathology was created when they were found sometimes to possess a considerable abundance of apparently normal islands. It is now evident that the recovery of assimilation under fasting would be impossible if islands were not thus present; and these findings, formerly a ground of argument against the insular hypothesis, actually serve to support it. In the preliminary publications, it was deduced from this fact alone that the deficiency of the islands must be at least partly functional. (d) When some cells of the diabetic islands show hydropic degeneration, a functional insufficiency must be assumed also in the cells which appear normal. The accepted interpretation of the hydropic change in both man and animals implies that the cells are overtaxed functionally while they still appear normal, and the visible vacuolation follows. (e) Though it is possible to find animal specimens in which the exhaustion is universal, this condition has never been observed in man. Even when the diabetes is not only maximal by the usual tests, but furthermore so severe that it cannot be controlled by fasting, the islands contain not only exhausted cells but also others which appear structurally normal. The latter sort are frequently so numerous that a functional disability must be admitted.

²³ Allen, F. M., and Du Bois, E. F., *Arch. Int. Med.*, 1916, xvii, 1010-1059.

B. CHANGES DUE TO DIABETES.

The years 1900 and 1901 are epoch making in the microscopic pathology of diabetes, for in them appeared not only Opie's study of changes causing the disease, but also the first description by Weichselbaum and Stangl²⁴ of the hydropic degeneration, which later has proved to be a result of the diabetes. Those authors described the process as a vacuolation and liquefaction.

"There appear in the protoplasm of single or several epithelial cells of the islands small vacuoles, or, more objectively expressed, small, round spots, within which the protoplasm, which otherwise ordinarily shows a very close and fine granulation and stains lightly but distinctly with eosin, appears entirely transparent and colorless. These so called vacuoles then become confluent, and in the cell body are seen now only isolated granules and threads, which barely stain with eosin, while all other parts of the cell body appear entirely homogeneous, transparent and colorless, till finally also the individual granules and threads disappear, and the nucleus is now surrounded only by a perfectly transparent and colorless cytoplasm. Whether the latter in the condition just described is to be regarded as fluid, or has merely become extremely thin and transparent, we wish to leave undecided. But as the change begins with a vacuolation and a breakdown of the protoplasm, and furthermore often the chromatin of the nucleus becomes indistinct and finally a complete dissolution of the latter follows, we have chosen the designation, liquefaction. In such islands, the remaining, not yet liquefied epithelial cells show an exceedingly thin, delicate, but still not homogeneous and transparent protoplasm. It is therefore not improbable that a thinning of the protoplasm precedes the above described vacuolation and liquefaction."

These observations, beginning with 18 cases of diabetes, were extended so that in 1911 Weichselbaum was able to report 183 diabetic necropsies, with "a still larger number" of non-diabetic controls. Of the diabetic cases, 53 per cent showed hydropic degeneration or atrophy, 43 per cent fibrous, and 28 per cent hyaline changes. These were described, as was inevitable under the circumstances and in the absence of animal experiments, together as the three principal lesions causing diabetes. The recognition of the hydropic change was facilitated by the fact that the diabetic material was mostly from severe cases with termination in coma, and by the care taken for freshness

²⁴ For bibliography see Chapter I, also Allen, Glycosuria and Diabetes, Chapter XXI.

and fixation of tissue with a view to applying special stains. The broad plan of the work also contributed notably to its success, a careful study of the normal histology having been first made by Stangl, later the development was studied in the fetus and infant by Weichselbaum and Kyrle, and finally the pathology was closely investigated in the largest series of diabetic and non-diabetic cases on record. The admirable manner in which the research thus planned was carried out makes it a classic. Both the descriptions and illustrations show clearly and convincingly the exact appearances encountered in the study of any long series of typical cases of severe diabetes. The discussion is also worthy of such a foundation, the necessity of examining many sections from different parts of the pancreas, the non-specificity of hemorrhages in the islands, the pictures indicative of regeneration and hyperplasia, the consideration of quantitative changes, the answers to opponents of the insular hypothesis, and the etiologic suggestions, being still worthy of notice.

The investigation carried on at Harvard, 1909 to 1912, developed an improved form of experimental diabetes, in which hydropic degeneration of islands was found to occur. Descriptions and photographs were published in the former monograph.²⁵ The vacuolation was proved to be specific to diabetes and to run parallel to the clinical course, and was interpreted as exhaustion due to functional overstrain. Professor F. B. Mallory, with whose aid and advice the microscopic study was made, first suggested that the visible exhaustion of cells might be the result of the diabetes.

Reference was made in that publication to the work of Lane and Bensley, who proved by differential staining that the islands contain two types of cells. What they called the α cells are few in number, while the β cells make up the main mass of the island. The different affinity of the fine (presumably secretory) granules of these cells for dyes distinguishes them from each other and (along with mitochondrial and other characteristics) also from acinar, duct, centroacinar, and imperfectly differentiated island cells.

Homans²⁶ in 1912, using Bensley's stains, demonstrated the loss of granules of the β cells, so that they came to resemble duct cells,

²⁵ Allen, *Glycosuria and Diabetes*, 1913.

²⁶ Homans, J., *Proc. Roy. Soc. London, Series B*, 1912, lxxxvi, 73-87; *J. Med. Research*, 1914, xxx, 49-68; 1915-16, xxxiii, 1-51.

in dogs made diabetic by removal of all the pancreas except a small fragment at the tip of the uncinata process. He was inclined to interpret it as a specific exhaustion due to functional overactivity, but hesitated to regard the rôle of the islands in carbohydrate metabolism as positively proved. In 1914 he published a fuller investigation, altogether independent of that of Allen, showing that in cats mild diabetes is accompanied by thinning and later complete loss of granules from the β cells, while the nuclei and mitochondria remain normal, and more severe diabetes is marked by degeneration and disappearance especially of the β cells, though α granules may also remain in only a few cells. In 1915 he reported similar observations in dogs, indicating uniform preservation of α cells while β cells degenerated, the possible new formation of small islands composed only of α cells, and the production of the hydropic process by carbohydrate food, the sequence being defined as activity, exhaustion, and degeneration. An illustration was also given of an exactly similar vacuolation of the β cells in a human diabetic, confirming Weichselbaum and Stangl.

Hydropic degeneration has also been described in the above mentioned case of Ghon and Roman,¹⁰ and in an interesting and important instance of spontaneous diabetes in a dog studied by Krumbhaar.²⁷

Martin,²⁸ under the direction of H. M. Evans at Johns Hopkins, tested various pure dyes of the group used by Bensley, and determined that the best for the purpose is a combination of ethyl violet with either orange G or azofuchsin. The latter may be particularly recommended as an improvement upon Bensley's original stains, in that it is easier and more reliable in application and gives more vivid and distinct pictures. This work was continued in connection with the diabetic investigation in this Institute. The existence of the two kinds of granules in normal island cells was confirmed. The work being incomplete, Martin did not reach a conclusion whether the granules were confined strictly to different cells. He suspected that there might be gradations, and that two sorts of granules might be present sometimes in the same cell, but owing to possible overlapping of cells and other elements of doubt, he did not feel justified in opposing

²⁷ Krumbhaar, E. B., *J. Exp. Med.*, 1916, xxiv, 361-365.

²⁸ Martin, W. B., *Anat. Rec.*, 1915, ix, 475-481.

Bensley's carefully formed opinion that the two cell types are wholly distinct. Homans' discovery that only the β cells are subject to the characteristic exhaustion and degeneration was corroborated, and this fact favors Bensley's view of the independence of the two types. Often the α cells persist with if anything heavier than normal granulation among the swollen and vacuolated β cells, as described by Homans. This investigation was applied to dogs in which the metabolism and clinical condition had been carefully studied, in the hope of gaining information of the function of the α cells, but no definite relation between them and any phase of the diabetic disturbance was observed. Even the persistence of α cells in dogs showing a "total" D: N ratio could not prove them unconcerned in carbohydrate metabolism, since there is the possibility of a functional disability, such as must sometimes be assumed for the β cells, and also of functional interrelations normally between the two types of cells. In the extreme stages of experimental diabetes, vacuolation occurs in the small ducts and cell-cords, suggesting a real or attempted internal secretory function in them, though this is uncertain.

The vital and differential staining methods open important fields of research. Knowledge of the normal and the comparative histology of the pancreas is by no means complete. Though the essential independence of the islands is established by the work of Bensley and by their specific degeneration in diabetes, the frequency and extent of new formation of both islands and acini from ducts, the behavior of the islands in inflammation, regeneration, etc., and the exact border line between normal and pathologic processes, may be mentioned as unsettled problems. In diabetes and other pathologic states, it is still sometimes impossible to distinguish between acinar and island cells; the problem of regeneration and hyperplasia of island tissue has practical as well as theoretical bearings; and the function and relations of the several types of island cells, together with the duct and centroacinar cells, will be learned only by studying abnormal as well as normal organs. A point of particular interest was whether the special stains would furnish the long sought infallible anatomic diagnosis of diabetes. There was a chance that the islands which cause confusion in some diabetic cases might prove to be composed of α cells only; also that sparseness of granulation

might reveal diabetes in some instances where ordinary stains showed normal appearances. These conditions may in fact occur to some extent; but on the whole it is found, in agreement with conclusions expressed by Homans in conversation, that the special stains do not remove the difficulties of diagnosis. They furthermore are rather difficult and laborious in application, they demand a freshness of tissue and perfection of fixation seldom attainable in human autopsies, and even under ideal conditions in pathologic material they often fail to give the differentiation desired.

It is fortunate for practical convenience that routine methods carefully applied are sufficient. More or less can be learned from ordinary pathologic specimens in Zenker or formaldehyde solution, and neutral formaldehyde or Müller-formol mixtures are preferred by some. Instead of the usual 5 per cent acetic Zenker, the fixative of choice in the present work has been either a plain solution of 2.5 per cent potassium bichromate and 5 per cent mercuric chloride, or the same solution with addition of 1 or 2 per cent acetic acid just before using. Lane and Bensley have found that stronger acidity tends to dissolve out the specific island granules. The most important consideration for the study of hydropic degeneration is the freshness of the tissue. The autopsy should be performed immediately after death if possible, and the first step in it should be the removal and weighing of the pancreas, followed by immediate fixation of the pancreas specimens. It is advisable to take specimens from different parts of the gland in separate bottles. The procedure here has unconsciously imitated Weichselbaum and Stangl in taking them in three sets, from the head, body, and tail respectively. It is also desirable to take two kinds of specimens from each location: one, pieces of ordinary size, for the purpose of examining the number of islands and the general pathology; the other, tiny bits of tissue, only a few millimeters in dimensions for the sake of the quickest possible penetration of the fixative for the study of the cytology of the islands with either special or routine stains. For the latter the combination of eosin and either hematoxylin or methylene blue has been satisfactory in the present work. The fixation of other specimens in formaldehyde for fat or in absolute alcohol for glycogen stains, and other special measures, are of course added when desired. Persons

contemplating an investigation will do well to begin with animals, in which the diabetic change is plainest, and then to examine some human specimens showing it in typical advanced form, after which they will be better equipped to judge more doubtful material.

Information concerning hydropic degeneration may be summarized under six headings, as respects its description, nature, cause, mechanism, consequences, and significance.

1. *Description.*—Histologically, the process begins with a thinning of the fine granules, supposedly of internal secretion, shown in the island cells by the Bensley methods, or a paling and clearing of the finely granular cytoplasm seen with ordinary stains. The finest routine preparations probably reveal the change almost as early and delicately as the special dyes. The progress of the vacuolation or loss of granules is as described by Weichselbaum and Stangl and by Homans. The swelling of the individual cells, seemingly by imbibition of fluid, is apt to be more prominent in the dog and especially the cat than in other species, such as man, monkey, and raccoon, but occurs in all. In the most extreme degree, the islands composed of swollen empty cells somewhat resemble adipose tissue; Homans compares the network of cell membranes to a coarse meshed sieve; or the exhausted islands may seem to blaze out against the dark background of the acinar tissue like snowballs or hydrangeas in full bloom. Differences between species and between individual examples in the same species are governed largely (though perhaps not solely) by the acuteness of the process, giving both a more intense swelling and a greater number of simultaneously exhausted cells than when the change is slower. The alteration in the nucleus seems to be strictly secondary. An apparently normal nucleus can sometimes be seen naked, after the cell membrane has burst. The nucleus does not, as might be implied by Weichselbaum and Stangl's description, simply dissolve; but ordinarily at some, generally an advanced, stage of vacuolation of the cytoplasm, it becomes markedly dense and shrunken, and this pyknosis is one of the prominent features of the process. The shrivelled nucleus then dissolves, and is the last part of the cell to disappear. The observation of Weichselbaum and Stangl, that the hydropic change first begins in occasional cells, while most cells in the same island and all cells in

many islands still appear normal, holds for all species. Many β cells remain free from vacuolation even when many others have completely disintegrated. In the more advanced stages, recourse to the differential stains may be necessary to determine whether the remainder are the usual α cells, or β cells persisting with slight alteration or none. The order of precedence in which cells are affected is not governed by their position at the center or periphery of the island, or any obvious relation to the blood supply, or other known rules. The loss of cells is not replaced by fibrous tissue; neither, except in the most acute stage, are visible gaps left; but the acinar tissue crowds in on all sides, whether by new formation of acini or otherwise is unknown, and the reduced island remains as a compact group of cells, until finally it may consist only of a barely distinguishable clump of α cells and more or less framework, or may disappear without a recognizable trace.

2. *Nature*.—There is nothing to oppose Weichselbaum and Stangl's assumption that the vacuolation represents essentially water. The ordinary appearances, in addition to Sudan stains, suffice to rule out fat. Tests for protein and salts have not been made. Most observers are immediately impressed with the similarity to the Armani or Ehrlich change in certain cells of the renal tubules. Glycogen has not been demonstrable by Best's carmine in the vacuolated islands. The cause or nature of the renal picture calls for investigation. It has been commonly accepted as "glycogenic infiltration" because of Ehrlich's demonstration of the presence of glycogen in diabetes. The renal and pancreatic phenomena are not on a par, since the former may be found in various conditions while the latter is specific to diabetes. The truest resemblance is probably to the empty cells found in the adrenal medulla when nervous or other stimuli exhaust the fine granules which supposedly represent the precursor of epinephrine stored in the chromaffin tissue. Bensley in conversation suggested the possibility that the Langerhans vacuoles may contain the internal secretion in too great dilution for deposition in granules.

3. *Cause*.—Experimentally, the hydropic change can be shown to be specific to diabetes. It does not follow pancreatic operations unless diabetes is produced. Dogs made potentially diabetic by such operations can be kept even for years, and the preservation of their islands

can be demonstrated not only microscopically but also by the unchanged or increased food tolerance. But after any interval, early or late, the characteristic change can be produced by adding to the diet any kind of food beyond the assimilation, or by anything else that brings on active diabetic symptoms. Its independence of digestion is shown by its occurrence in fasting animals after removal of sufficient pancreatic tissue to cause active diabetes during fasting. It is likewise independent of other pathologic processes, such as give rise to diabetes. For example, hydropic degeneration does not give rise to fibrosis, neither does it ever result from simple fibrosis of any island, no matter how extreme. But when diabetes occurs, the presence of fibrous or other changes does not prevent the typical hydropic process, which in fact is generally found side by side with the fibrous and hyaline changes in the type of cases in which the latter have been most emphasized by Opie and others. A point of particular practical importance is that simple prolonged hyperglycemia, without glycosuria, regularly and definitely produces this change in diabetic animals; it is merely slower than with the more intense condition of hyperglycemia plus glycosuria. A slight degree of vacuolation may also be found in transitory diabetes, not only with glycosuria, but even when the animals for some days following operation show merely a considerable hyperglycemia on carbohydrate diet. The change may be demonstrated in a tiny bit of pancreas removed at this time without affecting the condition. Subsequently it may be impossible to bring on diabetes by any amount of starch and sugar feeding, and though temporary hyperglycemia may result, the island cells are not vacuolated. It must be concluded that the condition following operation was a genuine mild diabetes, even if evidenced only by hyperglycemia; and that subsidence of inflammation and functional and structural restoration and perhaps hypertrophy in the pancreas remnant resulted in a final cure.

4. *Mechanism.*—Experiments have been conducted to show the possible rôle of humoral and nervous agencies. Of the former, it might be supposed that the blood sugar is predominant, and that hyperglycemia *per se* is the stimulus to the islands. The evidence is against such an assumption. Vacuolation of the islands does not follow even the most prolonged hyperglycemia in normal animals,

one example being the experiment described in the former monograph by one of the authors, in which glycosuria was maintained by glucose injections in a cat during the greater part of 17 months, without producing vacuolation in the pancreatic cells or any other accompaniments of diabetes. Adrenalin and other forms of glycosuria likewise do not cause this change. Phloridzin has given useful results. Phloridzin poisoning, continued even for many months, does not cause hydropic degeneration; the unchanged sugar tolerance thereafter would be sufficient proof, even without the microscopic examinations. But when dogs are made severely diabetic by removal of all but a small fragment of pancreas, and, beginning even before operation, receive phloridzin in small doses so as not to produce fatal acidosis or intoxication and yet keep the blood sugar continuously at an actually subnormal level, hydropic degeneration occurs in fully typical fashion. Of nervous influences, it was shown in the former monograph that the Bernard puncture ordinarily causes no vacuolation in the islands, but in the single predisposed dog in which true diabetes followed the puncture, the characteristic hydropic change occurred. Homans,²⁶ producing hyperglycemia and glycosuria by 7 to 10 hours faradic stimulation of the splanchnic nerves in animals possessing an entire pancreas or only a half or a fifth of it, was unable to demonstrate positive alterations in the islands. Even potentially diabetic animals, however, fail to show vacuolation from hyperglycemia due to glucose injections within such an interval. The questionable swelling and diminished granulation of the cells mentioned by Homans may possibly indicate a positive effect, which was prevented from becoming manifest only by the time limitations. A paralytic injury seems to be excluded by both denervation and graft experiments. The best procedure for this purpose is to leave a small remnant about the lesser duct to aid digestion, and to transplant the button of duodenum bearing the main duct along with the entire uncinata process beneath the skin of the abdomen, preserving the blood supply of the graft through the inferior pancreaticoduodenal vessels, and removing all the rest of the pancreas. Division of this pedicle some weeks later isolates the graft from all intra-abdominal connections. Removal of successive portions from both the duodenal remnant and the subcutaneous graft then shows that both diabetes

and island changes are absent until the total remaining pancreatic tissue is reduced to the degree required to produce diabetes in an ordinary operation; food then shows the usual influence, and the usual hydropic changes occur in both the duodenal remnant and the subcutaneous graft. The graft of course acquires a nerve supply, presumably vasomotor, along with the blood supply from the subcutaneous tissue. Also the intrapancreatic ganglia survive, and no experiments have succeeded in eliminating the possibility of their regulating action. What is proved is that both the normal internal secretion and the hydropic process go on apparently unchanged in the absence of any possible specific stimulus or control from centers outside the pancreas. It may be conjectured that the regulation of the function of the islands, as probably of endocrine organs in general, is both nervous and humoral. Both experimental and clinical evidence suggests the possible influence of nervous stimuli, at least for harm. The humoral agency is proved; but it does not lie in hyperglycemia, which is merely a symptom of active diabetes. A special hormone is conceivable. But as mass action is an explanation of growing importance for physiological regulations, it may be that variations in the concentration of the internal secretion (whether this be combined with food substances such as sugar, or free) in the blood serve to govern the formation and discharge of this substance by the cells.

5. *Consequences.*—The hydropic degeneration results in numerical atrophy and finally almost complete disappearance of the islands of Langerhans. Weichselbaum and Stangl did not distinguish between this clear-cut process and the more recondite "atrophy" in which the island cells resemble lymphocytes. It seems probable that in the earlier stages compensatory regeneration and hyperplasia also occur. This view is supported clinically by the marked recovery of tolerance often possible at such a stage, developmentally by the formation of islands from ducts, which Laguesse and Bensley proved to continue in postembryonic life, and pathologically by the rather frequent finding of enlarged, seemingly hyperplastic islands, and of others that appear as if newly formed. Duct-like strands of cells, and small, compact, generally oval islands, unlike those usually seen normally and sometimes looking definitely like proliferations from ducts, have been mentioned by Homans and are a familiar observa-

tion in diabetic animals. In man such islands seem to be as a rule spherical, since their cut section is approximately round. It has seemed fitting descriptively to refer to them as the "morula" type of islands. They are not merely contracted islands with empty capillaries, but conform to Bensley's description of secondarily developed islands, and in their most typical form they are pushed in between the acini as morula-like masses of cells without capsule or the ordinary capillary and trabecular framework. They are strikingly frequent in some cases of diabetes, being sometimes almost the only type of island present. The finding of a considerable proportion of such islands may create a suspicion of diabetes; but, even granting the interpretation of them as "young" islands, it is not surprising that they may be found in the absence of diabetes, since regeneration need not be limited to the diabetic pancreas, and may in fact sometimes be the means of preventing diabetes. The islands of this type may suffer hydropic change and be lost like the others. Whether they are functionally equal to the ordinary islands, whether the cells are commonly paler and more subject to exhaustion and degeneration, are only speculative suggestions at present. Regeneration, even if a reality, fails in the later stages. Apart from the uncertainties of this question, two important facts are fully established. On the anatomical side, the deficit in number and mass of islands demonstrated in diabetes by Opie, Weichselbaum, Heiberg, and others, as far as it is not due to destructive processes causing the diabetes, is the result of the diabetes itself through hydropic degeneration; and in many cases, especially some of the worst type in young persons, this latter process is responsible for the loss of most of the islands. On the physiological side, this phenomenon explains clearly the progressive loss of tolerance caused by improper diet, and enforces the lesson of the difficulty or impossibility of repairing the damage.

6. *Significance.*—Active diabetes must first be present in order for the hydropic change to occur. In the partially depancreatized animal, a small fragment of pancreas evidently attempts unsuccessfully to carry the whole metabolic burden. In human patients, the islands present are apparently likewise stimulated to meet a demand beyond their capacity. Presumably the cells respond with an actual or attempted increase of secretory activity for a longer or shorter time

while appearing morphologically normal. At length secretion is discharged more rapidly than it can be formed, so that the normal fine granulation becomes more sparse and is replaced by vacuolation. Finally nuclear degeneration and complete disintegration of the cell result. This interpretation is so clearly suggested by the anatomic appearances, and so plainly confirmed by the feeding experiments, that there has been full agreement on the point among recent investigators. For this reason, the term "exhaustion" has come to be used as synonymous with vacuolation.

Physiologically, this phenomenon may be compared to the discharge of the acinar cells of the pancreas by secretin. There is a difference, in that secretin or other hormones have never been known to cause destruction of cells and actual disappearance of the tissue upon which they act. Whether the difference lies in intensity or duration of stimulation or in peculiarities of the cells is unknown. A further distinction is that an internal secretory function is here concerned, and the process is a clear-cut example of anatomic breakdown of an endocrine organ by functional overstrain. A strikingly clear relation between function and structure is thus shown, and the conception of diabetes as the overstrain of a metabolic function, long probable on clinical grounds, is strongly confirmed. The experiments with partially depancreatized animals are so simple and definite that this biologically important phenomenon is made easy to study.

III. Clinical Application.

This includes practical deductions concerning the etiology, anatomic diagnosis, and treatment of diabetes.

A. CLINICAL ETIOLOGY.

The etiology of diabetes will probably become fairly clear as soon as the pathology of the pancreas is adequately studied. Notwithstanding all the past work, the pancreas remains a neglected and little known organ from the simple anatomic-pathologic standpoint, as may easily be seen from the cursory remarks on it in text-books. The normal variations must first be better known. Occasional atypical appearances were noted by Opie and others, and Oertel and

Anderson²⁹ are the most recent authors to interpret these as indicating a natural sequence of degeneration and regeneration, though a question of their true normality is raised by the statement that they occur chiefly after middle life. A comprehensive investigation must be comparative. The present war, for example, may afford unusual opportunity for extensive observations on the pancreas of supposedly healthy individuals; but even if a high proportion show peculiarities, the question whether these are normal phenomena or reactions to morbid influences can be answered only by comparison with a series of animal species. The same military opportunity might be utilized to obtain a series of specimens from the more primitive races of man. It might then be possible to judge whether the erect posture, civilized habits, or other factors render man specially liable to pancreatic disorders and hence to diabetes.

An elementary fact, which seemingly should have attracted notice before, is that the pancreas is one of the most frequently diseased organs in the body. There is even ground to question whether a strictly normal pancreas may not appear as the exception rather than the rule in miscellaneous autopsies. Doubtless the percentage of abnormalities is lower in the young and rises with age, just as the incidence of diabetes is known to increase with age. The clinical diagnosis is missed in the great majority of cases, because of the deep situation of the organ hindering physical examination, the absence or slightness of digestive disturbance, and the fact that only the most violent forms of pancreatitis give the symptoms recognized as characteristic, while in milder or more chronic cases the local or general signs are indefinite or imperceptible, or if present are obscured by other morbid conditions. With due regard for nervous, hereditary, and other contributing influences, the central problem of the practical etiology of diabetes is the cause of the pancreatitis which may be predicated in every case, as a rule with no exceptions yet demonstrated.

Three forms of injury are distinguishable. One is the well known inflammation produced by bile or obstructed pancreatic secretion, the immediate harmful agency being chemical but the cause back of it

²⁹ Oertel, H., and Anderson, C. M., *Royal Victoria Hospital (Montreal), Scientific Reports*, 1916, *Series B*, 163-173.

generally bacterial.³⁰ Another is damage by bacterial products, locally or from a distance. There can be no doubt of the occasional rôle of organisms, as those of syphilis, lying in the parenchyma, or of colon or other bacteria in the ducts. Also any pathogens circulating in the blood might perhaps attack either the capillaries or the epithelium. Injury by soluble toxins from remote foci seems more vague and dubious. Such a possibility is supported by threefold evidence: (a) familiar lesions in viscera, including the pancreas, from extensive burns and other severe intoxications; (b) the frequent hyaline and rare amyloid changes, often affecting particularly the islands, and best explained as of toxic origin; (c) the easily demonstrable impairment of assimilation which so often accompanies even slight infections. The injury seems to be direct, since it is difficult to imagine any important metabolic alteration from a trivial cold, for example. It also appears to be functional, since rigid control of symptoms by dietary restriction during the attack ordinarily permits recovery of the full tolerance thereafter, while any permanent lowering resulting when symptoms are not thus controlled is readily explainable by hydropic degeneration. It is possible, however, to conceive of intoxication causing first functional deterioration and then structural decay, in the form of pyknosis of nuclei, atrophy of cells, and fibrosis of capillaries and islands.

Miscellaneous localized infections found in a certain proportion of diabetics may be variously interpreted as pure accidents such as befall numerous non-diabetics, or as a result of the lowered resistance characteristic of diabetes, or as a source of infection or intoxication directly causing the diabetes. It is probable that each of these three possibilities is sometimes correct. The demonstrable fact of damage to the islands of Langerhans by infectious disturbances, and

³⁰ Concerning pancreatitis from bile, see Halsted, W. S., *Bull. Johns Hopkins Hosp.*, 1901, xii, 179-182; Opie, E. L., *Ibid.*, 182-188; *Am. J. Med. Sc.*, 1901, cxxi, 27-43; Flexner, S., *J. Exp. Med.*, 1906, viii, 167-177.

Concerning pancreatitis from injection of bacteria, acids, alkalis, and other irritants, see Flexner, *Johns Hopkins Hosp. Rep.*, 1900, ix, 743-771; Flexner and Pearce, *Univ. Penn. Med. Bull.*, 1901-02, xiv, 193-202. Glycosuria is frequent with acute pancreatitis, according to Flexner's experiments and the clinical experience of Emerson, *Bull. Johns Hopkins Hosp.*, 1908, xix, 95-96.

the need and benefit of clearing up discoverable foci in any case, do not prove, however, that the focus or organism in question is the original cause of the diabetes. Removal of infectious foci responsible for continuous or recurrent intoxication naturally prevents the injury due to such intoxication. The clearing up of slighter foci, as dental caries or pyorrhea, in the absence of perceptible systemic symptoms, though advisable on general principles, seldom has much influence upon the assimilation. The rule with all foci is that their treatment gives relief from a distinct aggravating influence, but never a cure of the diabetes or a subsequent course different from cases without known foci. It is reasonably certain that a diabetes due exclusively to gall stones from typhoid or colon bacillus infection, or to pancreatitis from syphilis, pneumonia, or mumps, would show precisely the usual aggravation from a staphylococcus middle ear abscess or a streptococcus tonsillitis. Therefore conclusions should not too lightly be drawn that such a focus is the primary cause of the diabetes, either as a source of circulating toxin or as a portal of entry of organisms.

This problem can only be solved by more careful investigation of the incidence and causes of pancreatitis.³¹ Whipple's study, already mentioned,¹⁷ consisted in examinations of the pancreas in 230 unselected autopsies. Of these, 105 appeared normal; the others showed more or less pancreatitis, classified in five groups. The 6 cases of acute diffuse pancreatitis, occurring with pneumonia or other infections without recognizable symptoms, were mentioned above in connection with the similar inflammation which in animals is proved to be productive of diabetes. The three other classes of acute changes were 41 cases of focal necrosis, apparently not serious in degree, 5 cases of fat necrosis, and 7 cases of acute hemorrhagic pancreatitis. The remaining group of chronic pancreatitis embraced the majority of cases. Feiling³² expresses the opinion that mumps is the commonest cause of pancreatitis in childhood. He cites authors who have diag-

³¹ Cf. Egdahl, A., A Review of One Hundred and Five Reported Cases of Acute Pancreatitis, with Special Reference to Etiology; with Report of Two Cases, *Bull. Johns Hopkins Hosp.*, 1907, xviii, 130-136; McCrae, T., Acute Pancreatitis in Typhoid Fever, *Assn. Am. Phys.*, May 7, 1918.

³² Feiling, A., *Quart. J. Med.*, 1914-15, viii, 263-264.

nosed pancreatitis in respectively 4 out of 60 and 5 out of 33 cases of mumps. Autopsies on cases of mumps are rare, and it is reasonable to suppose that pancreatitis escapes notice more often than it is recognized. There have, however, been only a few reports of glycosuria or diabetes with mumps. The hyperglycemia or glycosuria frequently reported in connection with other infections is sometimes diabetic, more often doubtful in character.³³

The occurrence of acute pancreatitis without diagnostic symptoms is highly suggestive in regard to the etiology of diabetes. It is conceivable that the condition occurs either with general infections or independently, and that diabetes may result immediately or after various intervals. In delayed cases, the acute inflammation may render the organ susceptible to later injuries, or time may be required for the damaged islands to break down under metabolic strain. Thus, in children particularly, it is imaginable that an infection occasioning slight or imperceptible symptoms may leave the patient apparently as well as before, yet really with pancreatic deficiency which months or years later, under the burden of growth, becomes manifest as diabetes, seemingly of acute onset. The possibility was mentioned that with diabetic heredity such inflammations may be either more frequent, or, by reason of an inherently subnormal functional power of the organ, more serious in their consequences; and accordingly there will be special interest in examinations of the pancreas of both the non-diabetic and the diabetic members of diabetic families. The hardness of the pancreas so often noted by surgeons in operations is likewise of interest, though internists and pathologists dispute the reliability of such observations. While the commonest origin of chronic pancreatitis may be gall stones and biliary infections, there is room for inquiry concerning other prolonged causes, and also to what extent acute inflammations are responsible for progressive later changes, through obstruction of circulation or secretion by fibrous tissue.

However uncertain the symptoms, there is reason to believe that pancreatitis of any marked degree is not a matter of indifference for the general health; and the pathologic facts warrant the prediction

³³ Allen, *Glycosuria and Diabetes*, pp. 564 and 798.

that it will some day receive more attention as a cause of acute and chronic illness. When an adequate diagnostic method is developed, the new domain of pancreatitis will largely be carved out from the diagnoses which today are essentially expressions of ignorance, *e.g.* "dyspepsia," "nervous indigestion," "neurasthenia," "gastroenteritis," "autointoxication," "biliousness," "catarrhal jaundice," as well as other indefinite abdominal troubles or vague general impairment of health. Particularly with regard to "catarrhal jaundice," it is worth while to question how often the stasis of bile is due to swelling of the head of the pancreas, or, if due to primary bile duct infection, how often this spreads to the pancreas, and whether in all such cases thought should not be directed to the pancreas as the organ chiefly in danger. Clinical observations (*cf.* table, Chapter III) support the view that diabetes and indigestion generally do not occur together, partly because, as Opie showed, the type of pancreatitis is often different, and also doubtless because the malnutrition of pancreatic indigestion opposes the development of active diabetes.

The frequency of pancreatic inflammation may give reason for surprise that the damaged organ is so often able to prevent diabetes, but removes the principal element of mystery from the cases that occur.

B. ANATOMIC DIAGNOSIS.

Three chief difficulties have hindered the study of pancreatic pathology.

First, the organ is subject to incidental changes which may efface its ordinary characteristics. Thus, Oertel³⁴ describes cellular atrophy and collapse of structure to such an extent that islands and acini are not distinguishable. These changes, which have nothing to do with diabetes, but are purely the expression of pancreatic involution from cachexia or other cause, are necessarily an obstacle in diagnosis, especially important because terminal cachexia is so common in diabetes. Here the islands may show appearances like Weichselbaum's atrophy, with shrunken cells and pyknotic nuclei, without proving any specific disease in them. It is necessary also to be critical of

³⁴ Oertel, H., *Royal Victoria Hospital (Montreal), Scientific Reports*, 1916, *Series B*, 155-162.

reports of the gross weight of the pancreas, since this may be found low without indicating anything more than emptiness of the organ and general malnutrition.

Second, cytological observations have not been considered in the purpose or in the preparation of material of most researches in the past. Autopsy specimens are seldom ideal, often for reasons outside the power of the pathologist. In the main, however, attention has been centered upon the grosser structural disorganization, and the carelessness of pathologists regarding finer cellular changes is responsible for their overlooking the vacuolation accurately described and pictured by Weichselbaum and Stangl. It is furthermore important, in estimating dearth of islands, to recognize the pseudo-islands which occur in some cases, probably from proliferation of duct cells, and which lack both the structure and function of true islands.

Third, the clinical grouping of cases has been misleading. Inherently mild diabetes has been classed as severe merely because of acetonuria or perhaps an unnecessary death in coma. Maximal severity has been attributed to certain cases on the ground of their rapid course and early fatal termination. Since such patients when given the opportunity by proper treatment often manifest a surprisingly high assimilative power, the finding of numerous islands in their pancreas is now seen to be in strict accord with the insular theory, instead of inimical to it as formerly supposed. With a truer clinical classification, and with treatment preventing a large proportion of early unnecessary deaths, pathologists will find the microscopic diagnosis much simpler. On the other hand, the clinical statement that diabetes was absent need not be accepted as infallible. Generally it means only absence of glycosuria. Tests of the blood sugar and glucose tolerance have seldom been made, and even these may be vitiated by cachexia or other disturbances. Weichselbaum records one instance in which the pathologic findings pointed to diabetes, which was not clinically evident during the final illness in the hospital, but careful inquiry of the relatives elicited a history of typical diabetic symptoms previously. In most diseases the pathologist corrects the clinician, not *vice versa*; and this will be increasingly true of diabetes as the morbid anatomy is better understood.

The diagnostic import of the island exhaustion resulting from diabetes, and of the lesions causing diabetes, may be summarized as follows:

1. *Hydropic Degeneration.*—It is necessary to define the significance of the presence and absence of this change.

Its Presence.—Vacuolation of cells is an appearance which pathologists are likely to view with suspicion as an accidental or unreliable phenomenon. Fortunately the islands of Langerhans are little subject to non-specific vacuolation. Fry³⁵ mentions vacuolation and degeneration of the islands in a case of myxedema. The bare possibility of masked diabetes must be considered; or, as vacuolation of the adrenals is similarly mentioned, it is conceivable that the change in the islands may have been fatty. Extensive examination of miscellaneous autopsy specimens has thus far confirmed Weichselbaum's conclusion in favor of the specificity of the true hydropic alteration. Careful study is still needed to decide whether actual fluid accumulation ever takes place in the island cells from any cause other than diabetes, and whether fatty or other changes ever simulate the real exhaustion. The most frequent cause of uncertainty is imperfect preservation of tissue. Shrinkage, as from formaldehyde, small breaks in the sections, and other artefacts may be confusing. Especially, with only a little delay in fixation, the delicate membranes of exhausted cells may break down first of all; and with later autopsies blurring and fragmentation of the islands may make pictures hard to interpret. Under these circumstances simple pallor of island cells, and the finding of naked nuclei, is suggestive but not conclusive. With abundant islands present, there may then be justified hesitation between two extreme judgments; one, complete absence of diabetes, with perhaps nothing wrong but a trivial pancreatitis; the other, diabetes of the most intense rapid type with early death in coma. Diagnosis is sometimes demanded not only from poorly fixed tissue but also from single slides, whereas search through all portions of the pancreas is required by the fact that certain areas sometimes reveal pictures not seen in the others. It seems safe to say that the typical picture of vacuolation in some cells and pyknotic

³⁵ Fry, H. J. B., *Quart. J. Med.*, 1914-15, viii, 276-299.

nuclei and degeneration in others is absolutely diagnostic of diabetes. Furthermore, if in satisfactorily prepared tissue an observer familiar with this process finds a single island cell which is unmistakably swollen and vacuolated, with a nucleus (generally normal) surrounded by a halo of clarified cytoplasm inclosed within a distinct cell membrane, in sharp contrast to the other normal appearing island cells, the existence of diabetes is established. Only, the warning against accidental appearances more or less closely imitating the true picture must here be emphasized. As the sign is one of active diabetes, the clinical record regularly agrees; but if any exception is found, the clinical diagnosis should be subjected to fully as close scrutiny as the pathologic diagnosis.

Its Absence.—In animals the hydropic change is a fairly reliable and delicate index of diabetes, beginning with slight vacuolation of a few cells in the early mild stage, and advancing parallel with the duration and severity. It appeared puzzling that a considerable proportion of human cases, surpassing in both these respects many of the animals, show entire absence of visible exhaustion; yet the explanation is simple. In the strictest sense, the hydropic degeneration is an expression not of diabetes but of cellular dissolution due to diabetes. It is unknown at what point repair becomes impossible; but in animal experiments a cell evidently persists only a few days in its terminal stage of extreme vacuolation and swelling. Under sharp dietary restriction, gradual recovery seems to be possible even at this stage, apparently corresponding to the marked transformation and gain of tolerance in some human cases on fasting. Otherwise, cells and islands break down and are permanently lost, as already explained. Human cases seldom progress as rapidly as the experimental diabetes of animals, in which the destruction of islands may be practically complete within a few weeks or months, as proved anatomically and by the inability to become sugar-free on fasting. The human cases are more likely to last months and years, and even in the worst forms to retain enough island tissue to enable control by fasting. Accordingly, the visible degeneration could not be so striking in the human pancreas as in animals unless the clinical progress were as rapid. Moreover, the intensity of clinical symptoms is not a sole criterion of the anatomic effects. Not only may a dog

with a 2.8 or lower D: N quotient show more rapid and extensive island destruction than a man with a 3.65:1 ratio, but the differences between human patients are still greater. It is well known that cases with similar hyperglycemia, glycosuria, and acidosis differ widely in progressiveness, such differences being most familiar between elderly and youthful patients, but sometimes equally prominent between different cases at the same age. Specific differences in the susceptibility of the island cells to anatomic breakdown from functional overstrain must be recognized. Therefore it is impossible to establish any rule as to the proportion of cases in which hydropic changes will be found. It can only be said that they are invariably present when the intensity and the duration of the diabetes are sufficient. They are practically always present in typical coma, though when this follows only a short period of intense symptoms, they may sometimes be surprisingly slight and hard to demonstrate. Specimens from severe cases of diabetes treated by the old methods show them in the majority of instances. They are less frequent in proportion as the diabetes is milder or the treatment more efficient. The previous statement that persistent hyperglycemia without glycosuria causes degeneration of islands is a deduction as applied to human cases. The evidence for it is that diabetic animals under these circumstances show gradual loss of tolerance, and slight hydropic changes are demonstrable in their islands. Human patients show a similar injury of assimilation, which is sometimes so slow that it may appear doubtful but is nevertheless real; but the anatomic process has not as yet been observed in them under these conditions. Such a gradual loss, probably no more than the disintegration of an occasional scattered cell, though real, will necessarily be seldom convincingly visible. Diminished frequency of hydropic degeneration should be the accompaniment and proof of improved treatment.

In brief, the presence of hydropic degeneration may be held to establish a positive diagnosis of diabetes, but its absence is not proof that diabetes is absent.

2. *Lesions Causing Diabetes.*—All pathologic researches on the subject have agreed concerning the occurrence of pancreatitis, and notably of fibrous, hyaline, fatty, pigmentary, malignant, or other

changes affecting the islands, in a variety of conditions without positive diagnostic significance, but on the whole more frequently and extensively in diabetic than in non-diabetic cases. In the nature of things, it has been impossible to establish any uniform rule for the diagnosis of diabetes from such observations, for several obvious reasons. First, valid judgment of the extent of island destruction requires unusually painstaking study, because of the differences even between closely adjacent areas of the normal pancreas, as shown by Bensley, and still more so in pathologic material. Second, some allowances must be made for functional influences and differences, as mentioned previously. Third, the pathologist cannot be expected to estimate concomitant clinical conditions. The characteristic active symptoms of diabetes may be absent with emaciation from anorexia, impaired food absorption, or any form of cachexia, when the pancreatic destruction is such as would certainly bring on these symptoms in a patient otherwise healthy. The condition is entirely similar to the apparent absence of diabetes in cachectic dogs possessing only insignificant atrophic remnants of pancreas. This is doubtless the chief explanation of the usual lack of diabetic symptoms with pancreatic cancer. In the main, the inability to draw a sharp pathologic line between diabetes and non-diabetes merely expresses the fact that no such line exists. There are all gradations between normal and diabetic, with or without demonstrable impairment of food assimilation. With a certain allowance for functional variations, any person or animal is diabetic in proportion as islands of Langerhans are lacking, and this anatomic fact is so thoroughly established that it is independent of clinical complexities. Whereas the uncertainty of diagnosis might formerly be imputed solely to the ignorance of the pathologist, the latter should now be able to recognize diabetes positively in any case of fatal severity, without regard for functional differences, from the anatomic deficiency of island tissue alone, and to form also some idea of the degree of true severity. When islands are so abundant as to make the diagnosis on this basis doubtful, the pathologist may say positively that, barring disobedience, complications, or other uncontrollable accidents, death was due to inadequate treatment and not to actual severity of the diabetes.

Several trials have been made of the diagnosis of unlabelled pancreas specimens from various sources. In brief, when the fixation has been good and the diabetes severe, the distinction from miscellaneous non-diabetic material, on the combined basis of vacuolation and scarcity or "atrophy" of islands, has succeeded in almost 100 per cent of cases. When either the fixation was poor or the diabetes mild, mistakes have been so numerous that the results were largely unreliable.

The confusion concerning pancreatic pathology in the past has wrongfully cast doubts upon the pancreatic origin of diabetes, notwithstanding the wide discrepancies between structure and function freely recognized for other viscera. More accurate correlation of all the facts, clinical, experimental, and anatomic, justifies the inquiry with what other organ or disease is the relation between function and structure so clear and demonstrable as in the case of the pancreas and diabetes.

C. RELATION TO TREATMENT.

For their therapeutic significance, the anatomic changes are again conveniently divisible into those caused by and causing the diabetes.

1. Hydropic Degeneration.—Clinically, three lessons stand out. One is the establishment of diabetes as an independent condition with a pathology of its own. On the one hand, this contributes further to clear away the pernicious confusion of diabetes with non-diabetic forms of clinical and experimental glycosuria. On the other hand, diabetes is raised above the rank of a mere symptom of pancreatic disease. Its right to recognition as a distinct morbid entity has long been generally acknowledged because of its importance and its broad clinical characteristics. It is now seen to have a pathologic course independent of the inflammatory or other basis on which it arose. Treatment of diabetes by diet therefore is not mere palliation of a symptom, but is a genuine means of checking the progress of a definite pathologic change.

Second, anatomic guidance is given for the direction, ideals, and limitations of dietotherapy. It emphasizes the need of beginning at the earliest possible stage, when islands are most abundant and the power of regeneration perhaps also exists. The fact should be

emphasized that, whatever excuses may be made for lax treatment, it is responsible for progressive destruction of islands of Langerhans. With grossly excessive diet and flagrant symptoms the loss is rapid; with only hyperglycemia and perhaps traces of acidosis it is slower; also the susceptibility to functional overstrain differs widely in different cases; but the ultimate injury manifests itself clinically, without exceptions other than a few cases so mild that they tend strongly to recover. Frequently the patient comes under thorough treatment only after his own carelessness or a physician's mistakes have caused irreparable downward progress. In the stage of greatest severity, exemplified by most of the cases of the present series, the remaining island tissue is very scanty, and any capacity of regeneration seems to be exhausted. The inability to recover assimilative power, and the difficulties in any research aiming at a cure of such cases, are made clear by this depletion not only of islands but apparently also of the cells in ducts or elsewhere which are able to form islands. The purpose of diet is therefore to prevent the specific degeneration of the islands by relieving functional overstrain. It obviously cannot check destruction by progressive inflammatory or other processes. There is also a bare possibility that Weichselbaum's "atrophy" may represent a hopelessly progressive disease of the islands. Experience shows, however, that the signs of progressive inflammatory change are usually greatest in the more elderly patients, whose diabetes is as a rule milder and easier to control, while in a large proportion of youthful patients the progressive loss of islands is due chiefly to hydropic degeneration. As mentioned, the animal experiments demonstrate the possibility of preserving the islands and the tolerance by restriction of all classes of food in the absence of any progressive tendency. Though the clinical results are marred by faults of patients and by mistakes in the application of the treatment, they prove that in at least a large proportion of cases an existing downward progress can be checked and a stationary or improved assimilation maintained through months or years. To date, as far as the principle of total dietary regulation has been faithfully carried out, only one case has yet been observed of apparent "spontaneous downward progress" in absence of the metabolic injury of improper diet or infectious complications. Therefore, whatever

part may be assigned to the causes back of the diabetes, it must be concluded that degeneration of islands due to errors in dietetic management has been a leading factor in the supposedly "spontaneous" aggravation of the condition.

Third, a verdict on the treatment can in large measure be given from the autopsy. Weichselbaum and Stangl's cases were doubtless treated by the former orthodox method, and the hydropic degeneration found in a majority of them is positive proof of rapid destruction of islands due directly to the diet. Allowance must be made for disobedience, intercurrent infections, and other uncontrollable accidents. Otherwise, the finding of hydropic changes condemns the treatment. Vacuolated islands are not present with thorough dietary control. It seems possible also to form a correct anatomic judgment of the true severity of the diabetes. With close distinctions between prepositions, it may be said that many patients die with or from, but very few of diabetes. They die with diabetes if they are carried off by some extraneous cause. They may die from diabetes indirectly, if death results, for example, from infection for which diabetes is responsible through lowering resistance; or more directly, if the diabetes reaches such intensity that fasting fails to avert coma, even though the pancreas contains numerous islands and, if coma is barely escaped, a correspondingly high food tolerance is subsequently attainable. These deaths, in other words, are due essentially to avoidable accidents of infection, fat intoxication, etc. But with the fundamental definition as deficiency of the internal secretion of the pancreas, a patient can be said to die strictly of diabetes only when this secretion is absolutely too scanty to support life. These are the patients who cannot be free from active symptoms except at the price of extreme emaciation, who cannot gain appreciably in assimilative power, and who sometimes die finally of inanition in spite of unbroken fidelity on their own part and the best skill of the physician. Irrespective of any assumed functional alterations, the few autopsies upon such patients to date have invariably shown an organic dearth of island tissue fully sufficient to explain the hopeless clinical severity. The failure of treatment has thus been due to inability to replace the islands, which have been lost probably to some extent in an inflammatory process, but in most cases largely through previous errors in dietetic management.

Certain points should also be mentioned in which the autopsy is not decisive concerning treatment. First, absence of discoverable hydropic change does not prove that the diet was suitable, since, as mentioned above, a certain intensity of overstimulation is necessary before this change is apt to be discoverable. Second, even extreme dearth of islands along with absence of vacuolation does not necessarily relieve the physician of responsibility for the death. It largely absolves from any accusation of acute death due to avoidable accidents. But it has been a common mistake to feed patients slightly beyond their true tolerance, permitting hyperglycemia and slight acidosis for the sake of temporary subjective comfort, and checking more serious symptoms by occasional fasting or reduced diet. In this way downward progress is merely delayed; the breakdown of islands by functional overstrain occurs more slowly but just as inevitably. Finally, the most rigid treatment may be unavailing because the pancreatic capacity has fallen actually too low to support life; but the cause may have been not a chronic progressive tendency of the disease but a chronic inefficiency of treatment.

2. *Changes Causing Diabetes.*—The inflammatory origin of diabetes carries distinct therapeutic significance. Islands once destroyed cannot be replaced by any means now known. All that can be hoped is to spare the function of the remainder as effectually as possible by diet, and thus also to provide the most favorable conditions for spontaneous regeneration. Acute inflammation as a cause of diabetes offers three suggestions: first, the importance of sparing the weakened function from the outset; second, the desirability of finer methods for the diagnosis of pancreatitis, along with surgical or other procedures to mitigate the consequences; third, the chance that in at least some cases the organic lesion may not progress further and the subsequent welfare may be purely a question of whether the remaining islands are spared or destroyed by diet. As far as diet was properly conducted, the present series supports this expectation, by showing the apparent absence of inherent progressive tendency in a considerable proportion of cases. With early efficient dietary care, it is to be hoped that the small number of more or less complete cures, such as cases Nos. 40 and 76 in this series, case No. 203 of Joslin,³⁶

³⁶ Joslin, E. P., *Treatment of Diabetes Mellitus*, 1917, p. 52.

and the extreme example of Jonas and Pepper,³⁷ may somewhat increase. Chronic inflammation makes a direct appeal for some therapeutic intervention to stop it. With improved dietetic control, more attention is undoubtedly going to be paid to the diagnosis of chronic pancreatitis and to attempts to prevent the injury which it produces as respects both diabetes and the general health. By reason of the relative safety with which operations can now be performed upon properly prepared diabetics, explorations for the cause of pancreatitis, the removal of otherwise quiescent gall stones and the drainage of infected bile will probably become more common, especially perhaps in cases at or beyond middle life. The conception of diabetes as due chiefly to pancreatic inflammation creates a more hopeful general view-point than before. The pathologic study thus offers the first well grounded hope that, as constantly better control of infectious disease is achieved, the race may some time be free of diabetes.

Conclusions.

1. The status of the islands of Langerhans as an internal secretory organ and as the seat of the specific diabetic disturbance is now as firmly established as any fact in physiology or pathology. In addition to the older extirpation and ligation experiments, which were not conclusive, the new evidence consists in the production of diabetes with large masses (up to one-third of the pancreas) of normal appearing acinar tissue present when only islands are deficient, and especially in the occurrence of visible exhaustion and degeneration of the island cells in demonstrable parallelism with variations in diet and the course of the diabetes.

2. Clinical diabetes apparently arises regularly on a basis of pancreatitis, either acute or chronic; and with accurate correlation of clinical and anatomic examinations, a generally logical association of function and structure is perceptible.

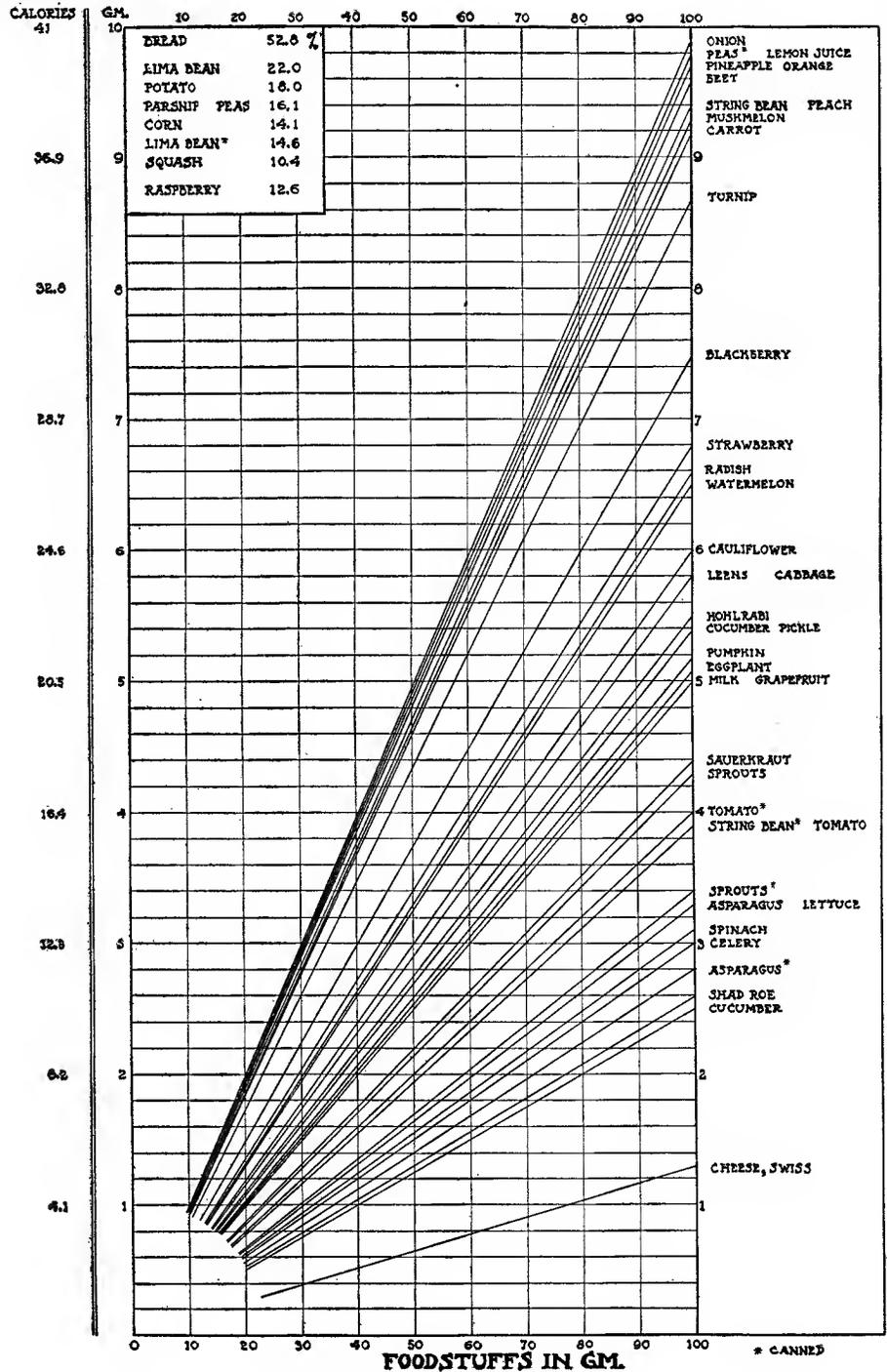
3. The explanation of the permanent lowering of assimilation resulting from excess of any kind of food in diabetes is the specific degeneration of the islands of Langerhans thus produced. Regulation of the total diet is not merely the treatment of a symptom, but is the essential means of preventing the principal cause of downward progress.

³⁷ Jonas, L., and Pepper, O. H. P., *J. Am. Med. Assn.*, 1917, lxviii, 1896-1897.

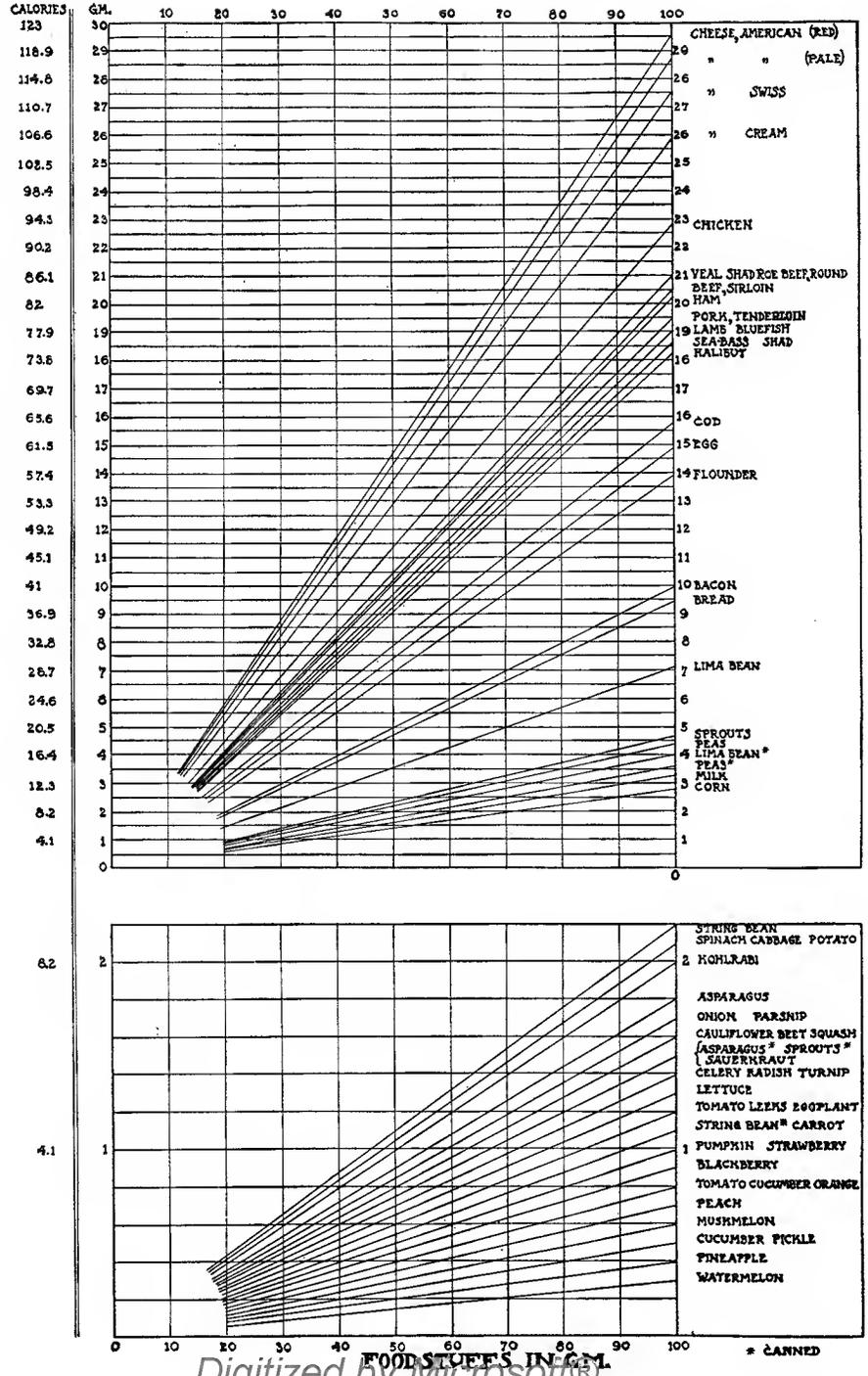
TABLE III.

Urine.													Blood.													Remarks and clinical notes.										
Gm.			Total N.	D : N	FeCl ₃	Nitroprusside.	NH ₄ -N	Urea-N	Acetone bodies as acetone.				Albumin.	Remarks.	Plasma.							Total fatty acid.			Cholesterol.			Lecithin.								
3	4								gm.	gm.	gm.	gm.			gm.	gm.	gm.	gm.	cc.	Sugar.	Combining power for CO ₂ .	Acetone + di-acetic per 100 cc.	β-oxybutyric as acetone per 100 cc.	Acetone bodies per 100 cc.	Nitroprusside.		Lipemia.	Hemoglobin.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.	Whole blood.
H. Faint.	Mod. Neg.	12.87	5.03 6.02		H. Mod.	V.H. H.	1.05 0.71		1.05 2.48	3.12 1.04	4.11 3.52	205 215	Neg.	10:30 a.m. 11:30 "	0.227 0.106	64.3 58.6	12 12.5	26.0 43.7	38.0 56.2	++ ++	+ Neg.	85 103	44.6 46.2	1.63 0.95	1.75 1.02	1.32 0.93	0.60 0.55	0.65 0.59	0.42 0.51	0.25 0.21	0.19 0.14	0.31 0.26	Patient admitted.			
Neg.	"	0	5.57		Sl.	"	0.63		1.49	1.96	3.45	199	"																				Carbohydrate test begun.			
"	"	0	4.77		Faint.	Mod.+	0.20		1.71	1.34	3.05	200	"																							
"	"	0	5.61		"	H.	0.27		1.19	0.75	1.94	195	"																							
"	"	0	4.09		"	"	0.24		0.30	0.35	0.85	130	"																							
"	"	0	3.25		"	"	0.21		0.42	1.08	1.50	117	"																							
"	"	0	4.66		"	Mod.+	0.14		0.44	0.51	0.95	65	"																							
faint.	"	0	5.14		"	Mod.	0.11		0.31	0.63	0.94	35	"																							
Neg.	V. faint.	0	6.30		"	"	0.13		0.13	0.29	0.42	75	"																							
Faint.	"	0	5.41		Neg.	"	"		0.18	0.27	0.45	51	"																							
Neg.	Neg.	0	5.48		Faint.	"	0.21		0.27	0.37	0.64	160	"	9:30 a.m.	0.133	63.2	Tr.	36.2	36.2	0	0	99	45.3	0.57	0.63	0.52	0.42	0.45	0.39	0.19	0.13	0.23		End of carbohydrate test. Beginning of low calory diet to clear up hyperglycemia and ketonuria.		
"	"	0	9.41		Neg.	"	0.63		—	—	—	220	"																							
"	"	0	9.62		"	Sl.+	0.56		—	—	—	231	"																							
"	"	0	7.14		Faint.	"	0.39		—	—	—	216	"																							
"	"	0	9.77		"	"	0.16		—	—	—	211	"																							
"	"	0	—		Neg.	V. Faint.	—		—	—	—	—	"																							
"	"	0	—		"	Sl.	—		—	—	—	—	"	5:00 p.m.	0.123	64.4	Neg.	13.2	13.2	0	0	98	47.7	0.55	0.61	0.50	0.38	0.41	0.37	0.23	0.17	0.29				
"	"	0	—		"	Sl.+	—		—	—	—	—	"	12:00 n.	"	71.0	"	11.3	11.3	0	0	"	51.0	0.57	0.60	0.55	0.40	0.43	0.39	0.21	0.16	0.24		Weekly fast-day.		
"	"	0	—		"	Faint.	—		—	—	—	—	—	10:00 a.m.	0.083	69.1	"	7.0	7.0	0	0	96	52.0	0.61	0.65	0.59	0.32	0.36	0.30	"	0.19	0.23				
"	"	0	—		"	"	—		—	—	—	—	—																							
"	"	0	—		"	Neg.	—		—	—	—	—	—																							
"	"	0	—		"	"	—		—	—	—	—	—	9:30 a.m.	0.076	68.1	—	—	—	0	0	101	44.5	0.51	0.56	0.49	0.26	0.30	0.21	0.30	0.28	0.38				
"	"	0	—		"	"	—		—	—	—	—	—	10:15 "	0.123	62.4	—	—	—	0	0	98	37.2	0.53	0.54	0.51	0.28	"	0.26	0.29	0.24	0.32				
"	"	0	—		"	"	—		—	—	—	—	—	10:00 "	0.104	62.3	—	—	—	0	0	96	39.8	0.49	"	0.45	0.31	0.36	0.29	0.21	0.18	0.27		Weekly fast-day.		
"	"	0	—		"	"	—		—	—	—	—	—																							
"	"	0	—		"	"	—		—	—	—	—	—	5:15 p.m.	0.114	67.2	—	—	—	0	0	98	46.0	0.52	0.56	0.49	0.25	0.27	0.21	0.32	0.27	0.38				

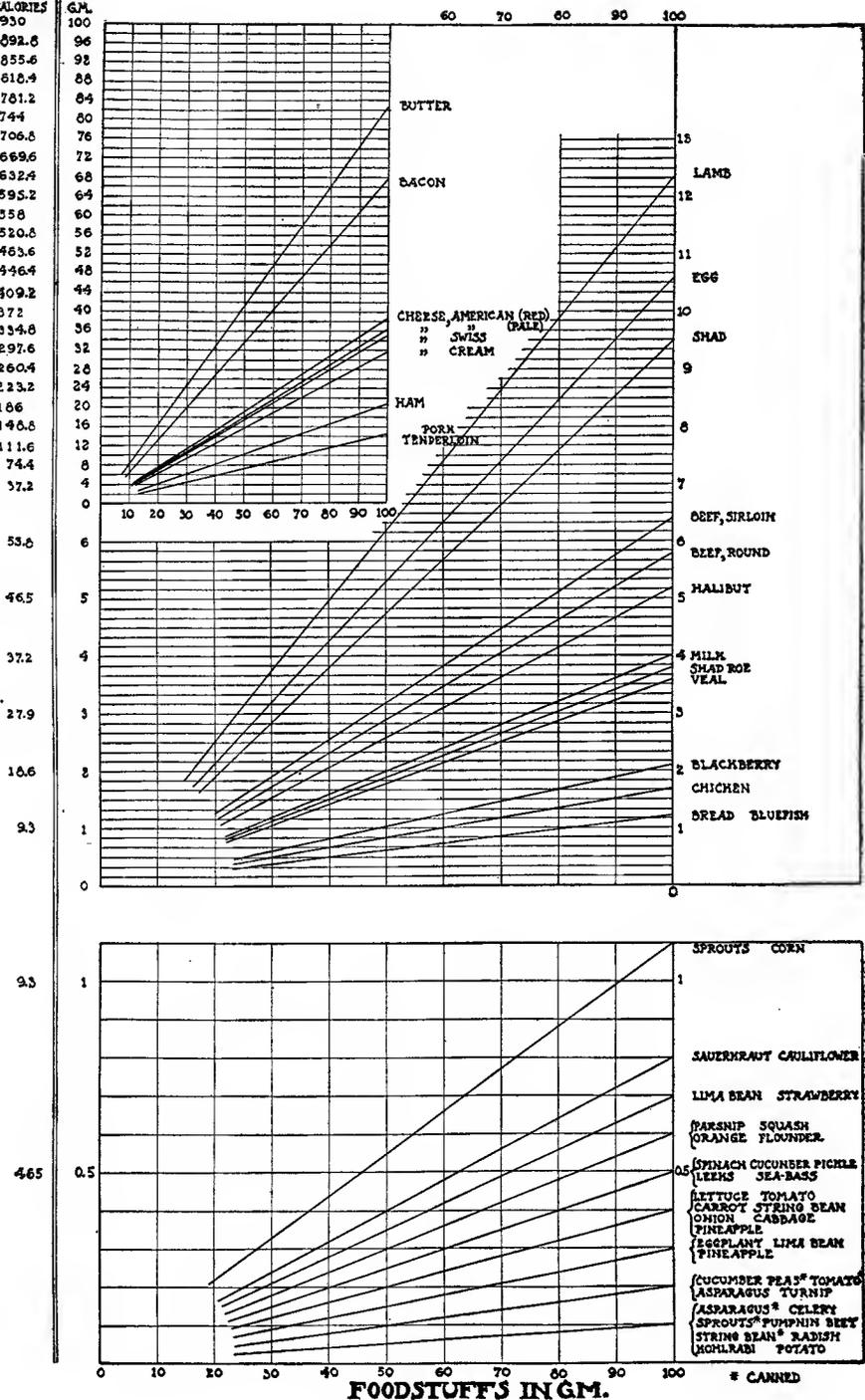
CARBOHYDRATE



PROTEIN



FAT



Diabetic No.	General data.				Family history.				Past history.											
	Sex.	Nationality or race.	Age.	Occupation.	Diabetes.	Obesity.	Tuberculosis.	Other disorders.	Infections and accidents			Nervous system.	Activity.	Habits.			Figure.	Digestion.	Bowels.	
									Childhood.	Adult.	Wassermann test.			Alcohol.	Tobacco.	Appetite and diet.				
1	F.	American.	28 yrs.	None.			Uncle (1).	Father, tendency to melancholia. Sister, nephritis.	Measles, diarrhea.			Naturally nervous; unhappy love affair.	Overstrenuous socially.			Fond of eating; excess in sweets.	Thin.	Good.	Moderate.	
2	"	Italian.	17	Sewing machine operator.		Father; brother (moderate).			"		-	Phlegmatic.	Sweat-shop.	Slight.		Moderate.	Slightly obese.	"	Regular.	
3	"	American.	26	None.			Maternal grandfather; father; uncle.	Maternal aunt died of melancholia. Brother nervous.	" mumps; chicken-pox; typhoid; tonsillitis.	"Colitis;" grippe; intercostal rheumatism; appendicitis; appendectomy; oophorectomy; phlebitis.		Sensitive.	Some social strain.			Much candy.	Normal.	"	"	
4	M.	"	12	"	Sister; paternal grandfather; uncle.			Maternal grandmother, cancer. Neurotic on father's side.	Abscess on neck; bronchitis; rheumatism; measles; chicken-pox; tonsillitis.		-	Precocious; neurotic.	Normal.			Sweets restricted.	Plump.	"	"	
5	"	"	34	Customs inspector.					Measles; tonsillitis.	Gonorrhea; acute pancreatitis (?).	-	Neurotic.	"	Occasional excess.	Moderate.	Irregular.	Normal.	Poor.	Constipated.	
6	F.	Italian.	48	Housewife.	(Husband now diabetic. Patient very ignorant.)				Unknown.				Phlegmatic.	Tenement life.	Slight.		No excess.	Slightly obese.	Good.	Regular.
7	"	American (Swedish).	36	Saleswoman.					Scarlet fever.	Miscarriage.	-	Nervousness perhaps due only to diabetes.	Unhappy married life.	Excess (?).		Light eater; coffee to excess.	Obese.	"	"	
8	M.	American.	29	Printer.				Mother, simple goiter.	Measles; chicken-pox; mumps.	Slight pleurisy.	-	Normal.	Normal.	Little.	Little.	No excess.	Thin.	"	Slightly stippled.	
9	"	Jew.	24	Tailor.					(Memory uncertain.) Rheumatism.	Gonorrhea; bronchitis; frequent colds.		Neurotic.	"	"	Moderate.	Ordinary.	Normal.	"	Constipated.	
10	"	American (Irish).	17	Plumber.					Measles; whooping-cough.			Normal.	Healthful.			Large; much sweets.	"	"	Regular.	
11	F.	Austrian.	55	Housewife.		Obese family.			Measles.	4 miscarriages.		"	Ordinary.	Slight.		Excess denied.	Very obese.	"	"	
12	M.	Jew.	49	Tailor.		Moderate.				Partial tonsillectomy.	-	"	"	"	Moderate.	No excess.	Obese.	"	"	

TABLE I—General Summary.

Past history.								Diabetic history.																
system.	Activity.	Habits.			Figure.	Digestion.	Bowels.	Onset.		Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Ac.	
		Alcohol.	Tobacco.	Appetite and diet.				Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.									Degree.	Draw-siness.
nervous; love	Overstrenuous socially.			Fond of eating; excess in sweets.	Thin.	Good.	Moderate constipation.	Acute.	Jan., 1913	July 6, 1913	Polydipsia; polyphagia; pruritus.	56.8		40.1	+	+	Marked.	—	Stopped May, 1913.		Marked.	Heavy.	+	
ic.	Sweat-shop.	Slight.		Moderate.	Slightly obese.	"	Regular.	Gradual.	Dec., 1912	Mar. 14, 1913	Weakness; loss of weight; polyphagia; polydipsia.	5.45	40.9	42.6	+	+		—	Stopped Feb., 1913.	Headaches.		Moderate.	—	
	Some social strain.			Much candy.	Normal.	"	"	Acute.	Jan., 1913	May, 1913	Weakness; loss of weight.	54.5	49.5	46.5	+	+		—	Normal.		Marked.	"	—	
is; neu-	Normal.			Sweets restricted.	Plump.	"	"	"	Summer, 1907	Immediate.	Polyphagia; polyuria.	31.8		23.8	+	+		Two ulcers.	Slight 1st 15 days; slight terminal.		Neuritic in legs.	Slight.	Heavy at times.	+
	"	Occasional excess.	Moderate.	Irregular.	Normal.	Poor.	Constipated.	"	July, 1913	Sept., 1913	Polydipsia; loss of weight and strength.	79.5	72.3	60.4	+	+		Faint 1st 11 days.	Lessened libido.	Back and legs.	Present, but not connected with diabetes.	Slight.	—	
ic.	Tenement life.	Slight.		No excess.	Slightly obese.	Good.	Regular.	Unknown.		July 25, 1914	Hospital routine.			58.8	—	—		Faint 1st 15 days.	Climacteric 1913.		"	—		
ess per- lue only etes.	Unhappy married life.	Excess (?).		Light eater; coffee to excess.	Obese.	"	"	Acute.	Dec., 1913	Mar., 1914	Pruritus; loss of weight.	76.3		52.8	—	+	Vulvar, marked.	Superficial vulvar; also styes.	Faint, transitory.	Normal.	Severe in legs.	Marked.	"	—
	Normal.	Little.	Little.	No excess.	Thin.	"	Slightly constipated.	"	June, 1913	June, 1913	Polydipsia.	68.2		50	+	+		—	Absent.		Slight.	Heavy.	+	
	"	"	Moderate.	Ordinary.	Normal.	"	Constipated.	"	Oct., 1913	Oct., 1913	Bronchitis.		68.2	53.6	+	+		—		Headaches.		"	—	
	Healthful.			Large; much sweets.	"	"	Regular.	"	Jan., 1914	June, 1914	Polydipsia; loss of weight.	60.5		41.6	+	+		Cervical swelling of unknown nature.	Moderate 1st 3 days.			"	+	
	Ordinary.	Slight.		Excess denied.	Very obese.	"	"	Gradual.	1904	1907	Bitter taste; constipation.	91.3		74.2	—	—		Heavy.	Stopped.	Head, thorax, and abdomen.	Beginning.	"	+	
	"	"	Moderate.	No excess.	Obese.	"	"	Acute.	1911	Immediate.	Weakness; polydipsia.	91		86	Transitory.	Transitory.	Slight.	Lichen planus of arms; ulcers of feet.	Faint	Normal.	Neuritic in back and legs.	Present, not due to diabetes.	Slight.	—

Date.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Physical examination.														Remarks.
				Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.	Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Blood pressure.				
																		Systolic.	Diastolic.			
	Stopped May, 1913.		Marked.	Heavy.	+	+	-	Pale.	Emaciated.	Normal.	Good.	Normal.	Normal.	Normal.	Normal.	Normal.	Normal.	Normal.	103	80	Lower pole of right kidney palpable; incipient coma.	
	Stopped Feb., 1913.	Headaches.		Moderate.	-	-	-	Good.	Medium.	"	"	Slightly hypertrophied.	"	"	"	"	"	"			Strong peasant type.	
	Normal.		Marked.	"	-	-	-	"	Good.	"	"	Normal.	"	"	"	"	"	"	120		Temporary weakness of vision.	
15		Neuritic in legs.	Slight.	Heavy at times.	+	+	Vomiting.	Sallow.	Emaciated.	"	Poorly developed.	Slightly hypertrophied.	"	"	"	"	Slight cervical enlargement.	Diminished.			Chronic nephritis; nearly total blindness from retinitis.	
11	Lessened libido.	Back and legs.	Present, but not connected with diabetes.	Slight.	-	-	-	"	Fair.	"	Poorly developed.	Hypertrophied; no pus foci.	"	"	"	Normal at first; subsequent hypertrophy and atrophy.	Slight general adenopathy.	Normal.	150	115	Cirrhosis of liver.	
15	Climacteric 1913.			"	-	-	-	Cyanotic.	Good.	"	Caries; pyorrhea.	Hypertrophied; congested; no pus foci.	Hypertrophied.	Lobar pneumonia.	Edge felt at costal margin.	Normal.	Sluggish.	115	70	Admitted for pneumonia.		
transi-	Normal.	Severe in legs.	Marked.	"	-	-	-	Fair.	Fair.	"	Fair; considerable tartar.	Normal.	Normal.	Normal.	Normal.	Slight posterior cervical enlargement.	Normal.			Uterus retroflexed and retroverted.		
	Absent.		Slight.	Heavy.	+	+	Nausea.	Pale.	Emaciated.	"	Good.	"	"	"	"	Slight epitrochlear enlargement.					Pulmonary tuberculosis later developed.	
		Headaches.		"	-	-	Colic; nausea; vomiting.	Flushed.	Poor.	"	Caries; pyorrhea.	"	"	Bronchial râles at apices.	"	Normal.	Absent.	80	60	Hemoptysis once; persistent bronchitis, clearing up on treatment; tuberculosis never demonstrated.		
1st 3				"	+	+	Nausea.	Pale.	Emaciated.	"	Caries.	"	"	Normal.	"	"	"	85	75	Dangerous weakness and acidosis at admission.		
	Stopped.	Head, thorax, and abdomen.	Beginning.	"	+	+	" vomiting.	Cyanotic.	Obese.	"	All missing.	"	Mitral regurgitation.	Congested from heart failure.	Edge felt 2 cm. below umbilicus.	"	"				Orthopnea, hemoptysis, and all signs of heart failure.	
	Normal.	Neuritic in back and legs.	Present, not due to diabetes.	Slight.	-	-	-	Good.	"	"	Caries; pyorrhea.	Hypertrophied.	Normal.	Slight emphysema.	Normal.	"	Normal.	150	95	Chronic bronchitis; hemoptysis three times; varicose veins and eczema on legs.		

Diabetic No.	General data.				Family history.				Past history.										
	Sex.	Nationality or race.	Age.	Occupation.	Diabetes.	Obesity.	Tuberculosis.	Other disorders.	Infections and accidents.			Nervous system.	Activity.	Habits.			Figure.	Digestion.	Bowels.
									Childhood.	Adult.	Wassermann test.			Alcohol.	Tobacco.	Appetite and diet.			
13	F.	American.	11 yrs.	Schoolgirl.				Paternal grandfather, cancer.	Whooping-cough; measles; mumps; adenoids removed.		—	Normal.	Quiet life.			Normal.	Rather thin.	Good.	Regular.
14	M.	Jew.	51	Optician.					Scarlet fever.	Occasional sore throats; gonorrhoea twice; dry pleurisy.		"	Ordinary.	Moderate.	Moderate.	Rather small.	Thin.	Slight dyspepsia.	Constipated.
15	"	Scotch.	42	Bookkeeper.	(Nothing hereditary known to wife.)				(Healthy life. History imperfect.)			"	"	Little.	"	Normal.	Normal.	Good.	Regular.
16	F.	Jew.	47	Housewife.	Mother; brother.			Father, cancer.	Measles; mumps.	Syphilis.	++++	"	"	Moderate.		"	Slightly obese.	"	"
17	"	"	69	"	(Negative as far as known.)			Daughter, dementia præcox.	"	Pneumonia with empyema; 3 operations; laparotomy for tumor.		"	"	Little.		"	Slightly obese.	Slight indigestion.	Constipated.
18	M.	American.	16	Errand boy.				Father, cirrhosis of liver.	Chicken-pox; tonsillitis.			"	"		Little.	"	Normal or slightly thin.	Good.	Regular.
19	F.	Jew.	39	Housewife.					Measles; whooping-cough; typhus.	Peritonillar abscess; puerperal sepsis; 1 miscarriage.	—	"	"	Little.		Small.	Slightly obese.	"	"
20	"	American.	38	"			Brother.		Scarlet fever; measles; chicken-pox; whooping-cough; diphtheria. Fall at age of 2.	Recent sore throat.		Nervousness; migraine.	"			No excess.	Normal.	"	"
21	"	Scotch.	46	"					Measles; mumps; whooping-cough.	Scarlet fever; ventral hernia operation; sore throats.		Slightly nervous.	"			" "	Very obese.	"	"
22	M.	Jew.	52	Cigar manufacturer.				Mother, nephritis. Sister, cancer.		Gonorrhoea twice.	—	Very nervous.	Intense business strain.	Considerable.	Excess.	Luxurious living.	Thin.	"	Constipated.
23	"	American.	44	Insurance agent.	Mother.				Measles; chicken-pox; mumps.	Gonorrhoea; "bloody dysentery."	—	Normal.	Some business worry.	Moderate.	Moderate.	Normal.	Slightly obese.	"	Regular.
24	"	"	44	Manufacturer.	Father.			Paternal aunt, cancer.	Measles; mumps; otitis.	Gonorrhoea; acute articular rheumatism; sore throats; acute pancreatitis.	—	"	Ordinary.	Little.	Much.	"	Thin.	Poor.	Constipated.

TABLE I—Continued.

Case history.	Diabetic history.																								
	Habits.			Figure.	Digestion.	Bowels.	Onset.		Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.			
	Alcohol.	Tobacco.	Appetite and diet.				Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.									Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.
			Normal.	Rather thin.	Good.	Regular.	Acute.	Apr., 1914	Apr. 21, 1914.	Slight languor.	kg. 26.8	kg. 26	kg. 21.2	—	—			Moderate 1st 5 days.		Back and bladder.	Marked.	Heavy.	—	+	—
	Moderate.	Moderate.	Rather small.	Thin.	Slight dyspepsia.	Constipated.	Gradual.	1907	Summer, 1907	Backache.	63.6	51	50.8	—	—			—	Lessened libido.	Neuritic in back and legs.	Beginning.	Slight.	—	—	—
	Little.	“	Normal.	Normal.	Good.	Regular.	“	1912	1912	Slight loss of weight and strength.				—	—			—		Present, not known to be due to diabetes.	Heavy.	+	—	—	
	Moderate.	“	“	Slightly obese.	“	“	“	1909	1909	Weakness; loss of weight.	81.7	72.6	65	—	+	Vulvar, moderate.		Moderate to slight.	Regular till climacteric 1914.	Head and legs.	Beginning.	Slight.	—	—	—
	Little.	“	“	Slightly obese.	Slight indigestion.	Constipated.	“	About 1907	Oct., 1914	Gangrene.	82	49.1	53.6	—	++		Incipient gangrene of foot.	Slight.		Foot.	Probably only senile.	Insignificant.	—	—	—
		Little.	“	Normal or slightly thin.	Good.	Regular.	Acute.	Oct., 1914	Nov., 1914	Lassitude; polyphagia; polydipsia.	60.5		50.6	+	+		Slight.	Slight 1st 5 days.					—	—	—
	Little.		Small.	Slightly obese.	“	“	Gradual.	May, 1913	Oct., 1914	Pruritus; polyphagia; polydipsia; loss of weight.	66.3	49.1	47.2	+	+	Vulvar, marked.		Faint 1st 23 days.	Stopped.	Head and back.	Slight.	Insignificant.	—	—	Nausea; colic.
			No excess.	Normal.	“	“	“	Oct., 1913	“ 1913	Hospital routine.	77	72.8	53	—	—			Faint 1st 22 days.	Normal.	Head.		Slight.	—	—	—
			“ “	Very obese.	“	“	Acute.	Summer, 1914	“ 1914	Polyphagia; polydipsia; loss of weight.	121	105	108	+	+			Faint.	“ till menopause.		Slight.		—	—	—
business	Considerable.	Excess.	Luxurious living.	Thin.	“	Constipated.	“	1912	Nov., 1912	Ocular examination.			50	+	+			Moderate to negative.	Impotence for 2-3 yrs.	Cramps in legs.	Present, not due to diabetes.	Moderate.	—	—	—
business	Moderate.	Moderate.	Normal.	Slightly obese.	“	Regular.	Gradual.	1905	1906	Insurance.	88.5	75	70.5	—	—			—				“	—	—	—
	Little.	Much.	“	Thin.	Poor.	Constipated.	Acute.	1907	1907	Ocular examination.	75	63.5	44.2	+	+			—	Stopped.			“	—	—	—

Physical examination.

Date	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Blood pressure.		Remarks.
				Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.											Systolic.	Diastolic.	
1st 5		Back and bladder.	Marked.	Heavy.	-	+	-	Flushed.	Emaciated.	Normal.	Good.	Hypertrophied; no pus foci.	Normal.	Normal.	Normal.	Normal.	Diminished.	105	75	Attacks of urinary calculi.
	Lessened libido.	Neuritic in back and legs.	Beginning.	Slight.	-	-	-	Sallow.	Poor.	"	Many missing; caries; pyorrhea.	Normal.	"	Slight emphysema.	"	Slight general adenopathy.	Normal.	100	70	Slight hemoptysis at time of pleurisy.
			Present, not known to be due to diabetes.	Heavy.	+	-	-	Cyanotic.	Moderately emaciated.	"	Good.	"	"	Normal.	"	Normal.	Absent.			Received in coma.
to	Regular till climacteric 1914.	Head and legs.	Beginning.	Slight.	-	-	-	Pasty.	Good.	"	Several missing.	"	Hypertrophied; mitral regurgitation.	"	Edge felt at costal margin.	"	Normal.	225	110	Latent syphilis; chronic nephritis; mitral insufficiency; arteriosclerosis; cystitis.
		Foot.	Probably only senile.	Insignificant.	-	-	-	Poor.	Emaciated.	"	Many missing; caries; pyorrhea.	"	Hypertrophied.	Slight bronchitis; lower right lobe obliterated.	Normal.	Inguinal enlargement.	"	215	150	Senility; bad hygiene; incipient gangrene of right foot.
days.					-	-	-	Fair.	Rather poor.	"	Good.	Hypertrophied; no pus foci.	Normal.	Normal.	"	Normal.	Exaggerated.	135	60	Transitory dimness of vision.
23	Stopped.	Head and back.	Slight.	Insignificant.	-	-	-	Pale.	Poor.	"	Caries; pyorrhea.	Normal.	"	Emphysema.	"	"	Normal.	90	60	Slight edema and nephritic appearance, but no nephritis.
22	Normal.	Head.		Slight.	-	-	-	Fair.	Fair.	"	Caries; pyorrhea.	"	Mitral regurgitation.	Normal.	"	Axillary enlargement.	"	140	110	Marked xanthoma.
	" till menopause.		Slight.		-	-	-	Good.	Very obese.	Slightly enlarged.	Many missing; caries; pyorrhea.	Hypertrophied; no pus foci.	Slightly hypertrophied.	Emphysema.	"	Normal.	"	175	120	Bilateral arcus senilis; slight albuminuria without casts.
to	Impotence for 2-3 yrs.	Cramps in legs.	Present, not due to diabetes.	Moderate.	-	-	-	Sallow.	Emaciated.	Normal.	Several missing; caries; pyorrhea.	Slightly hypertrophied.	Hypertrophied.	Normal.	Edge felt 2 cm. below costal margin.	General adenopathy.	"	135	110	Chronic nephritis; arteriosclerosis; hysteric attacks.
				"	-	-	-	Good.	Good.	"	Slight caries.	Hypertrophied; no pus foci.	Normal.	"	Edge felt 3 cm. below costal margin.	Slight epitrochlear and inguinal enlargement.	"			
	Stopped.			"	-	-	-	Sallow.	Emaciated.	"	Good.	Normal.	"	"	Edge felt at costal margin.	Normal.	Sluggish.	70	55	Temporarily impaired vision; yellow skin; lipemia; erythrocytes 4,000,000; extreme weakness.

TABLE I—Continued.

Past history.								Diabetic history.																
System.	Activity.	Alcohol.	Habits.		Figure.	Digestion.	Bowels.	Onset.		Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Degree.	Drowsiness.
			Tobacco.	Appetite and diet.				Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.										
Nervous.	Ordinary.			Normal.	Obese.	Good.	Constipated.	Gradual.	1911	1911	Routine.	96	84.5	76	—	—		Slight.	Normal till climacteric.	Entire body.		Heavy.	+	
Slight	"			Much candy.	Thin.	"	"	Acute.	Feb., 1913	Mar., 1913	Polyphagia; polydipsia; loss of weight and strength.			31.2	+	+		Moderate 1st admission; negative subsequently.	Stopped Feb., 1913.		Moderate.	Moderate.	-	
	"	Little.	Moderate.	No excess.	Normal.	"	Regular.	Gradual.	1907	1907	Dental caries; infection of mandible.			59.6	—	—	Carbuncle.	—	Retained.		Slight.	"	-	
and a move-	Studious.			" "	"	"	"	Acute.	Jan., 1915	Jan., 1915	Polyuria.			29	+	+		—					-	
	Ordinary.			Starch, not sugar.	"	"	Constipated.	"	" 1915	" 1915	Weakness; polyphagia; polydipsia.	52.5		45.6	+	+		—	Normal.			Slight.	-	
	"	Moderate.	Moderate.	Simple.	Slightly obese.	Poor.	Regular.	"	June, 1914	Oct., 1914	Pruritus; polyphagia; polydipsia.	73	57	56.8	+	+	Vulvar, marked.	Faint.	"		Marked.	Heavy.	-	
	"	Little.	"	Normal.	Normal.	Good.	Constipated.	Gradual.	1912	1912	Debility.		68.4	53.4	—	—		Incipient gangrene of toe.	—	Great toe.	Slight.	"	-	
	"	"		Starch, not sugar.	"	"	"	Acute.	June, 1914	Oct., 1914	Amenorrhea.			53.2	+	+	Vulvar, marked.	Faint 1st 15 days.	Stopped Oct., 1914.			"	+	
	"			Much starch and sweets.	Obese.	Occasional indigestion.	"	Gradual.	1912	1912	Nervousness; lassitude; pains.	96		83	—	—		Faint 1st 15 days.	Normal till climacteric at 50.	Head; limbs.	Moderate.	Insignificant.	-	
	"	Little.	Moderate.	No excess.	Normal.	Good.	"	"	Nov., 1911	Oct., 1912	Pain in arms.			51.6	+	+		Slight.	Moderate 1st 3 days.	Libido lessened.	Arms.	Slight.	Heavy.	-
	Healthful.		"	Normal.	"	"	Regular.	"	1904	1905	Backache; polyuria.			66.4	—	—		—				"	-	
	Ordinary.	Little.	"	"	"	"	"	Acute.	Dec., 1913	Jan., 1914	Polydipsia; polyuria; loss of weight.	64		50.2	—	+		Colon bacillus wound infection; abscesses on neck.	Heavy at 3rd admission.	Absent.		Moderate.	"	-

Urinary.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Physical examination.												Remarks.
				Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.	Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Blood pressure.		
																		Systolic.	Diastolic.	
	Normal till climacteric.	Entire body.		Heavy.	+	Atypical.	Vomiting.	Cyanotic.	Obese.	Normal.	Marked caries and pyorrhea.	Hypertrophied; no pus foci.	Hypertrophied.	Emphysema; bronchitis.	Edge felt at costal margin.	Normal.	Absent.	250	110	Left hemiplegia; beginning atypical coma; fecal retention.
1st admission; severe subsequently.	Stopped Feb., 1913.		Moderate.	Moderate.	-	-	-	Sallow.	Emaciated.	"	Good.	Normal.	Normal.	Normal.	Normal.	"	Normal.	105	70	
	Retained.		Slight.	"	-	-	-	"	Fair.	"	Many missing; caries; pyorrhea.	"	"	"	Edge felt at costal margin.	"	"			Large carbuncle on neck, with fever.
					-	-	-	Good.	Good.	"	Good.	Hypertrophied; no pus foci.	"	"	Normal.	Slight epitrochlear enlargement.	Exaggerated.			
	Normal.			Slight.	-	-	-	Poor.	Fair.	"	"	Normal.	"	"	"	Slight axillary enlargement.	Active.	110	90	Tuberculosis not demonstrated.
	"		Marked.	Heavy.	-	-	-	Fair.	Slightly emaciated.	"	"	"	"	"	Edge felt at costal margin.	Slight axillary and epitrochlear enlargement.	Sluggish.	110	85	Fasting acidosis.
		Great toe.	Slight.	"	-	-	-	Sallow.	Emaciated.	"	"	"	"	"	Normal.	Axillary palpable.	"	90	75	Arteries palpably sclerotic.
1st 15	Stopped Oct., 1914.			"	+	+	-	Good.	Good.	"	Slight caries; pyorrhea.	Hypertrophied; pus exudation.	"	"	"	Axillary and epitrochlear enlargement.	Absent.	100	65	Tonsillectomy performed later.
1st 15	Normal till climacteric at 50.	Head; limbs.	Moderate.	Insignificant.	-	-	-	"	Obese.	"	All missing.	Normal.	Slight murmur.	Emphysema.	"	Normal.	Exaggerated.	190	100	Trace of albuminuria.
late 1st 3	Libido lessened.	Arms.	Slight.	Heavy.	-	-	-	High.	Thin.	"	Good.	"	Normal.	Normal.	"	"	Normal.	110	90	
				"	-	-	-	Ruddy.	Fair.	"	"	"	"	"	Edge felt 4 cm. below costal margin.	Slight axillary and epitrochlear enlargement.	Sluggish.	120	80	
at 3rd admission.	Absent.		Moderate.	"	-	-	-	Sallow.	Thin.	"	Impacted wisdom root.	"	"	"	Normal.	Normal.	Normal.	100	60	Diabetes dating from sepsis.

Diabetic No.	General data.				Family history.				Past history.										
	Sex.	Nationality or race.	Age.	Occupation.	Diabetes.	Obesity.	Tuberculosis.	Other disorders.	Infections and accidents.			Nervous system.	Activity.	Habits.			Figure.	Digestion.	Bowels.
									Childhood.	Adult.	Wassermann test.			Alcohol.	Tobacco.	Appetite and diet.			
37	M.	American.	16 yrs.	Schoolboy.					Measles; chicken-pox.	Alveolar abscess; severe cold.	—	Normal.	Healthful.			Normal.	Normal.	Good.	Regular.
38	F.	Jew.	39	Housewife.			Brother.			Visceroptosis.	—	“	Ordinary.	Little.		“	“	“	“
39	“	American.	27	Teacher.	Mother.			Father and brother nervous. Maternal grandfather, cancer. Paternal aunt, insanity.	Scarlet fever and others.		—	Neurotic.	Hard mental work.			“	Slightly obese.	“	“
40	M.	“	29	Doorman.	(Little known.)				Measles; whooping-cough; scarlatina.	Gonorrhea; chancre; colds.		Normal.	Ordinary.	Excess.	Moderate.	Small.	Normal.	Fair.	“
41	“	Irish.	52	Politician.			Sister.	Insanity on mother's side.	Measles; mumps; scarlet fever; chicken-pox; diphtheria.	Gonorrhea; syphilis; tuberculosis; grippe.	++++	“	Checkered life.	Moderate.	“	Normal.	Slightly obese.	Good.	“
42	F.	American.	11	Schoolgirl.					Measles; whooping-cough; scarlet fever.		—	Nervous.	Strain in school work.			Small.	Normal.	“	“
43	“	“	27	Nurse.	Maternal aunt.		Maternal grandmother.		Measles; mumps; whooping-cough; chicken-pox; diphtheria; pneumonia.	Malaria; septicemia with nephritis.	—	“	Ordinary.			Normal.	“	“	“
44	M.	“	53	Electrician.				Aunt, cancer.	Diphtheria.	Gonorrhea; colds; pleurisy with hemoptysis.	—	Moderately nervous.	“	Little.	Moderate.	Some excess in sweets.	“	“	“
45	“	Jew.	6	(Child.)	Paternal great grandmother; grandfather; uncle.	Family slightly obese.		Maternal grandmother, cancer.	None before diabetes; grippe and otitis media after.			Normal.	Healthful.			Much sweets.	“	“	Constipated.
46	“	“	48	Storekeeper.	Daughter.				Pneumonia.	Double inguinal hernia.	—	“	Sedentary.	Moderate.	Moderate.	No excess.	“	“	“

TABLE—1 *Continued.*

Past history.								Diabetic history.															
Nervous system.	Activity.	H abits.			Figure.	Digestion.	Bowels.	Onset.		Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Degree.
		Alcohol.	Tobacco.	Appetite and diet.				Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.									
Normal.	Healthful.			Normal.	Normal.	Good.	Regular.	Acute.	Mar., 1915	Mar., 1915	Polydipsia; polyuria; weakness; drowsiness.	55		47.4	—	+		—				Heavy.	
"	Ordinary.	Little.		"	"	"	"	Unknown.		Mar. 20, 1915	Hospital routine.				—	—		Slight.	Pregnant.		"		
Neurotic.	Hard mental work.			"	Slightly obese.	"	"	Gradual.	1910	1910	Headache; polydipsia; polyuria.	85		59.2	—	+	Vulvar, slight.	" with coma.	Stopped Mar., 1915.	Intense facial neuralgia.	Moderate.	Moderate.	
Normal.	Ordinary.	Excess.	Moderate.	Small.	Normal.	Fair.	"	Acute.	Apr., 1915	Apr. 12, 1915	Hospital routine.			45.4	—	—		Heavy 1st 10 days.			Heavy.		
"	Checkered life.	Moderate.	"	Normal.	Slightly obese.	Good.	"	Gradual.	1911	1911	Routine.	86.5		83	+	+		Ulcers on shins.	Slight.	Normal.	Present, not due to diabetes.	Slight.	
Nervous.	Strain in school work.			Small.	Normal.	"	"	Acute.	Feb., 1915	Feb., 1915	Polyphagia; polydipsia; polyuria.			26.8	+	+		Terminal with coma.			Beginning.	Moderate.	
"	Ordinary.			Normal.	"	"	"	"	Jan., 1915	Mar., 1915	Polyphagia; polydipsia; polyuria; loss of weight.	54	44	44	+	+	Vulvar, marked.	Trace for 1st few weeks.	Stopped.		Marked.	"	
Moderately nervous.	"	Little.	Moderate.	Some excess in sweets.	"	"	"	Gradual.	July, 1914	Apr., 1915	Pleurisy; polydipsia; polyuria.	77	73	62	—	+				Cramps in legs.	Slight.	Heavy.	
Normal.	Healthful.			Much sweets.	"	"	Constipated.	Acute.	Nov., 1914	Nov., 1914	Polyuria; loss of weight.	21.6	16.4	19.4	—	+		Incipient gangrene over sacrum.	Marked.			"	
"	Sedentary.	Moderate.	Moderate.	No excess.	"	"	"	"	Oct., 1914	Oct., 1914	Acute thirst.		68	51.2	—	+				Back and legs.	Present, not due to diabetes.	"	

Inuria.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Physical examination.														Remarks.
				Degree.	Drowsiness.	Hypernea.	Digestive symptoms.	Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Blood pressure.				
																		Systolic.	Diastolic.			
				Heavy.	+	+	-	High.	Fair.	Normal.	Caries; pyorrhea; alveolar abscess.	Hypertrophied; pus foci present.	Normal.	Normal.	Normal.	Slight general adenopathy.	Active.	120	90	Received with impending coma.		
	Pregnant.			"	+	+	-	Flushed.	Good.	"	Missing.	Normal.	"	Lobar pneumonia.	Edge felt 3 cm. below costal margin.	Normal.	Absent.	150	90	Admitted on pneumonia service. Otitis media; pericarditis; pregnancy; artificial delivery; diabetic coma.		
	Stopped Mar., 1915.	Intense facial neuralgia.	Moderate.	Moderate.	-	-	-	Good.	Fair.	Possible slight enlargement.	Slight caries; pyorrhea.	"	"	Normal.	Normal.	"	Normal.			Mentally irresponsible at times.		
1st 10				Heavy.	+	-	-	Cyanotic.	"	Normal.	Many missing; caries; pyorrhea.	"	"	Lobar pneumonia.	"	Slight epitrochlear enlargement.	Active.	125	70	Admitted on pneumonia service. Hematuria; diabetes transitory.		
	Normal.		Present, not due to diabetes.	Slight.	-	-	-	Good.	Slightly obese.	"	All missing.	Slightly hypertrophied; no pus foci.	"	Bronchitis; emphysema.	"	Slight adenopathy.	Normal.	125	70	Luetic.		
1 with			Beginning.	Moderate.	-	-	Vomiting.	"	Good.	"	Good.	Hypertrophied, with pus foci.	"	Normal.	"	A few palpable.	"			Tuberculosis later developed.		
or 1st weeks.	Stopped.		Marked.	"	-	-	-	Pale.	Poor.	"	"	Normal.	"	"	"	" " "	"			Tendency to edema.		
		Cramps in legs.	Slight.	Heavy.	-	-	-	Fair.	"	"	Many missing; moderate caries; pyorrhea.	"	"	"	"	Slight adenopathy.	"	90	62	Cough and night sweats preceding admission; tuberculosis not demonstrated.		
				"	+	-	-	Pasty.	Emaciated.	"	Spongy, bleeding gums.	"	"	Hydrothorax.	"	Normal.	Absent (?).	62		Extreme bicarbonate edema; alkalosis; nephritis; diabetic coma.		
		Back and legs.	Present, not due to diabetes.	"	-	-	-	Pale.	"	"	Many missing; caries; pyorrhea.	"	Hypertrophied.	Normal.	"	Slight general adenopathy.	"			Very feeble appearance; slight arteriosclerosis.		

Diabetic No.	General data.				Family history.				Past history.											
	Sex.	Nationality or race.	Age.	Occupation.	Diabetes.	Obesity.	Tuberculosis.	Other disorders.	Infections and accidents.			Nervous system.	Activity.	Habits.			Figure.	Digestion.	Bowels.	Acute gradu
									Childhood.	Adult.	Wassermann test.			Alcohol.	Tobacco.	Appetite and diet.				
47	F.	American.	31 yrs.	Saleswoman.			Maternal grand-mother.		Usual.		—	Normal.	Ordinary.			No excess.	Normal.	Good.	Regular.	Gradu
48	M.	"	20	Clerk.			Two uncles.		None remembered.	Sore throats; dental caries.		Degenerate.	"	Moderate.	Excessive.	" "	Thin.	"	"	Acute.
49	F.	"	30	Seamstress.					Measles; mumps; chicken-pox; scarlet fever; diphtheria.	Tonsillitis; two high forceps deliveries.		Nervous.	"			" "	Normal.	"	"	"
50	"	"	54	Teacher.					Usual.		±	"	"			" "	"	"	"	Gradual
51	M.	"	7	Schoolboy.					Whooping-cough.		—	Normal.	"			" "	"	"	"	Acute
52	F.	"	27	None.					Measles; chicken-pox.		—	"	"			" "	"	"	"	Gradual
53	"	"	9	Schoolgirl.					Measles; mumps; chicken-pox; tonsillitis; slight rheumatism.		—	Nervous.	"			" "	"	"	"	Acute.
54	"	"	29	Telephone operator.					Measles; whooping-cough.	1 miscarriage.	—	Normal.	"			Normal.	"	"	Constipated.	"
55	M.	"	26 mos.	(Infant.)	Paternal great grand-mother.						—	"	"			"	"	Regular.	"	
56	"	"	30	Clerk.			Maternal aunt, insanity. Two sisters, rheumatoid arthritis.		Whooping-cough; gastrointestinal attacks; swollen cervical glands; enuresis.	Grippe preceding diabetes.	—	"	"		Moderate.	Some excess in sweets.	Thin.	"	Constipated.	"
57	"	Jew.	37	Physician.	Mother; maternal uncle; maternal aunt; sister.	Family obese.		Paternal aunt, cancer. Father and mother, first cousins.	Measles.	Jaundice; tonsillitis.	—	Somewhat nervous.	"	Moderate.		Excess in food, sweets, and coffee.	Obese.	"	Regular.	"

TABLE—I Continued.

history.			Diabetic history.																					
Habits.			Figure.	Digestion.	Bowels.	Onset.		Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.			
Alcohol.	Tobacco.	Appetite and diet.				Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.									Degree.	Draw-siness.	Hyper-pnea.	Digestive symptoms.
								kg.	kg.	kg.														
		No excess.	Normal.	Good.	Regular.	Gradual.	1911	1911	Pruritus vulvæ; polyphagia; polydipsia; polyuria; loss of weight	84	66	67.3	+	+	Vulvar, marked.	Superficial, vulvar.	—	Normal.			Heavy.	—	—	—
Moderate.	Excessive.	“ “	Thin.	“	“	Acute.	1914	1914	Polyphagia; polydipsia; polyuria.			45	+	+		—					“	—	—	—
		“ “	Normal.	“	“	“	June, 1914	Dec., 1914	Polyphagia; polydipsia; polyuria; loss of weight.	68		52.4	+	+		Trace at first.	Normal.		Slight.		“	+	—	—
		“ “	“	“	“	Gradual.	1912	1912	Polyphagia; polydipsia; polyuria.			49.6	+	+		—	Stopped at onset of present illness.	Universal.	Moderate.	Moderate.	+	—	Vomiting.	
		“ “	“	“	“	Acute.	Oct., 1914	Oct., 1914	Coma.			18.3	+	+		Trace at admission.					“	—	—	—
		“ “	“	“	“	Gradual.	1911	“ 1911	Lassitude.	58		48.4	—	—		Slight.	—	Stopped June, 1915.		Slight.	Heavy.	—	—	—
		“ “	“	“	“	Acute.	1913	1913	Polyphagia; polydipsia; polyuria.			20	+	+	Vulvar.	—					“	—	—	—
		Normal.	“	“	Constipated.	“	June, 1915	July, 1915	Polydipsia; polyuria; loss of weight and strength.		65	49	+	+		—	Normal.				“	—	+	—
		“	“	“	Regular.	“	Oct., 1915	Oct., 1915	Polyphagia; polydipsia; polyuria.			11.8	+	+		—					“	+	—	—
	Moderate.	Some excess in sweets.	Thin.	“	Constipated.	“	1912	Jan., 1913	Weakness and depression.			51	+	+		—	Stopped.		Slight.		“	—	—	—
Moderate.		Excess in food, sweets, and coffee.	Obese.	“	Regular.	“	1899 1907	1899 1907	1899, accidental. 1907, furunculosis.	113.5	88	86.2	+	+	Slight.	Numerous boils and ulcers.	—	Lessened.		Moderate, not evidently due to diabetes.	Slight.	—	—	—

uria.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Physical examination.												Blood pressure.		Remarks.
				Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.	Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Systolic.	Diastolic.			
	Normal.			Heavy.	-	-	-	High.	Good.	Normal.	Slight pyorrhea.	Enlarged; no pus foci.	Normal.	Normal.	Normal.	Slight axillary enlargement.	Normal.	90	60			
				"	-	-	-	Pale.	Emaciated.	"	Fair.	Normal.	"	"	"	Normal.	"			Very inferior type.		
first.	Normal.		Slight.	"	+	-	-	"	Poor.	"	"	"	"	"	"	"	"			Transitory dimness of vision; cold and fever at admission.		
	Stopped at onset of present illness.	Universal.	Moderate.	Moderate.	+	-	Vomiting.	"	sallow.	Fair.	"	Many missing; caries; pyorrhea.	"	"	"	Edge felt 1½ cm. below costal margin.	"	90	75	Myxedema, treated with thyroid feeding.		
admis-				"	-	-	-	Very pale.	"	"	Good.	"	"	"	Normal.	"	"			Apparently very acute onset.		
	Stopped June, 1915.		Slight.	Heavy.	-	-	-	Pale.	"	Slight enlargement.	"	Slight hypertrophy; no pus foci.	"	"	"	Slight axillary and epitrochlear enlargement.	"					
				"	-	-	-	"	Emaciated.	Normal.	"	Normal.	"	"	"	Normal.	"			Appears constitutionally feeble.		
	Normal.			"	-	+	-	"	Fair.	"	"	"	"	"	"	"	Sluggish.	110	80	Progressive downward progress.		
				"	+	-	-	Flushed.	"	"	"	Hypertrophied; slight exudation of pus.	"	"	"	Slight epitrochlear enlargement.	Normal.					
	Stopped.		Slight.	"	-	-	-	Pale.	Emaciated.	"	Some caries.	Normal.	"	"	"	Slight adenopathy.	Diminished.	100	80			
	Lessened.		Moderate, not evidently due to diabetes.	Slight.	-	-	-	Florid.	Obese.	"	Marked caries and pyorrhea.	Greatly hypertrophied.	"	"	Edge felt at costal margin.	Moderate anterior cervical enlargement.	Sluggish.	120	85	Hyperidrosis with diabetes.		

Diabetic No.	General data.				Family history.				Past history.										Onset.		
	Sex.	Nationality or race.	Age.	Occupation.	Diabetes.	Obesity.	Tuberculosis.	Other disorders.	Infections and accidents.			Nervous system.	Activity.	Habits.			Figure.	Digestion.	Bowels.	Acute or gradual.	Date of onset.
									Childhood.	Adult.	Wassermann test.			Alcohol.	Tobacco.	Appetite and diet.					
58	F.	American.	72 yrs.	Housewife.					Whooping-cough.		--	Normal.	Ordinary.	Little.		Normal.	Slightly obese.	Good.	Regular.	Gradual.	June
59	M.	"	46	Physician.	Maternal aunt.		Father, cancer. Mother, gout and rheumatism. Sister, "acidosis."	Measles; whooping-cough; scarlet fever; gastrointestinal attacks; sunstroke.	Albuminuria; sciatica; gout; axillary abscess; boils and carbuncles.	--	Nervous.	Intellectual overwork.	Moderate.	Excess.	No excess.	Thin.	Rather poor.	"	"	"	Perh. 18
60	F.	"	43	Housewife.				Whooping-cough; measles; chicken-pox.	"Gastric fever;" tonsillitis.	--	Normal.	Ordinary.			Normal.	Normal.	Good.	"	"	Acute.	Apr.
61	M.	"	30	Papermaker.			Father, rheumatism. Mother paralysis.	Diarrhea; scarlet fever; rheumatism.	Measles; mumps (orchitis); rheumatism; trauma of elbow.		"	Heavy lifting.		Excess.	"	"	"	"	"	Gradual.	June
62	F.	"	19	None.		Maternal grandmother.		Whooping-cough; measles; chicken-pox; diabetes (?).		--	"	Easy life.			No excess.	Thin.	"	"	"	Acute.	"
63	M.	Polish.	13	Schoolboy.				Measles; chicken-pox; scarlet fever.		--	"	Ordinary.			" "	Normal.	"	"	"	"	Feb.
64	"	Jew.	12	"				Measles; mumps; fall on head.		--	"	Healthful.			Normal.	"	"	"	"	"	"
65	"	American.	53	Business.	Father.		Brother, Hodgkins' disease.	Measles; diphtheria; "gravel."			"	Ordinary.	Little.	Excess.	"	Slightly obese.	"	"	"	Gradual.	Oct.
66	"	"	15	Schoolgirl.	Paternal grandfather.			Tonsillectomy; measles; urticaria.		--	"	Healthful.			"	Normal.	"	"	"	Acute.	"
67	M.	Spanish.	46	Merchant.	Maternal aunt; paternal cousin.			Usual; mild.	Syphilis.	++	Nervous.	Business strain.	Considerable.	Considerable.	Large.	"	"	"	"	Gradual.	Dec.
68	"	Jew.	23 mos.	(Infant.)	Maternal great grandmother and grandmother.			Slight colds; vaccination.		--	Normal.	Normal.			Normal.	"	"	"	"	Acute.	May

TABLE I—Continued.

Habits.			Figure.	Digestion.	Bowels.	Diabetic history.																		Complexion	
Alcohol.	Tobacco.	Appetite and diet.				Onset.	Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.					
			Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.	Degree.	Drowsiness.									Hyperperna.	Digestive symptoms.				
							kg.	kg.	kg.																
		Normal.	Slightly obese.	Good.	Regular.	Gradual.	June, 1911	June, 1911	Failing vision.			68	—	+		Ulcers of foot.	Very faint.	Normal till climacteric.			Insignificant.	—	—	—	Pale.
rate.	Excess.	No excess.	Thin.	Rather poor.	"	"	Perhaps 1889	1910	Polyuria.			52.6	—	—		Boils and carbuncles.	—	Diminished.	Sciatica; gout.	Present, not evidently due to diabetes.	Moderate.	—	—	—	"
		Normal.	Normal.	Good.	"	Acute.	Apr., 1915	June, 1915	Loss of weight; polydipsia; pruritus vulvæ.	78		36.6	+	+	Vulvar, marked.		—	Stopped 1915.		Moderate.	Heavy.	+	+	—	"
	Excess.	"	"	"	"	Gradual.	June, 1915	" 1915	Polydipsia; polyuria; weakness.			74.0	—	+			Slight.	"				—	—	—	Slightly cyanotic.
		No excess.	Thin.	"	"	Acute.	" 1911	" 1911	Polydipsia; polyuria.		52.2	39.4	+	+			—	" 1912.			Heavy.	—	—	—	Flushed.
		" "	Normal.	"	"	"	Feb., 1915	Feb., 1915	Polydipsia; polyuria; loss of weight and strength.			27.8	+	+			Faint 1st 10 days.				"	+	+	—	Very pale.
		Normal.	"	"	"	"	" 1916	" 1916	Polydipsia; polyuria.			25.2	—	+			Faint at admission.				"	+	+	—	Flushed.
	Excess.	"	Slightly obese.	"	"	Gradual.	Oct., 1915	" 1916	Loss of weight.			61.1	—	—			—		Cramps in legs; headaches.	Not due to diabetes.		—	—	—	Good.
		"	Normal.	"	"	Acute.	" 1915	" 1916	Polydipsia.			50	—	+			—	Stopped Dec., 1916.			Trace.	—	—	—	Healthy.
derable.	Considerable.	Large.	"	"	"	Gradual.	Dec., 1913	Dec., 1913	Feverish sensation.	90	85	54.2	—	—			—	Diminished.	Headaches.	Not due to diabetes.	Slight.	—	—	—	"
		Normal.	"	"	"	Acute.	May, 1916	June, 1916	Polyphagia; polydipsia; polyuria; incipient coma.	11.3	9.1	8.5	+	+			Slight at first.				Heavy.	+	+	—	Flushed.

a.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Physical examination.														Remarks.
				Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.	Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Blood pressure.				
																		Systolic.	Diastolic.			
	Normal till climacteric.			Insignificant.	-	-	-	Pale.	Good.	Normal.	All missing.	Normal.	Normal.	Emphysema.	Edge felt 4 cm. below costal margin.	Normal.	Normal.	185	120	Double cataract and diabetic retinitis.		
	Diminished.	Sciatica; gout.	Present, not evidently due to diabetes.	Moderate.	-	-	-	"	Emaciated.	"	Slight pyorrhea.	"	"	Normal.	Normal.	Slight general adenopathy.	"	118	88	Insurance refused for albuminuria in 1899.		
	Stopped 1915.		Moderate.	Heavy.	+	+	-	"	"	"	Good.	Hypertrophied; no pus foci.	"	"	"	Normal.	Absent.					
	"				-	-	-	Slightly cyanotic.	Good.	"	Several missing.	Normal.	Arrhythmia; hypertrophy; mitral regurgitation and stenosis.	"	"	"	Active.	160	120	Admitted on cardiorenal service. Valvular disease; chronic interstitial nephritis.		
	" 1912.			Heavy.	-	-	-	Flushed.	Emaciated.	"	Caries.	Slightly enlarged; pus on pressure.	Normal.	"	Edge felt at costal margin.	"	Normal.			Pneumonia subsequently under treatment.		
10				"	+	+	-	Very pale.	Moderately emaciated.	"	Good.	Normal.	"	"	Normal.	"	Sluggish.			Received in coma.		
11				"	+	+	-	Flushed.	Moderately emaciated.	"	Poor; moderate pyorrhea.	Moderate in size; pus on pressure.	"	"	"	Slight general enlargement.	"			Received in incipient coma.		
		Cramps in legs; headaches.	Not due to diabetes.		-	-	-	Good.	Good.	"	Good.	Normal.	"	"	Edge felt at costal margin.	Normal.	Normal.	160	80			
	Stopped Dec., 1916.			Trace.	-	-	-	Healthy.	"	"	"	Missing.	"	"	Normal.	"	"	90	60			
	Diminished.	Headaches.	Not due to diabetes.	Slight.	-	-	-	"	Poor.	"	Much caries; marked pyorrhea.	Normal.	"	"	"	Slight inguinal enlargement.	Absent.			Troublesome insomnia; lues.		
b.				Heavy.	+	+	-	Flushed.	Fair.	"	Good.	Hypertrophied; no pus foci.	"	"	"	Slight cervical and axillary enlargement.	Normal.			Received in incipient coma.		

Diabetic No.	General data.				Family history.				Past history.											
	Sex.	Nationality or race.	Age.	Occupation.	Diabetes.	Obesity.	Tuberculosis.	Other disorders.	Infections and accidents.			Nervous system.	Activity.	Habits.			Figure.	Digestion.	Bowels.	Acute or gradual.
									Childhood.	Adult.	Wassermann test.			Alcohol.	Tobacco.	Appetite and diet.				
69	F.	Jew.	39 yrs.	Housewife.				Father, Bright's disease. Mother, cancer. 2 brothers, paralysis.	Usual.	"Vaginal cellulitis" twice; 5 abortions.	—	Very neurotic.	Worried, hectic life.	Moderate.		Restrained.	Tendency to obesity.	Good.	Regular.	Acute.
70	M.	American.	34	Physician.				Mother, tumor and Bright's disease.	Measles.		—	Normal.	Easy, quiet life.	Little.	Little.	Normal.	Normal.	"	"	"
71	"	"	9	(Child.)							—	"	Normal.			"	"	"	"	"
72	F.	"	12	Schoolgirl.					Measles mumps; chicken-pox.		—	"	"			"	"	"	Constipated.	"
73	"	"	3	(Child.)	Paternal grandfather.						—	"	"			"	"	"	Regular.	"
74	M.	"	23	Plumber.							—	"	"		Moderate.	"	"	"	"	"
75	"	Canadian (Irish).	33	Teamster.					Measles; numps.		—	"	"	Some excess.	Considerable.	"	"	"	"	"
76	"	American.	4	(Child.)	Maternal grandaunt; cousin.				Whooping-cough; otitis media.		—	"	"			"	"	"	"	"

TABLE I—Concluded.

Past history.							Diabetic history.																	
Activity.	Habits.			Figure.	Digestion.	Bowels.	Onset.		Glycosuria discovered.		Weight.			Polyphagia.	Polydipsia and polyuria.	Pruritus.	Skin infections.	Albuminuria.	Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.		
	Alcohol.	Tobacco.	Appetite and diet.				Acute or gradual.	Date of first symptoms.	Time.	Cause of examination.	Highest.	At onset.	At admission.									Degree.	Drowsiness.	Hypernea.
Worried, hectic life.	Moderate.		Restrained.	Tendency to obesity.	Good.	Regular.	Acute.	Dec., 1915	Jan., 1916	Polyphagia; polydipsia; polyuria; loss of weight and strength.	62.8	58.6	37.0	+	+	Extreme.	—	Stopped.	Head and limbs.	Marked.	Heavy.	—	—	
Easy, quiet life.	Little.	Little.	Normal.	Normal.	"	"	"	Sept., 1914	Sept., 1914	Polydipsia; polyuria.	60.0	59.0	42.2	—	+		—	"		Progressing.	"	—	—	
Normal.			"	"	"	"	"	Oct., 1914	Oct., 1914	Polyphagia; polyuria.			14.8	+	+		Trace.				"	+	+	
"			"	"	"	Constipated.	"	Nov., 1915	Nov., 1915	Lassitude.			31.6	—	—		" at 2nd admission.				"	—	+	
"			"	"	"	Regular.	"	Dec., 1915	Dec., 1915	Polydipsia; loss of weight.			9.8	—	—		—				Insignificant.	—	—	
"		Moderate.	"	"	"	"	"	Jan., 1916	Feb., 1916	Polydipsia; weakness.	63.8		43.6	—	+		—				Heavy.	+	—	
"	Some excess.	Considerable.	"	"	"	"	"	June, 1914	1914	Polydipsia; polyuria; loss of teeth.	59.2		37.6	—	+		—	Stopped.		Moderate.	Slight.	—	—	
"			"	"	"	"	"	Feb., 1917	Mar., 1917	Polyuria.			15	—	+		—				"	—	—	

Menstruation or sexual function.	Pains.	Alopecia.	Acidosis.				Physical examination.													Remarks.
			Degree.	Drowsiness.	Hyperpnea.	Digestive symptoms.	Complexion.	Nutrition.	Thyroid.	Teeth.	Tonsils.	Heart.	Lungs.	Liver.	Lymph glands.	Knee jerks.	Blood pressure.			
																	Systolic.	Diastolic.		
Stopped.	Head and limbs.	Marked.	Heavy.	-	-	-	Sallow.	Very emaciated.	Normal.	Normal.	Normal.	Normal.	Normal.	Normal.	Edge felt 2 cm. below costal margin.	Slight general enlargement.	Normal.	70	50	Highly hysterical
"		Progressing.	"	-	-	-	Pale.	Very emaciated.	"	Gums receding.	"	" action weak.	"	Normal.	Normal.	Normal.	Absent.	85	65	
			"	+	+	-	"	Moderately emaciated.	"	Gums receding.	"	Normal.	"	"	"	"	"			Received in coma.
nd			"	-	+	-	High.	Fair.	"	Poor; pyorrhea.	"	"	"	"	"	"	Feeble.			" with impending coma.
			Insignificant.	-	-	-	Pale.	Emaciated.	"	Good.	"	"	"	"	"	"	Absent.			Very feeble; chronic pot-belly.
			Heavy.	+	-	-	"	"	"	Fair.	"	"	"	"	"	"	"			Tuberculosis subsequently.
Stopped.		Moderate.	Slight.	-	-	-	Weather-beaten, yellowish.	"	"	All missing.	"	"	"	"	"	"	"	110	80	
			"	-	-	-	Pale.	Good.	"	Good.	"	"	"	"	"	Axillary and epitrochlear palpable on both sides.	Active.	90	70	

CASE NO. 2,204
1914

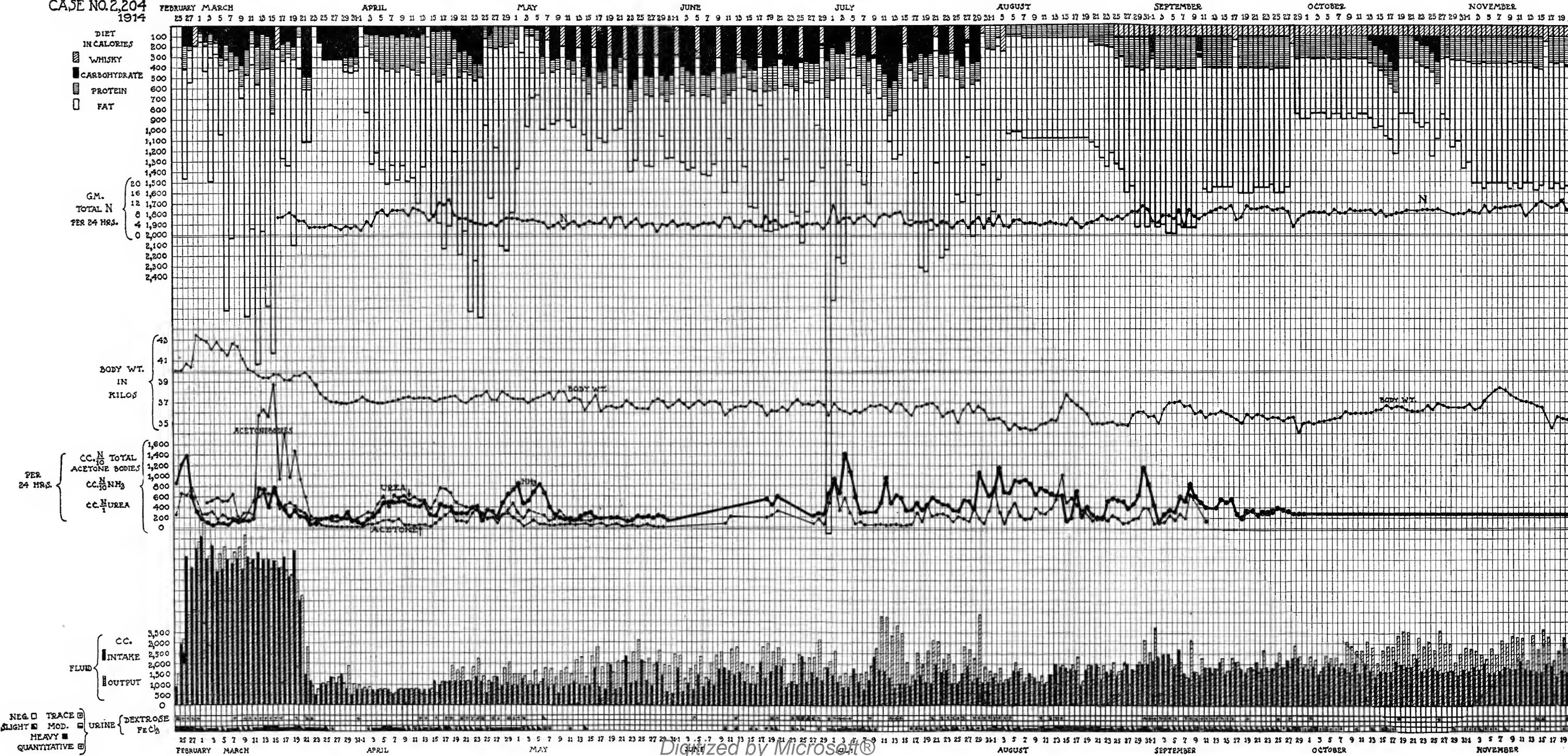
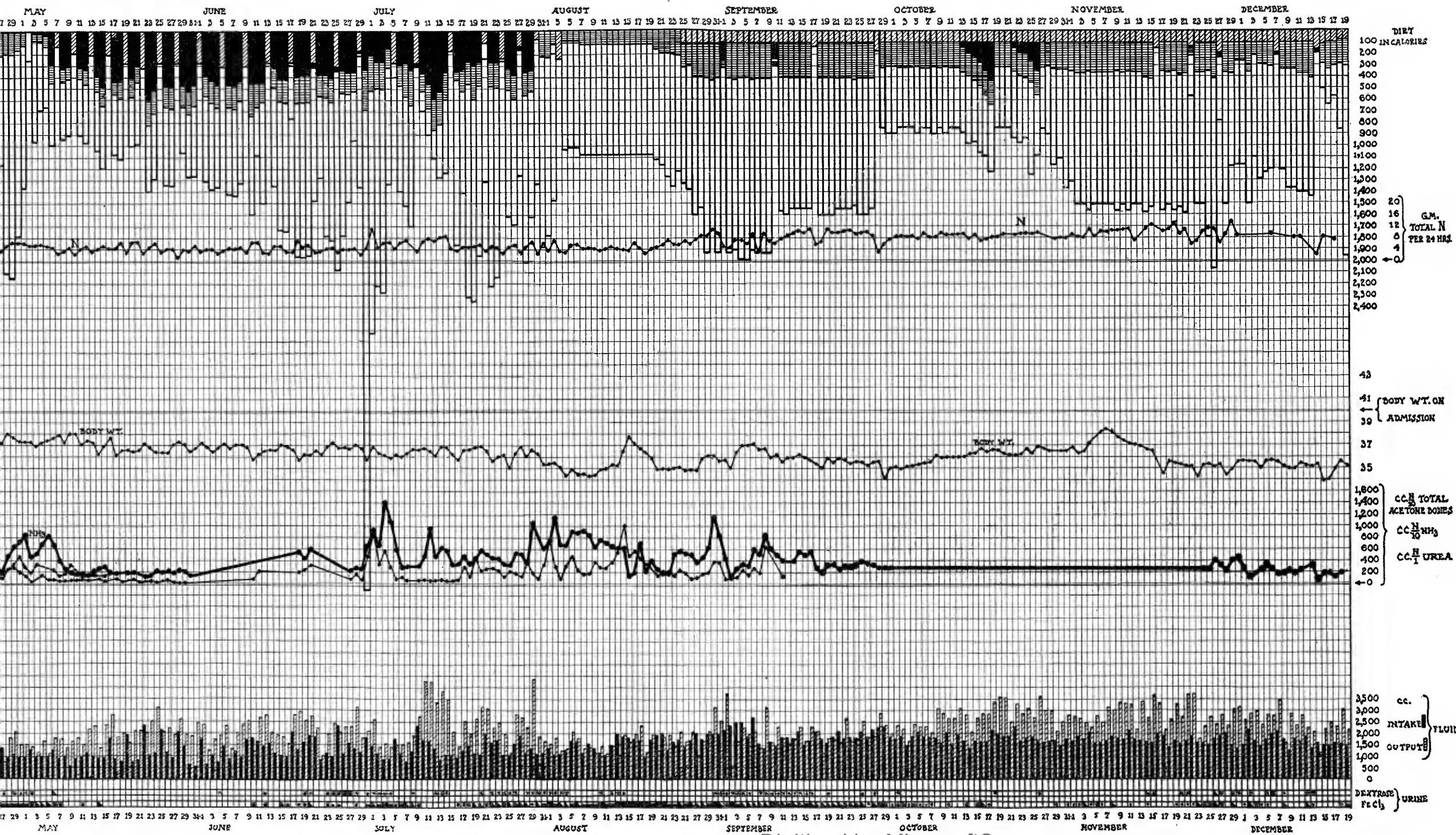


CHART 2. Case No. 1.



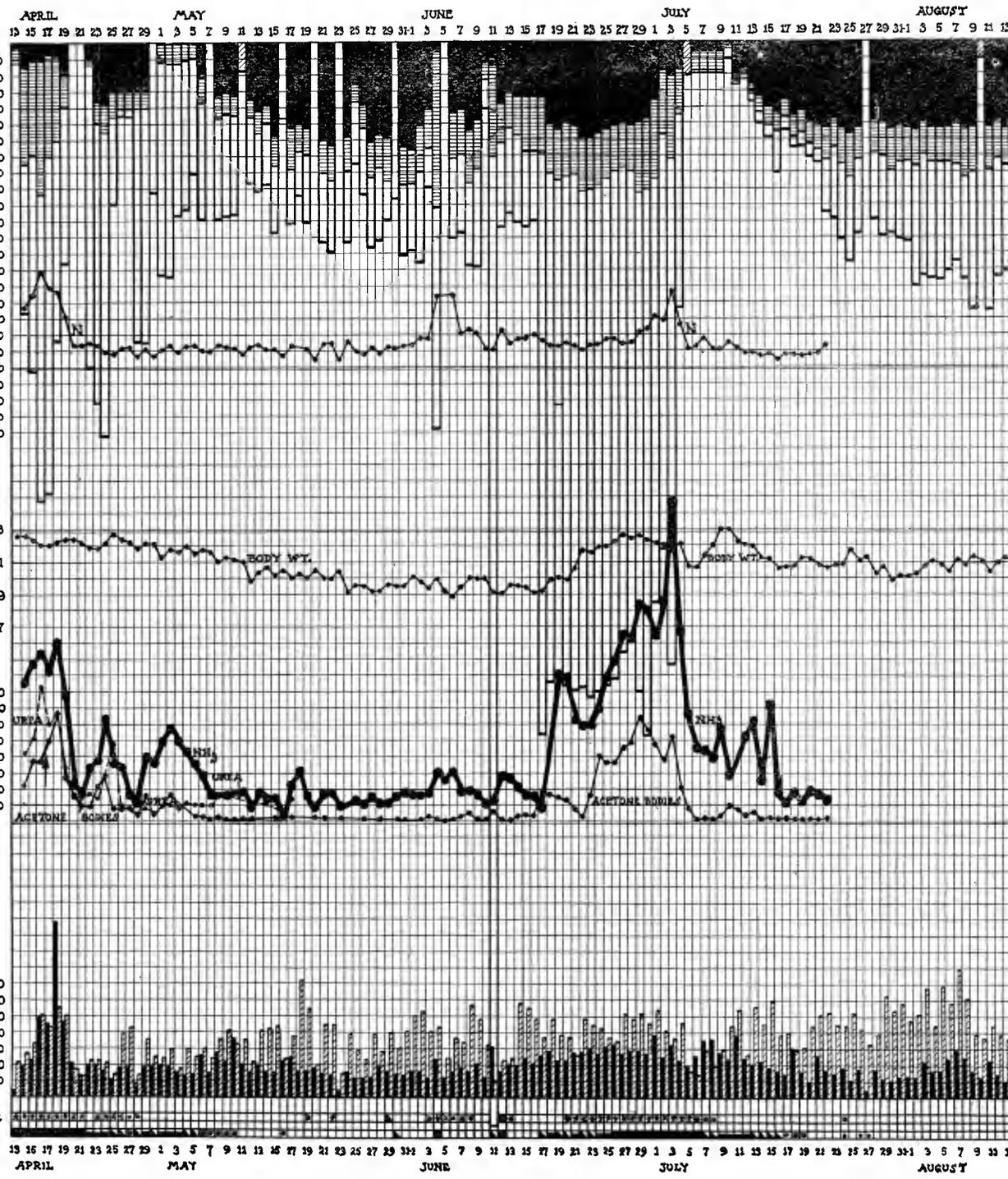
Date.	Glucose excreted in 24 hrs.	Date.	Glucose excreted in 24 hrs.
1914	gm.	1914	gm.
Feb. 24	27.0*	July 22	3.8
" 25	86.6	" 23	6.0
" 26	58.2	" 24	1.5
" 27	27.3	" 26	8.8
" 28	3.8	" 28	9.3
Mar. 7	1.2	" 29	28.0
" 9	3.0	" 30	0.8
" 10	15.0	" 31	3.7
" 11	9.0	Aug. 1	7.8
" 12	33.8	" 2	5.2
" 13	23.0	" 3	0.5
" 14	22.0	" 4	0.1
" 15	38.4	" 10	0.4
" 16	3.0	" 13	0.4
" 19	16.2	" 30	4.4
" 21	1.7	" 31	2.3
" 22	3.5	Sept. 1	0.9
" 31	1.4	" 2	0.6
Apr. 12	0.4	" 3	0.3
" 13	0.4	" 4	0.6
" 15	0.1	" 7	0.5
" 17	0.3	" 8	11.7
" 18	0.2	" 9	8.0
" 21	2.0	" 10	9.7
" 22	5.1	" 11	1.5
" 23	12.1	" 12	1.9
" 24	7.3	" 13	0.8
" 29	1.3	" 14	1.2
" 30	4.1	" 15	3.4
May 1	1.7	" 16	1.3
June 4	1.8	" 27	1.4
" 20	8.9	Oct. 1	2.4
" 24	6.0	" 26	1.1
" 28	3.3	Nov. 14	1.4
July 1	4.1	" 15	3.2
" 2	7.1	" 20	2.0
" 3	14.6	" 21	5.8
" 4	4.0	" 30	1.9
" 12	9.6	Dec. 2	2.8
" 13	5.5	" 5	3.9
" 14	7.4	" 12	6.5
" 20	3.3	" 13	3.2

* 12 hr. specimen.

CHART 2. Case No. 1.

CASE NO. 2,128

1st ADMISSION 1914



1914
2nd ADMISSION

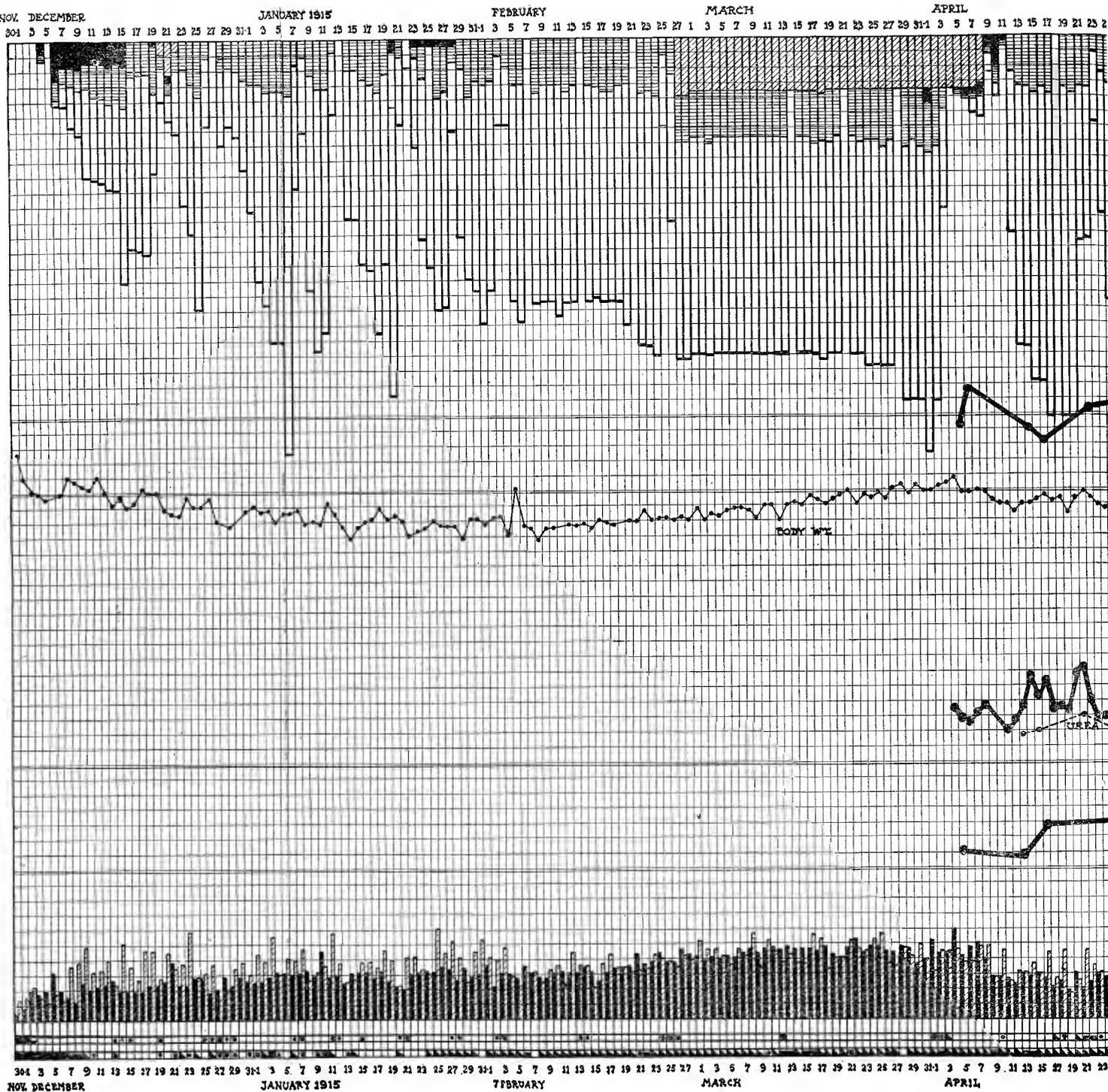
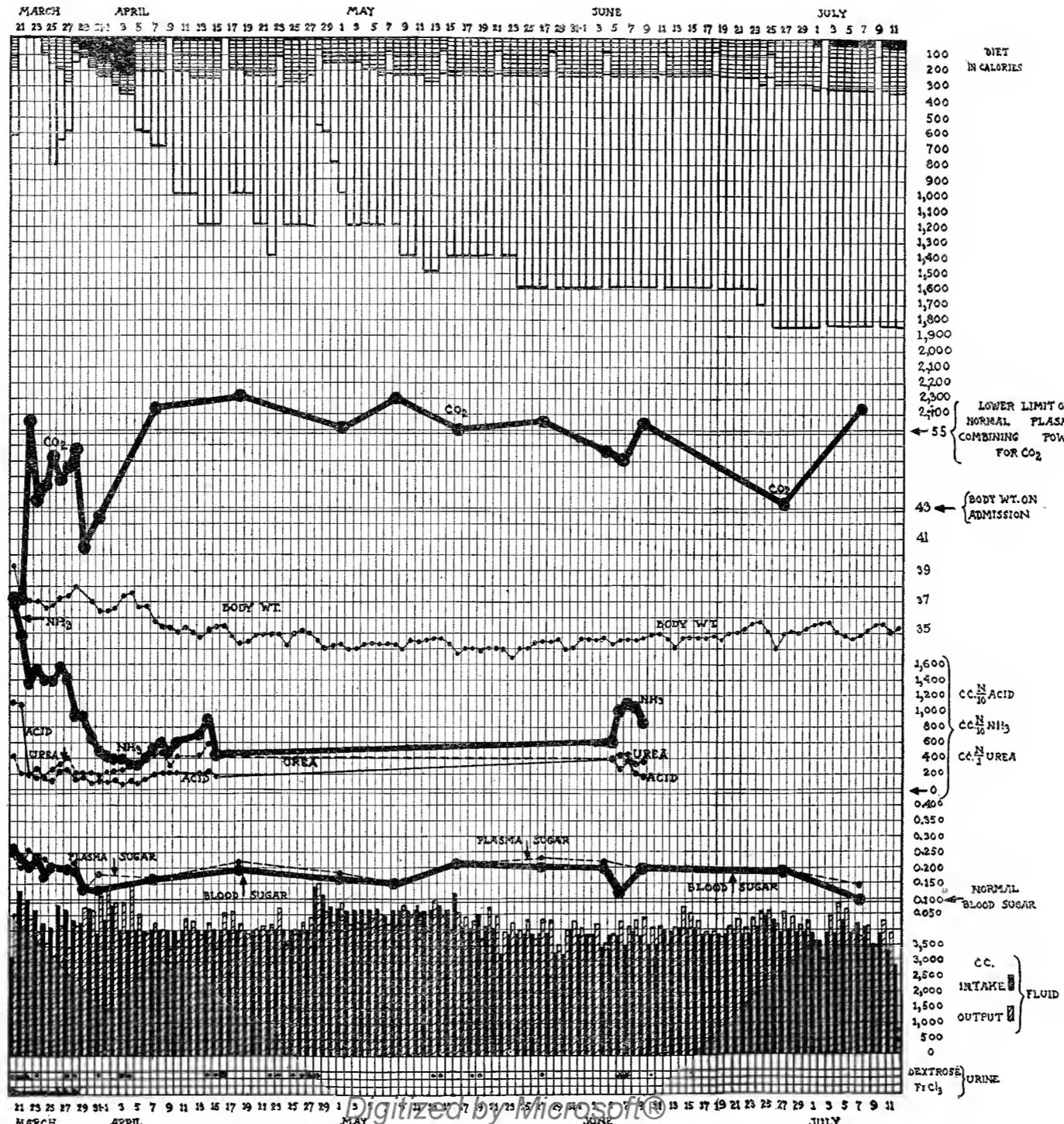
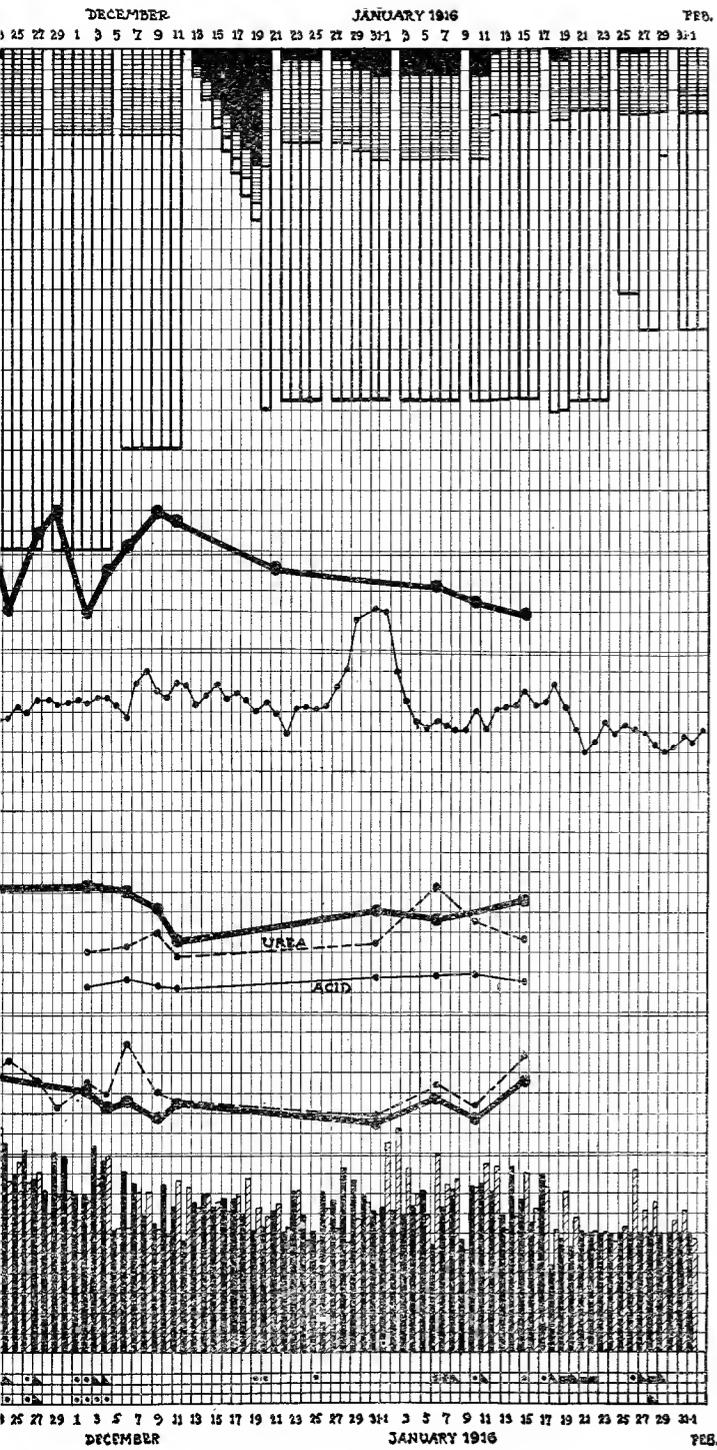




CHART 3. Case No. 2.



Date.	Glucose excreted in 24 hrs.	Date.	Glucose excreted in 24 hrs.
1st admission.			
1914	gm.	1914	gm.
Apr. 13	31.0*	June 22	16.9
" 14	36.0	" 23	22.9
" 15	51.9	" 24	19.8
" 16	78.0	" 25	19.6
" 17	51.6	" 26	19.5
" 18	42.5	" 27	28.6
" 19	31.7	" 28	24.9
" 20	5.0	" 29	29.0
" 21	0.5	" 30	34.6
" 24	1.9	July 1	32.9
" 25	0.7	" 2	20.7
" 26	3.1	" 3	37.9
May 22	3.8	" 4	13.0
June 4	12.2	" 5	3.6
" 5	2.0	" 6	1.0
" 20	7.9		
" 21	21.4		

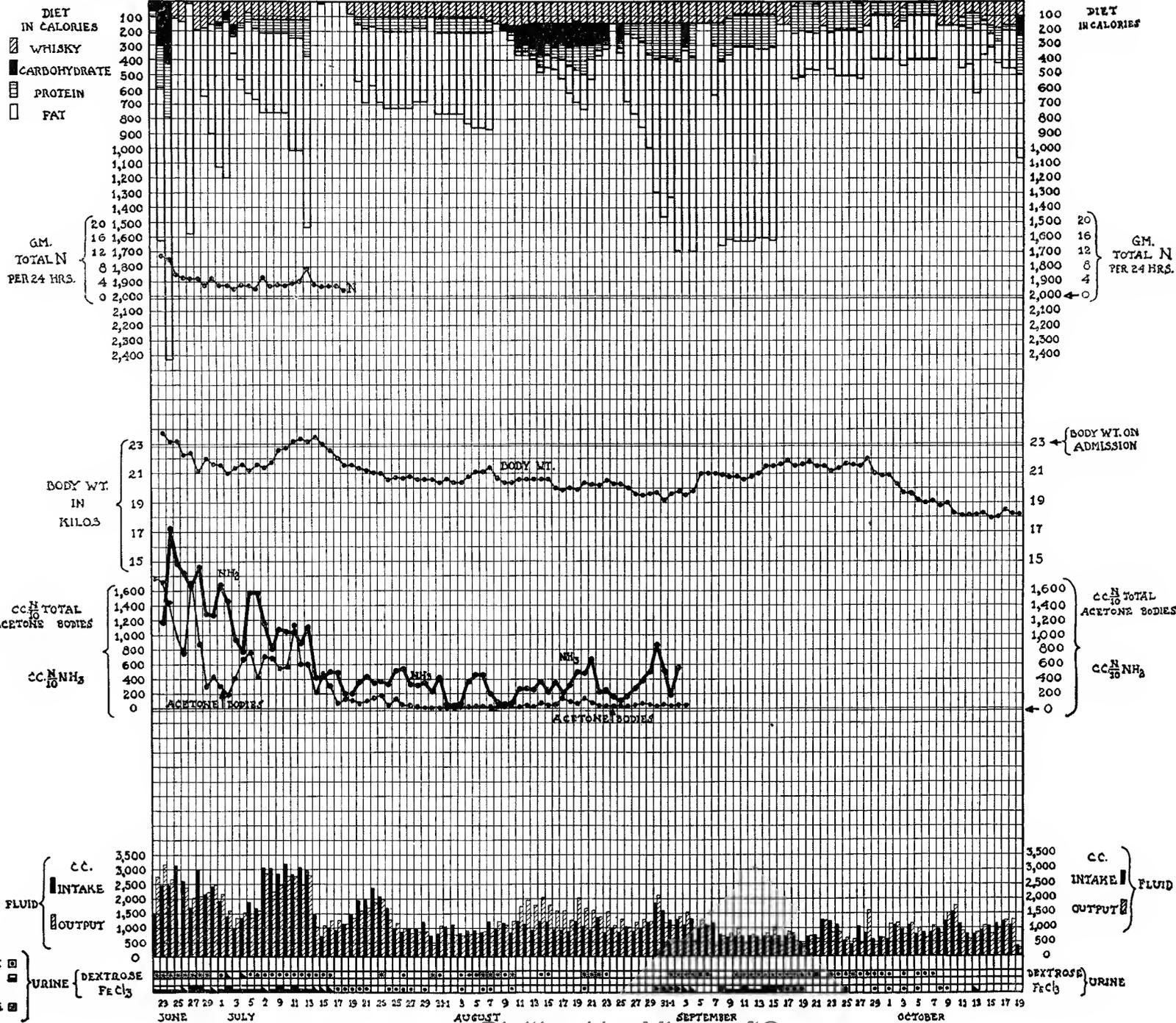
2nd admission.			
Date.	1915	Date.	1915
Dec. 14	7.7	Apr. 1	0.1
" 15	0.8	" 2	3.0
" 26	3.0	" 18	5.6
1915		May 28	5.8
Jan. 11	2.9	Sept. 2	2.2
" 21	1.0	1916	
" 28	2.4	Jan. 6	53.6
Feb. 13	2.2	" 7	42.5
" 24	0.4		

3rd admission.			
Date.	1916	Date.	1916
Mar. 20	38.3†	June 7	45.0
June 6	51.0		

* 17 hr. specimen.
 † 14 " "

CASE NO. 2162

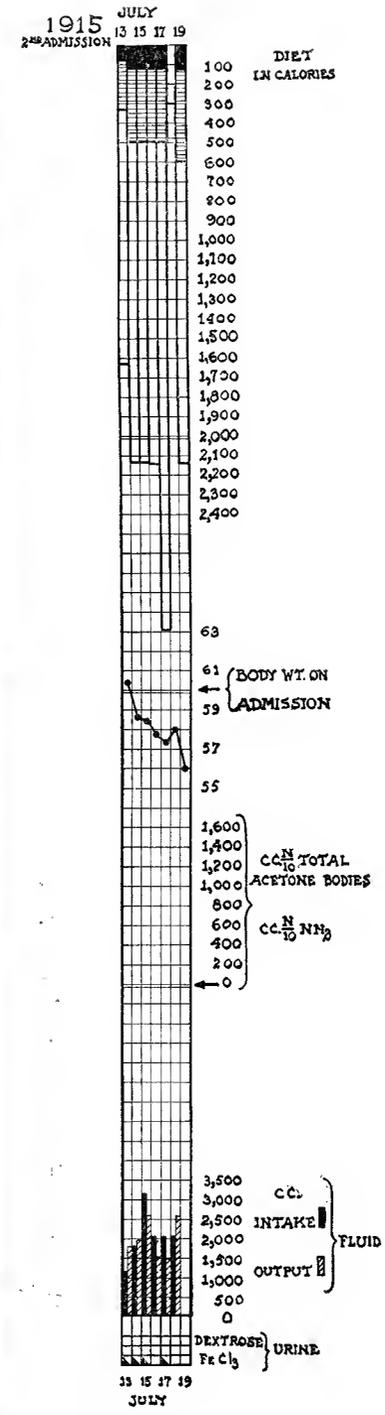
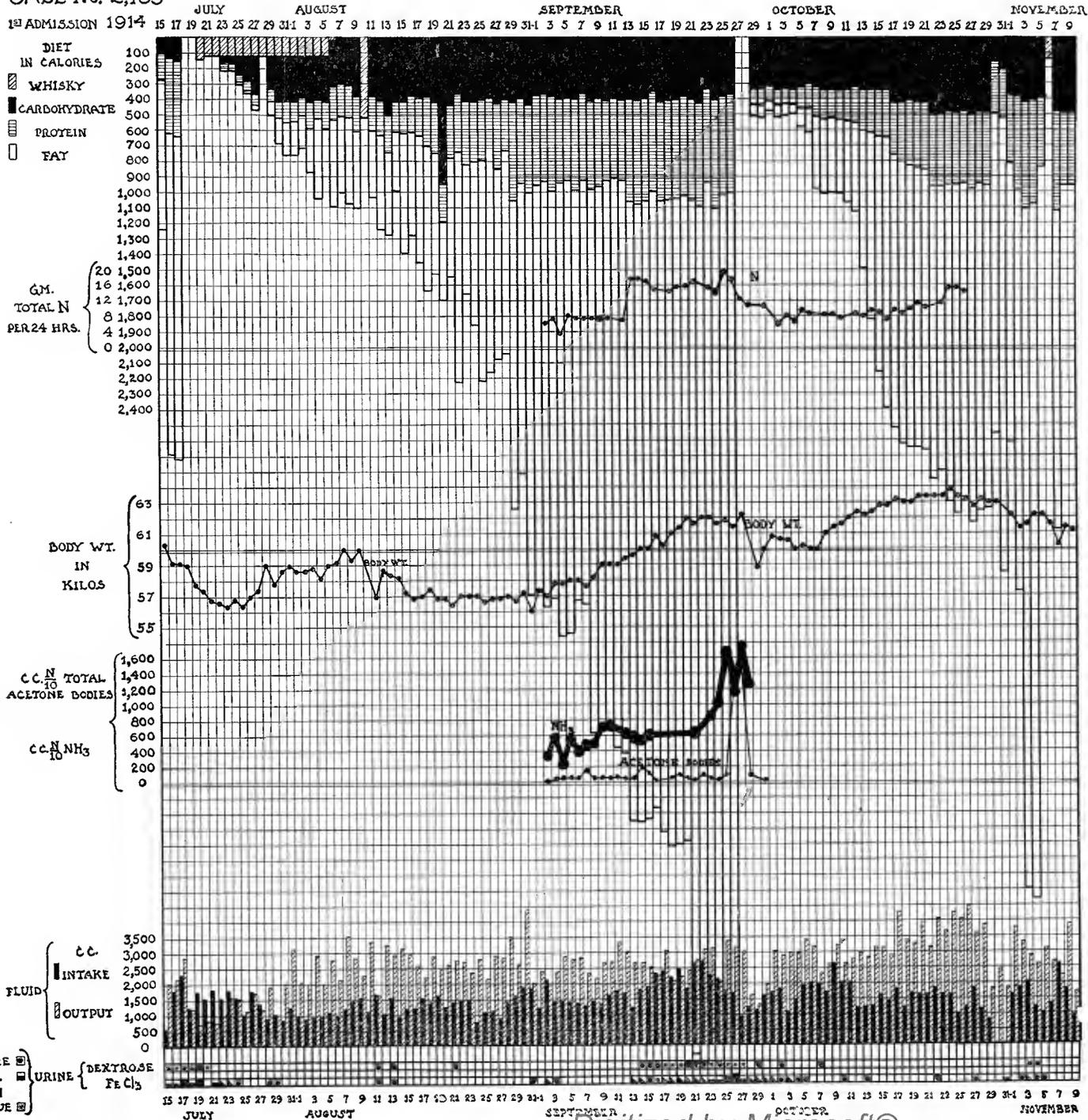
1914 JUNE JULY AUGUST SEPTEMBER OCTOBER
 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19



Date.	Glucose excreted in 24 hrs.
1914	gm.
June 22	39.2*
" 23	42.5
" 24	32.6
" 25	13.0
" 26	6.8
" 27	16.3
" 28	8.9
" 29	1.2
July 23	1.4
" 30	0.4
Aug. 6	0.4
" 7	0.7
" 8	0.6
" 10	0.1
" 20	3.7
" 21	2.8
" 22	2.2
Sept. 1	0.7
" 2	0.5
" 3	46.2
" 4	3.9
" 10	0.3
" 11	0.5
" 12	1.8
" 13	4.4
" 14	14.3
" 15	15.4
" 16	3.2
" 17	1.7
" 18	0.5
" 23	0.8
" 26	0.7

* 12 hr. specimen.

CASE NO. 2,169



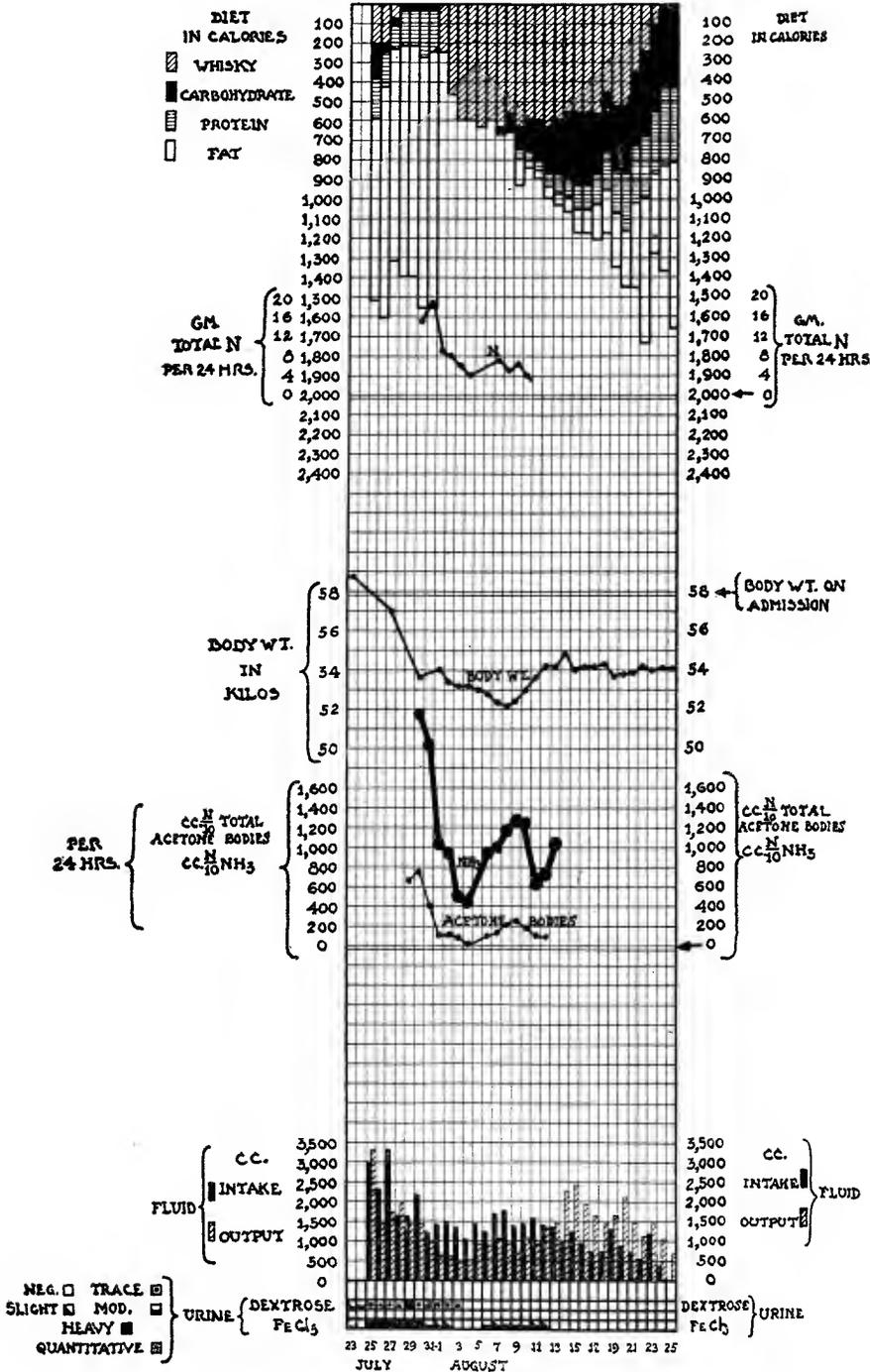
Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	
July 15	40.0*
" 16	32.3
" 17	60.8
" 18	10.2
" 19	2.9
" 20	1.6
Sept. 17	3.0
" 18	2.7
" 19	6.7
" 20	14.5
" 21	54.4
" 22	124.2
" 23	102.0
" 24	50.9
" 25	168.7
" 26	202.8
" 27	36.3

* 13 hr. specimen.

CASE NO. 2,134

JULY AUGUST

1914 23 25 27 29 31-1 3 5 7 9 11 15 17 19 21 23 25



Date.	Glucose excreted in 24 hrs.
1914	gm.
July 25	59.9
" 26	34.3
" 27	30.7
" 28	98.0
" 30	112.7
" 31	24.5
Aug. 1	8.7
" 2	2.4

CHART 6. Case No. 6.

CASE NO. 2,293

1914

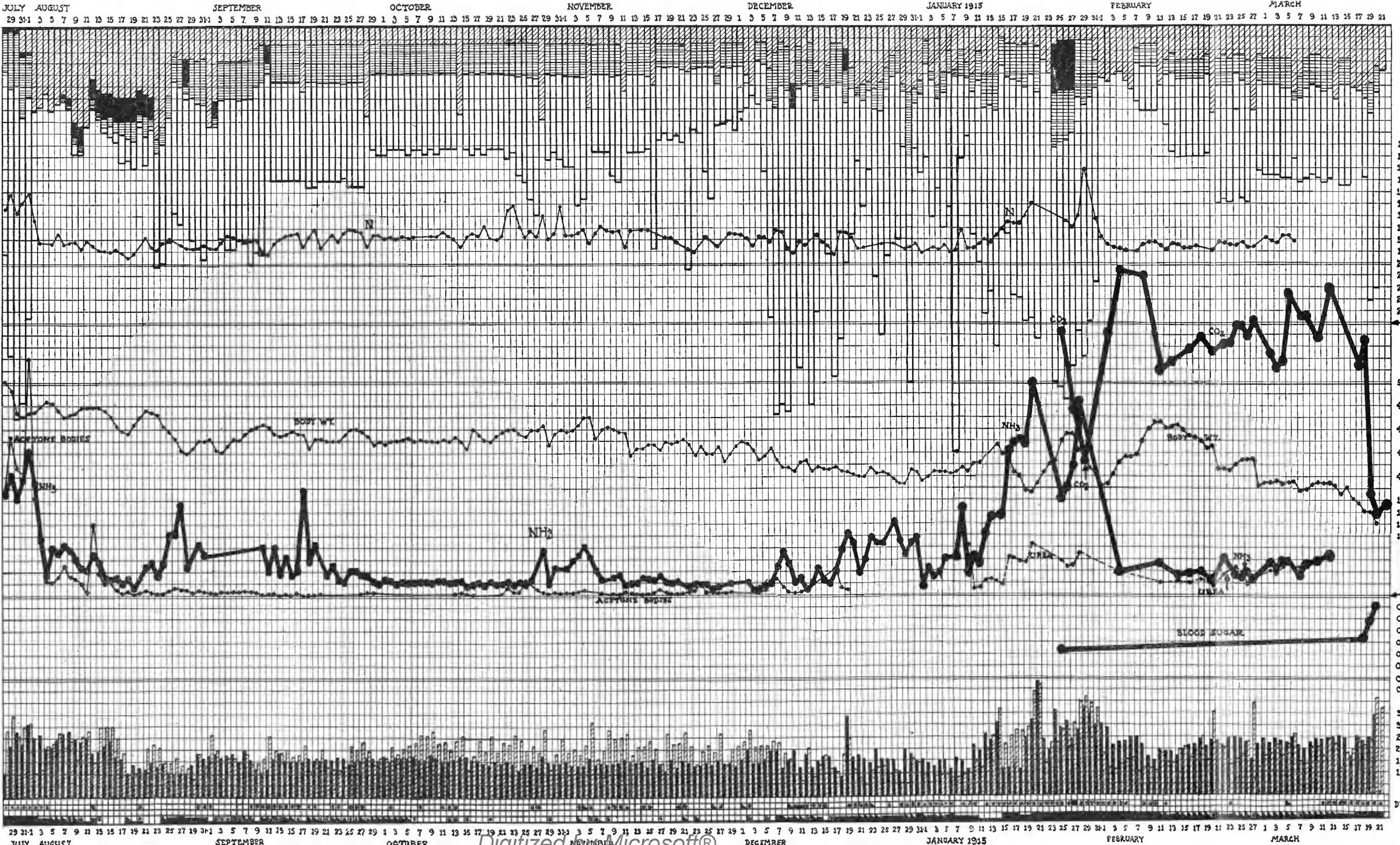
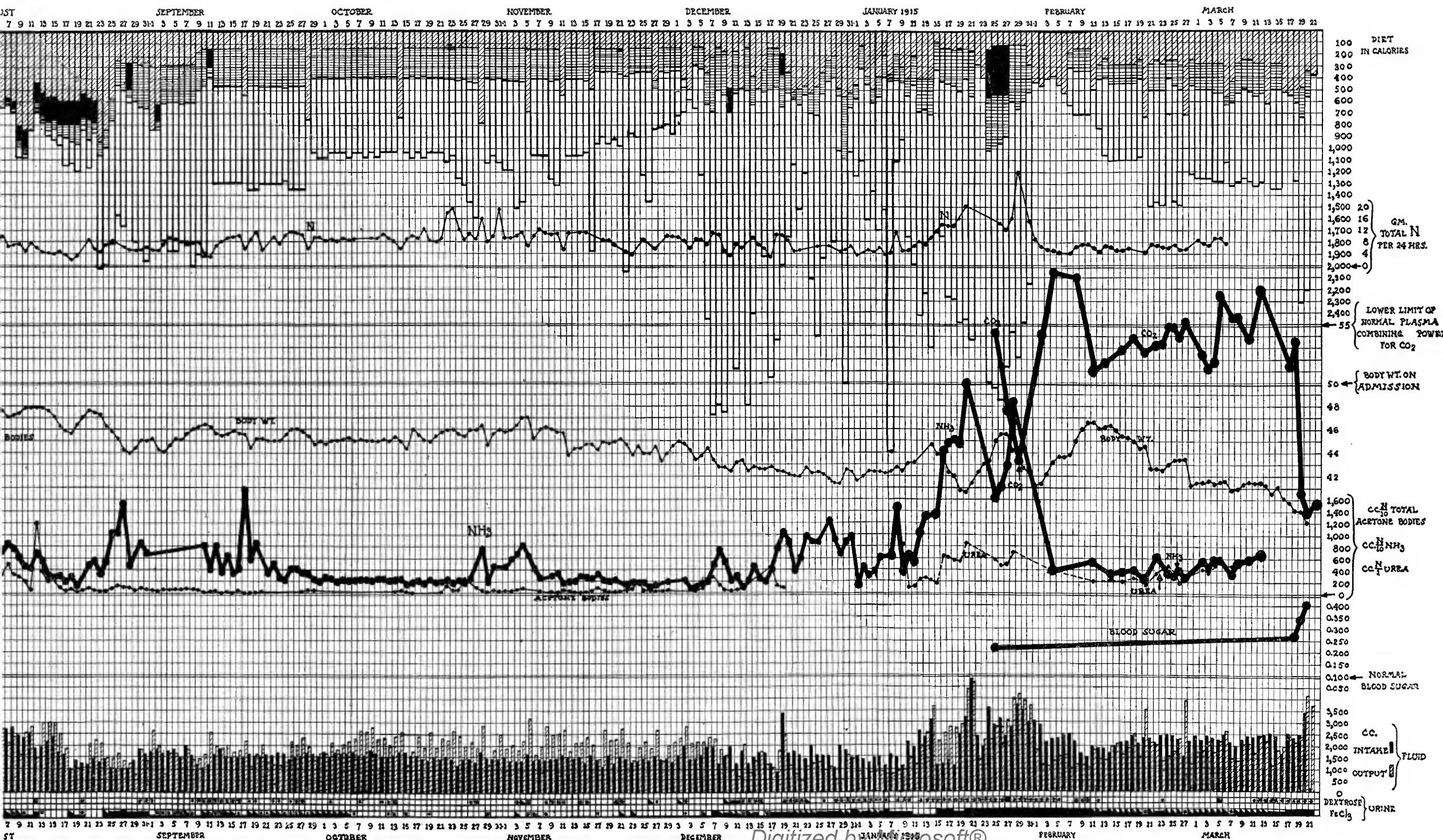


CHART 7. Case No. 8.

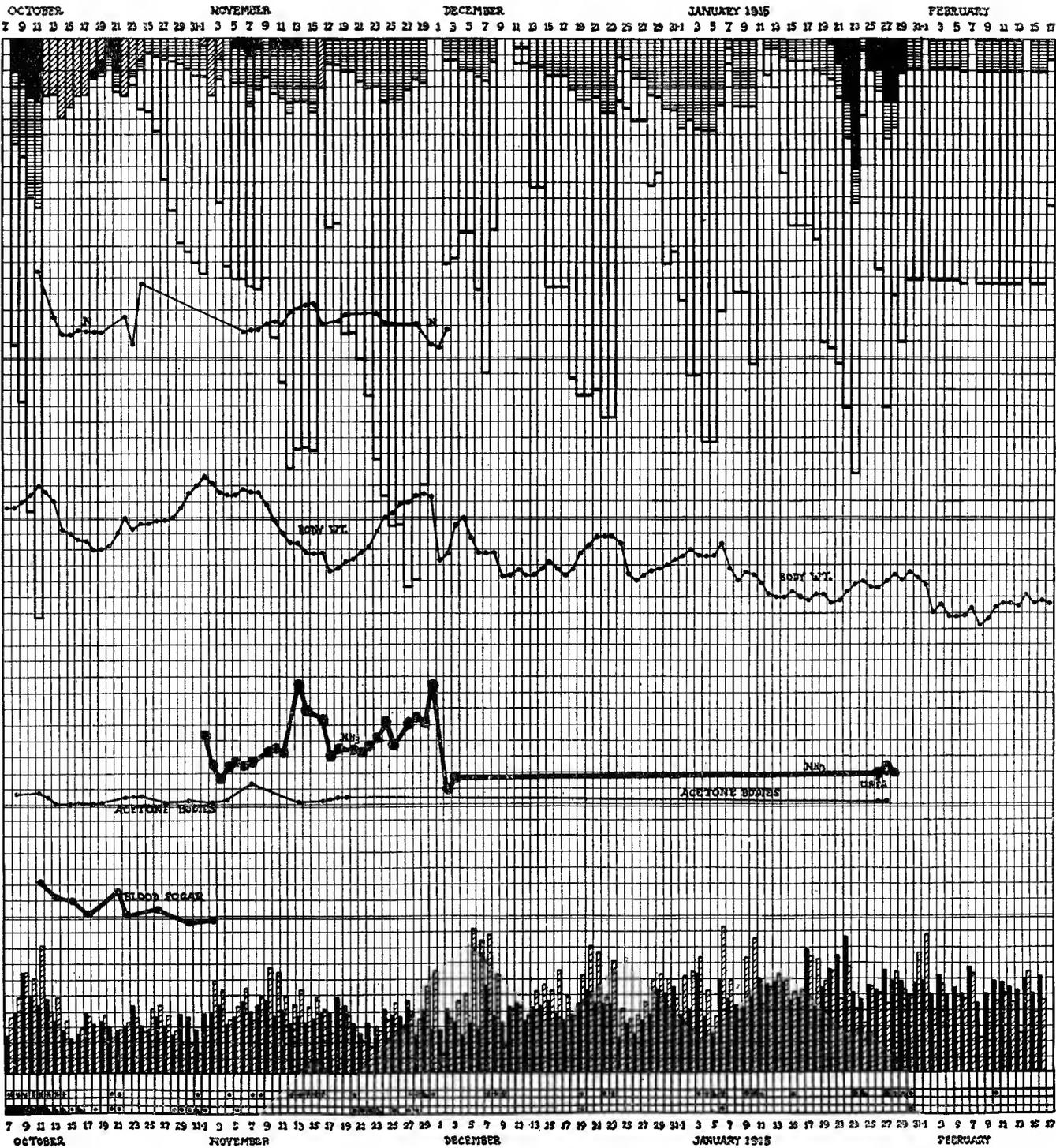


Date.	Glucose excreted in 24 hrs.	Date.	Glucose excreted in 24 hrs.
1914	gm.	1915	gm.
July 28	44.2*	Jan. 2	1.0
" 29	61.6	" 3	1.3
" 30	65.0	" 8	4.7
" 31	58.2	" 9	5.0
Aug. 1	60.6	" 10	5.0
" 2	17.8	" 12	11.4
" 3	1.9	" 13	15.3
" 4	2.0	" 14	23.0
" 20	0.4	" 15	12.2
" 30	6.6	" 16	43.8
" 31	8.1	" 17	44.4
Sept. 1	0.8	" 18	46.0
" 9	1.3	" 19	69.6
" 10	1.0	" 20	76.2
" 11	3.2	" 21	60.8
" 12	0.4	" 22	16.0
" 13	1.1	" 23	8.1
" 14	3.2	" 24	33.7
" 15	2.3	" 25	47.3
" 16	1.7	" 26	44.4
" 26	1.6	" 28	60.0
" 27	1.5	" 29	67.4
Oct. 26	1.1	" 30	49.4
" 27	1.8	" 31	42.5
Nov. 3	2.8	Feb. 1	16.5
" 9	5.4	" 2	8.2
" 10	3.7	" 3	6.8
" 14	1.5	" 4	2.8
" 15	2.4	" 10	1.5
" 20	1.8	Mar. 12	10.6
" 21	9.0	" 13	2.2
Dec. 2	5.7	" 14	7.3
" 12	1.5	" 15	18.6
" 13	1.7	" 16	22.2
" 14	4.4	" 17	33.2
" 15	1.1	" 18	62.9
" 19	21.8	" 19	64.9
" 20	8.5	" 20	84.9
" 22	0.6	" 21	54.4
" 28	0.5		
" 30	0.5		
" 31	3.5		

* 12 hr. specimen.

CHART 7. Case No. 8.

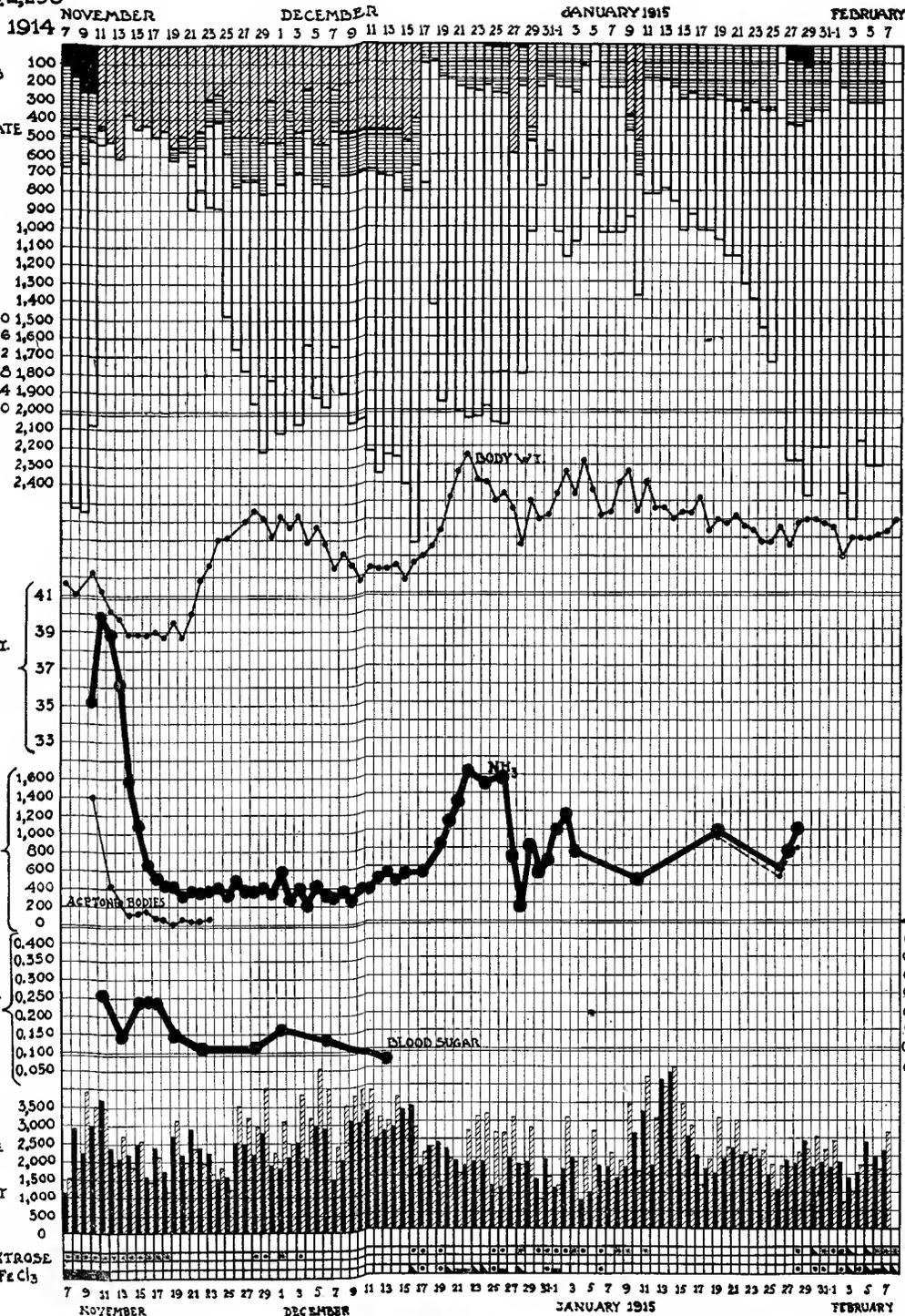
CASE NO. 2,269



Date.	Glucose excreted in 24 hrs.
1914	
Oct. 7	45.4*
" 8	79.4
" 9	77.3
" 10	75.6
" 11	98.0
" 12	16.7
" 13	7.0
" 14	3.4
Nov. 12	1.0
" 13	2.7
" 14	3.2
" 15	3.2
" 16	0.5
" 28	8.5
Dec. 7	6.8
" 8	12.5
" 9	0.9
1915	
Jan. 6	4.8
" 9	3.7
" 10	10.2

* 14 hr. specimen.

CASE NO. 2256



Date.	Glucose excreted in 24 hrs.
1914	
Nov. 7	44.4*
" 8	38.2
" 9	78.0
" 10	106.4
" 11	41.9
" 12	24.5
" 13	15.7
" 14	8.9
" 15	6.5
" 16	7.1
" 17	2.8
" 18	0.8
Dec. 1	1.7
" 28	0.8
1915	
Jan. 3	3.8
" 8	1.2
" 9	5.0
" 11	2.6
" 31	2.2
Feb. 6	9.3
" 7	26.0
" 8	12.0†

* 13 hr. specimen.

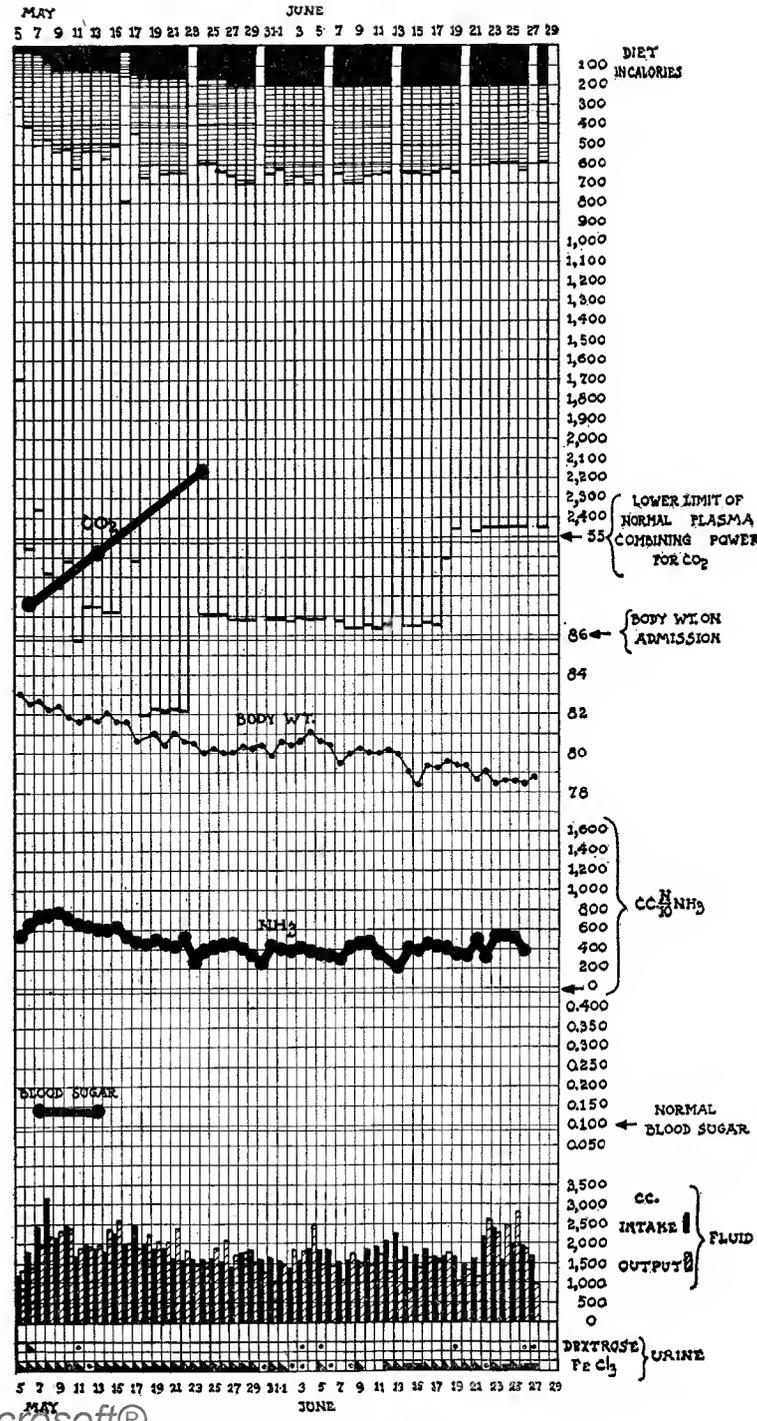
† 6 " "

CASE NO. 2,225

1st ADMISSION 1914



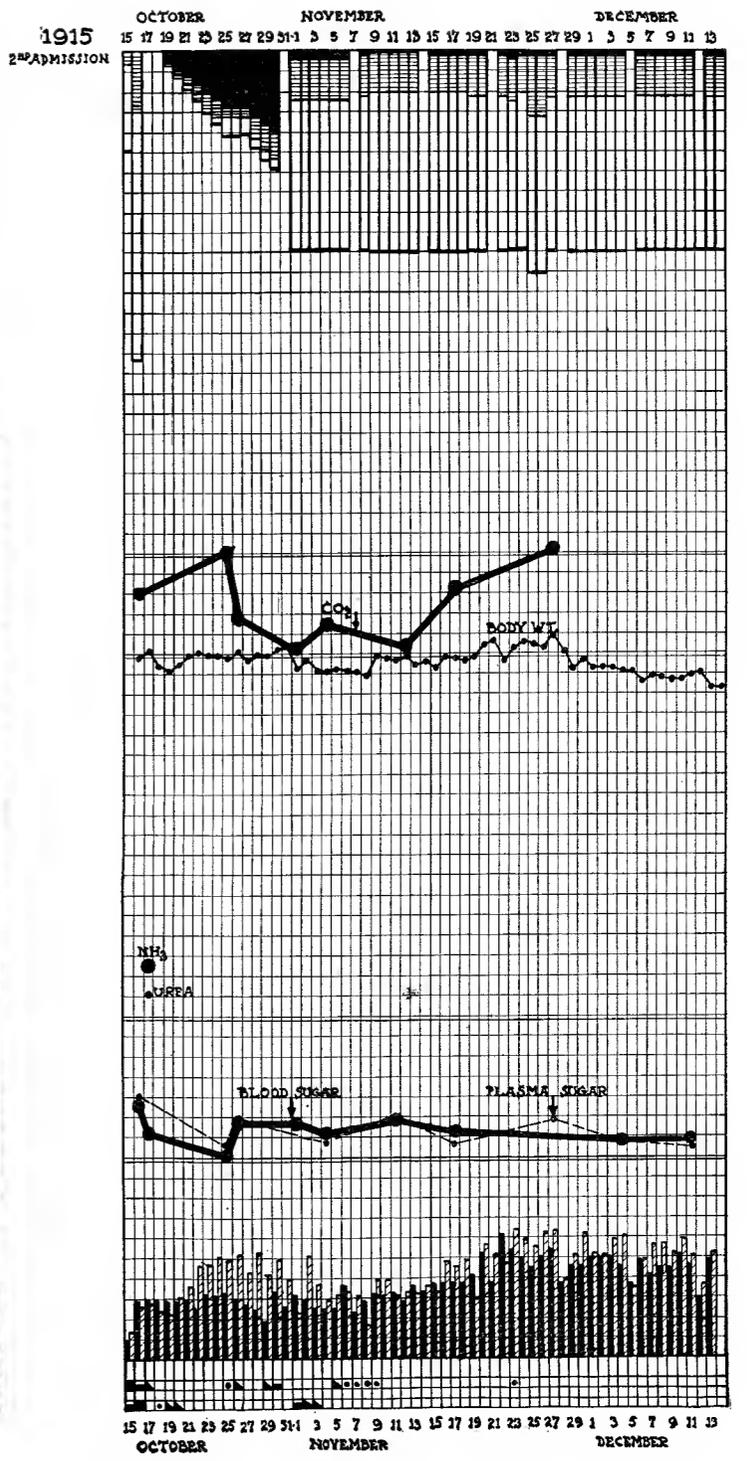
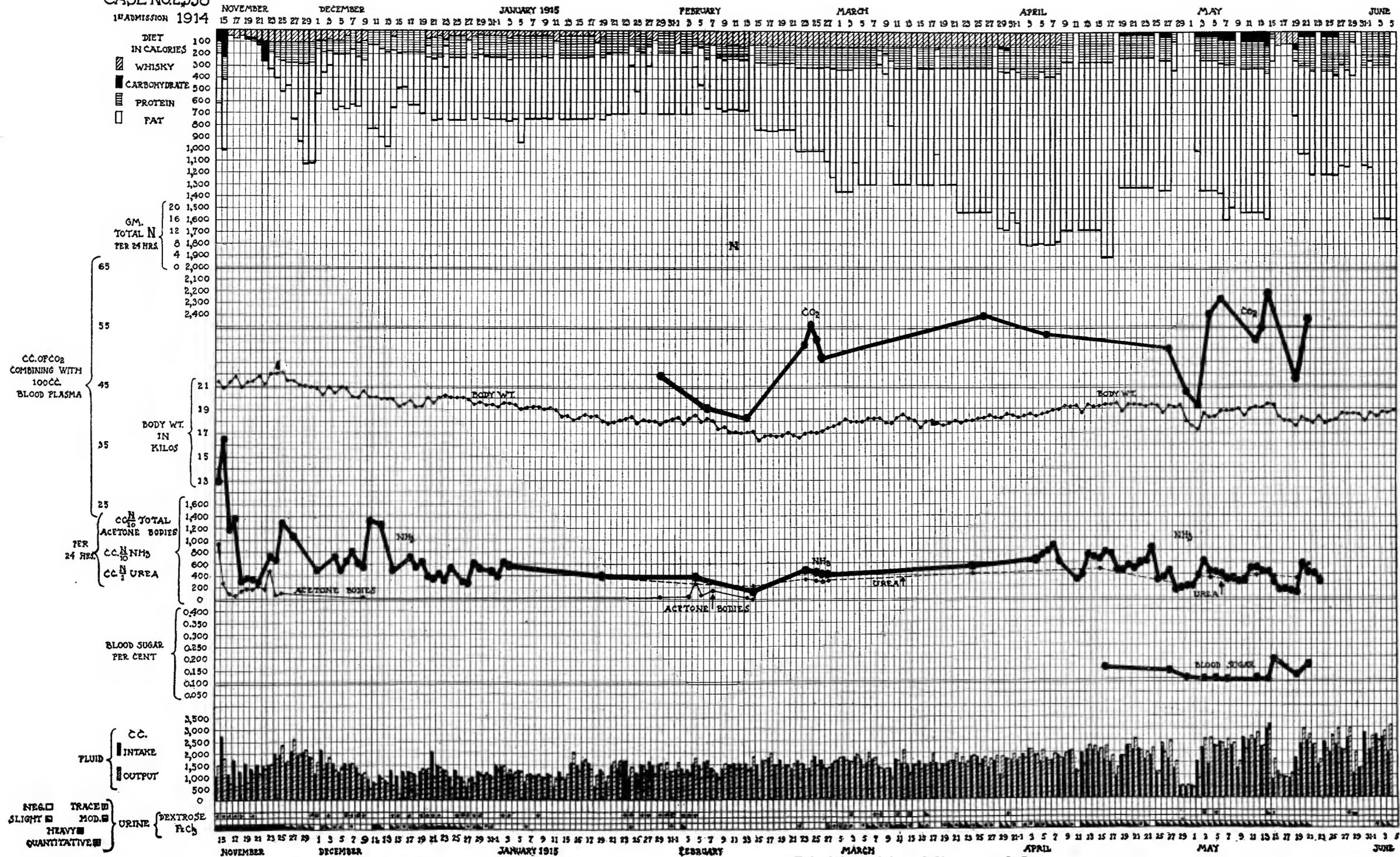
1915 2nd ADMISSION

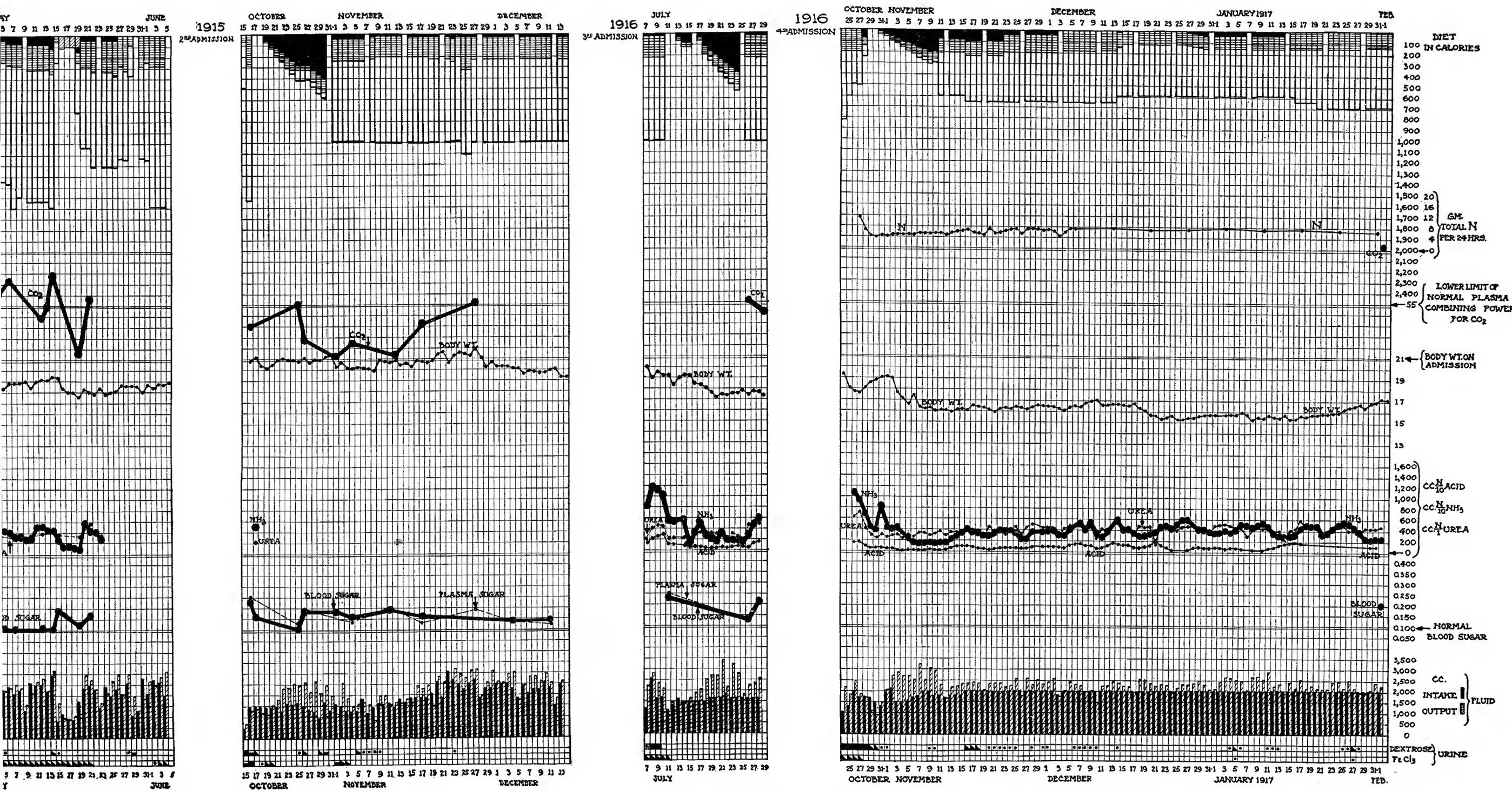


Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	gm.
Nov. 11	42.4*
" 12	26.0
" 13	6.9
" 18	0.8

* 13 3/4 hr. specimen.

CASE NO. 2358



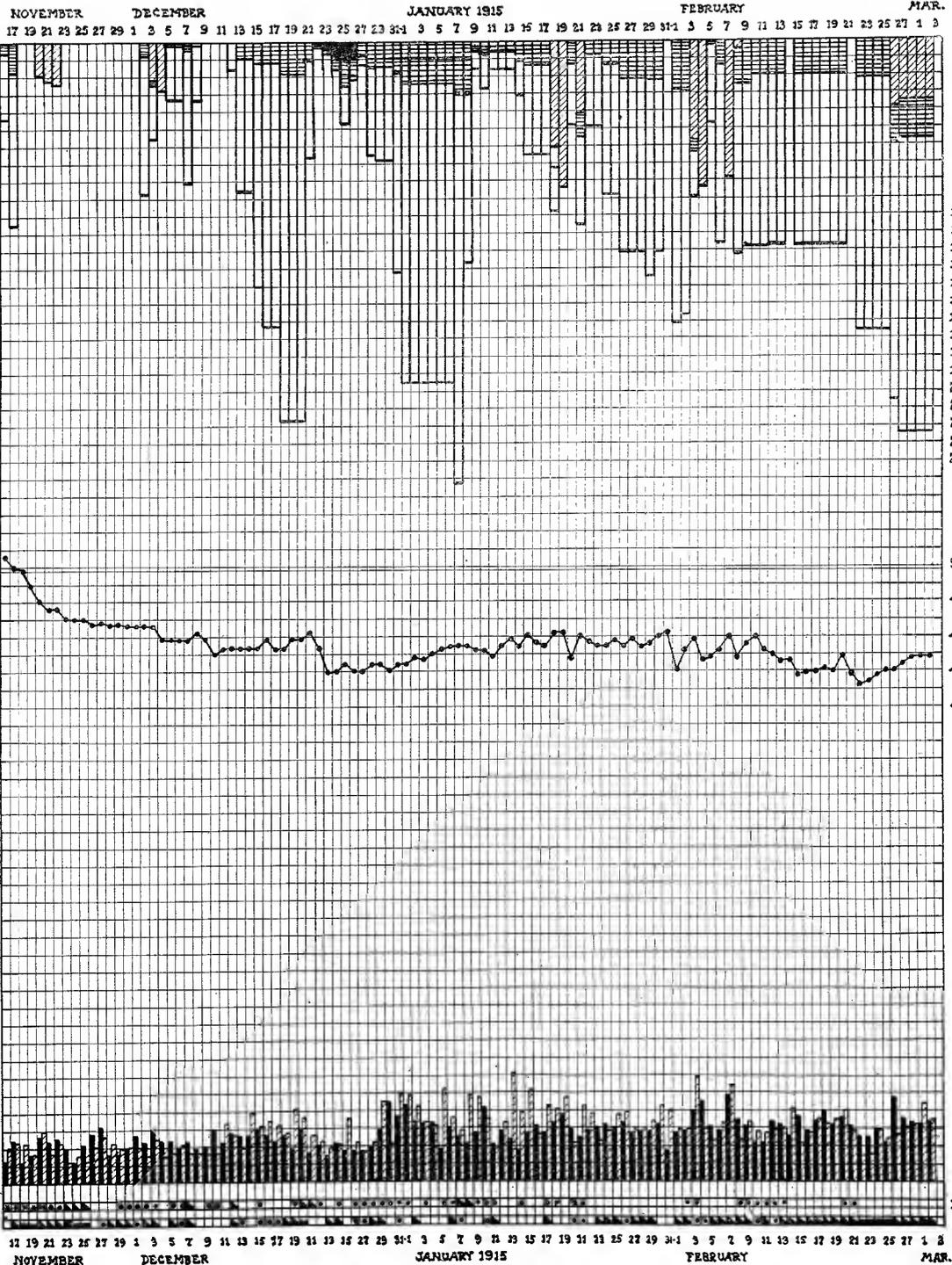


Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	gm.
Nov. 14	66.7*
" 15	46.8
" 16	2.2
" 17	1.1
" 18	0.5
" 20	0.3
" 30	0.1
Dec. 3	1.2
" 7	0.1
" 9	1.8
" 14	3.7
1915	
Jan. 31	1.4
Mar. 7	4.6
" 8	0.7
May 28	6.4
3rd admission.	
1916	
July 7	6.4†

* 13 hr. specimen.
 † 13½ "

CHART 11. Case No. 13.

CASE NO. 2,275
1914

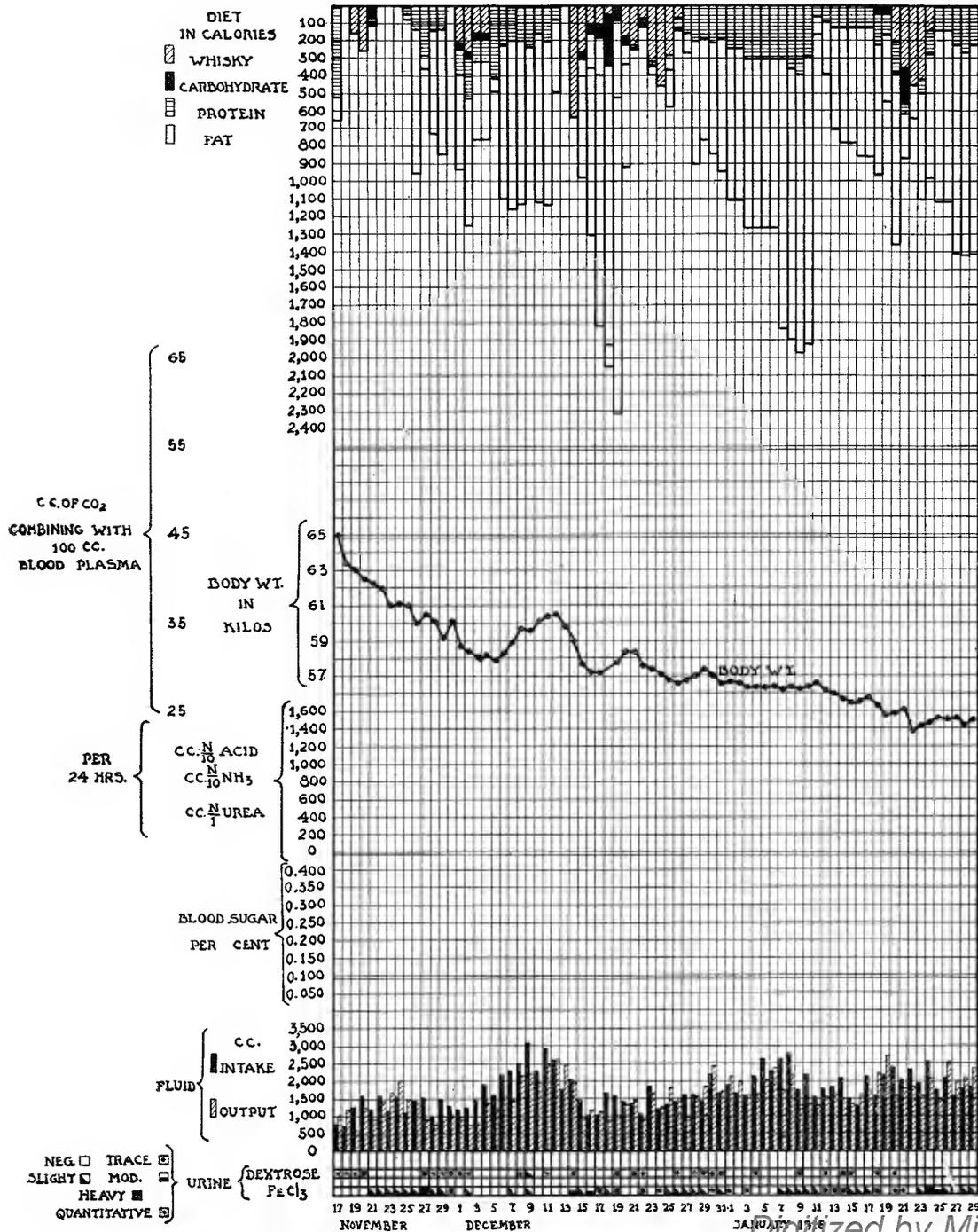


Date.	Glucose excreted in 24 hrs.
1914	gm.
Nov. 16	26.5*
" 17	28.9
" 18	7.7
" 19	3.3
" 20	2.7
1915	
Jan. 18	4.0
" 20	3.3

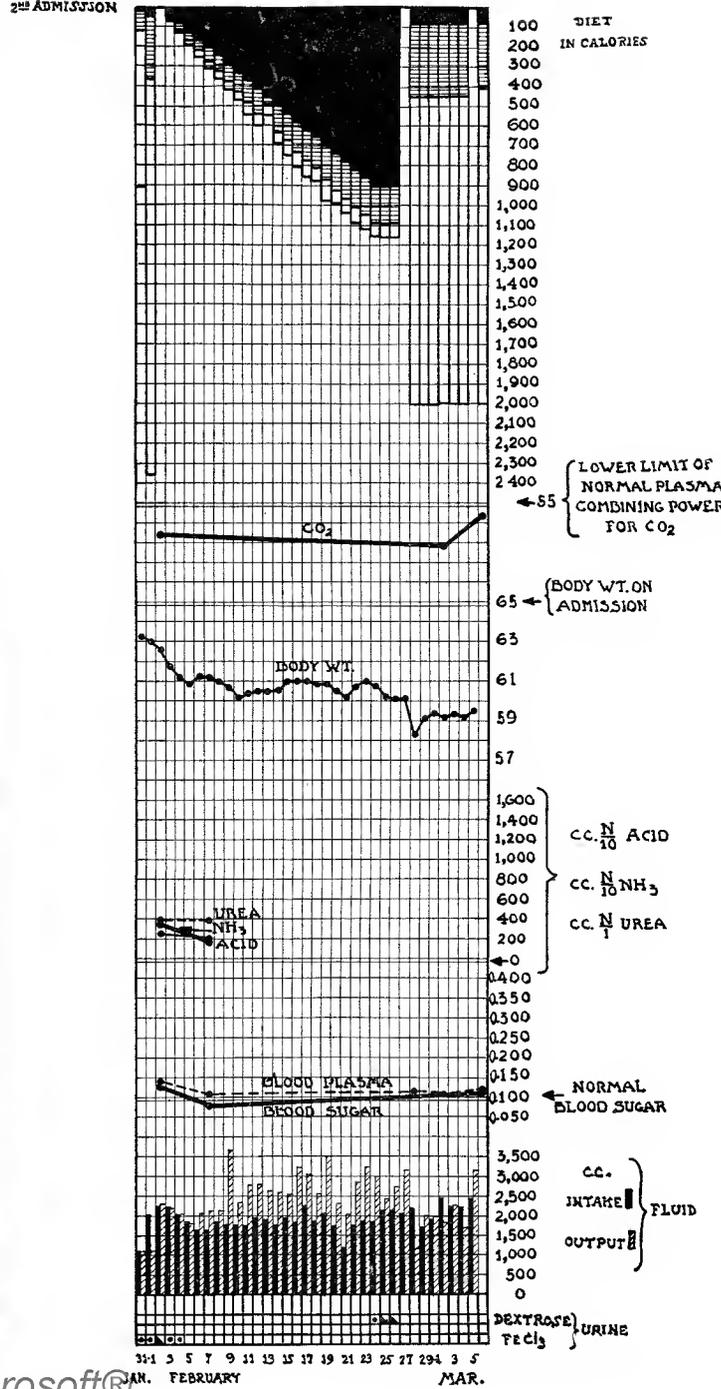
* 13 1/4 hr. specimen.

CASE NO. 2,248

1st ADMISSION 1914 NOVEMBER DECEMBER JANUARY 1915



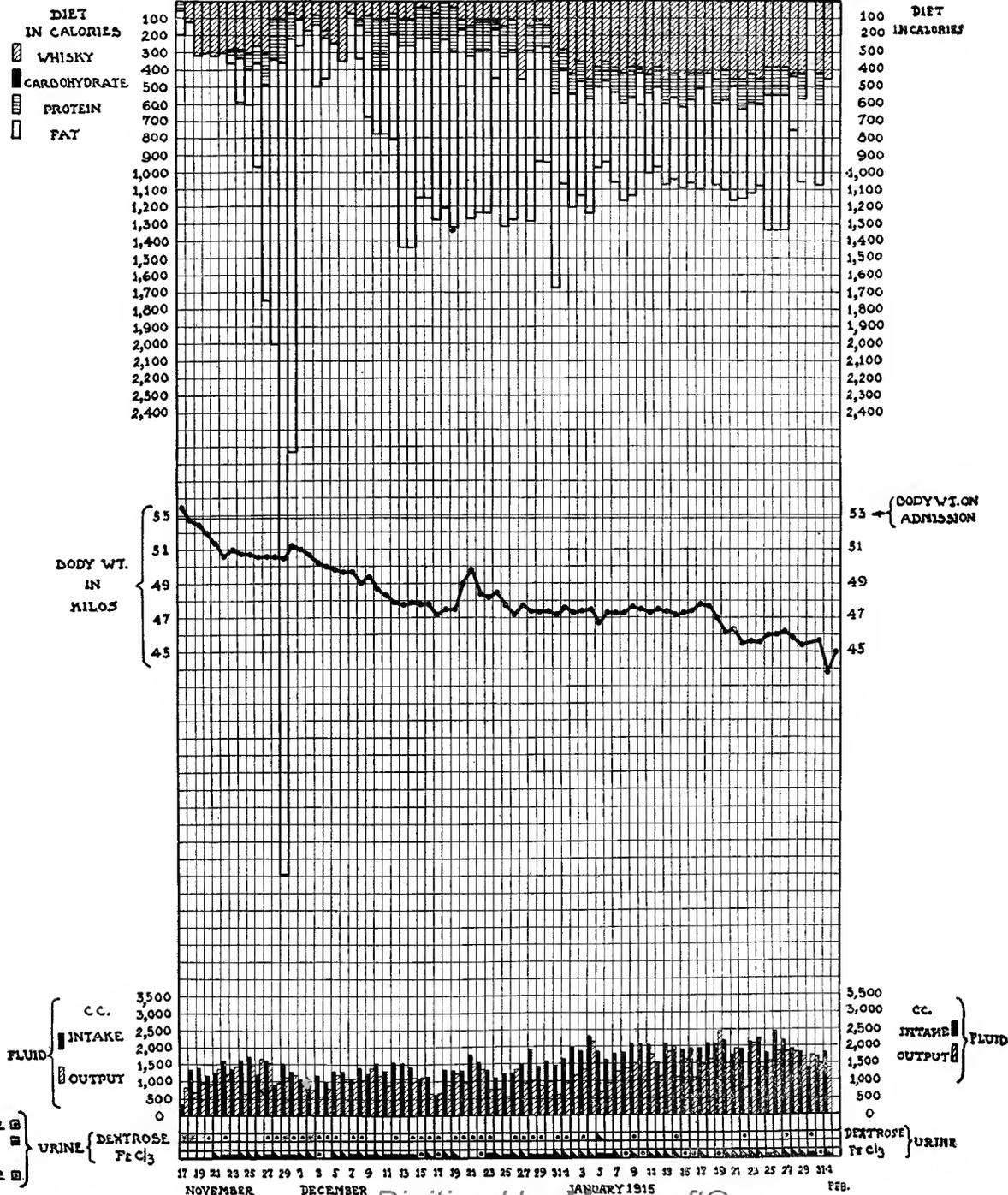
2nd ADMISSION 1916 JAN. FEBRUARY MAR.



Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	gm.
Nov. 17	101.0
" 18	9.5
" 19	4.5
" 28	3.0
" 29	10.5
Dec. 2	7.5
" 8	1.3
" 11	6.2

CASE NO. 2,252

NOVEMBER DECEMBER JANUARY 1915 FEB.
1914 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31

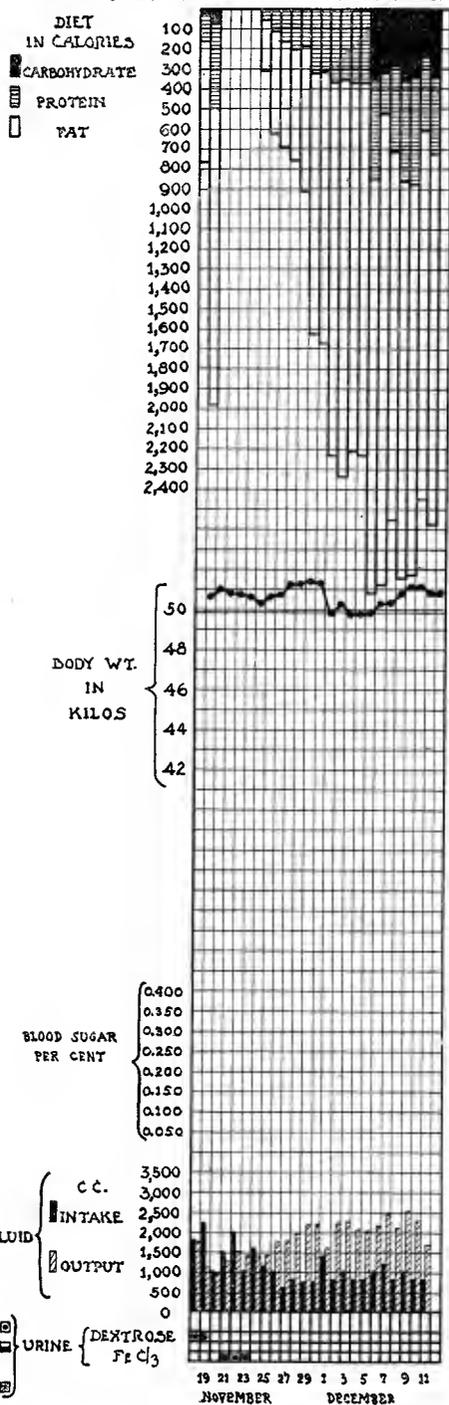


Date.	Glucose excreted in 24 hrs.
1914	gm.
Nov. 17	26.5*
" 18	7.4
" 29	11.1
Dec. 2	7.1

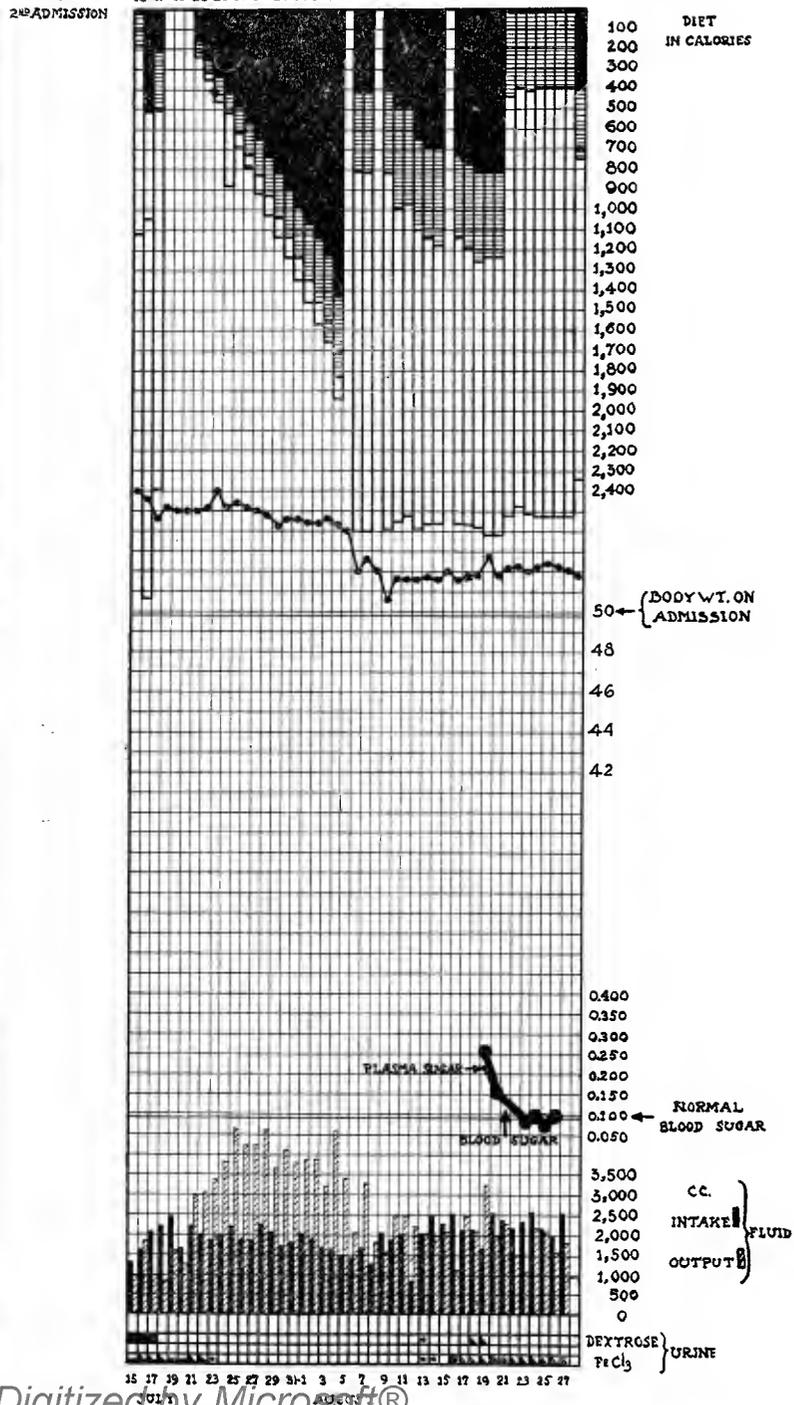
* 13 $\frac{1}{2}$ hr. specimen.

CASE NO. 2,196

1ST ADMISSION 1914 NOVEMBER DECEMBER
19 21 23 25 27 29 1 3 5 7 9 11



1915 2ND ADMISSION JULY AUGUST
15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15 17 19 21 23 25 27



Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	gm.
Nov. 18	64.5*

* 18 hr. specimen.

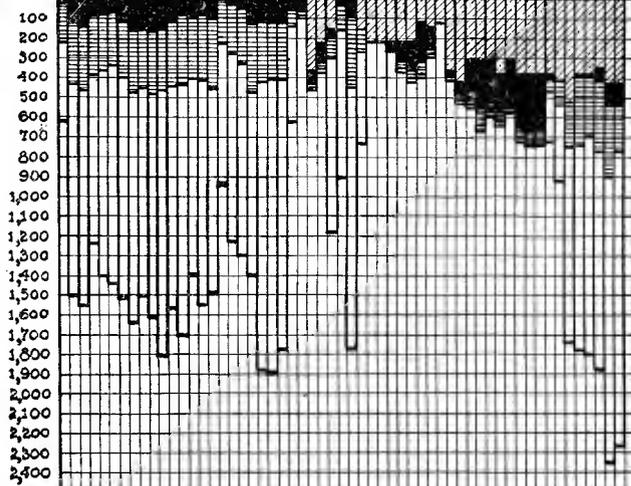
CHART 15. Case No. 18.

CASE NO. 2,233

1st ADMISSION 1914

NOVEMBER DECEMBER JANUARY 1915
19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15

DIET
IN CALORIES
WHISKY
CARBOHYDRATE
PROTEIN
FAT



CC. OF CO₂
COMBINING WITH
100CC.
BLOOD PLASMA

65
55
45
35
25

BODY WT.
IN
KILOS

33
31
29
27
25
23
21
19
17
15
13
11
9
7
5
3
1
0

CC. N₂
PER 24 HRS.

3,500
3,000
2,500
2,000
1,500
1,000
500
0

FLUID
INTAKE
OUTPUT

NEG. □ TRACE □
SLIGHT □ MOD. □
HEAVY □ QUANTITATIVE □

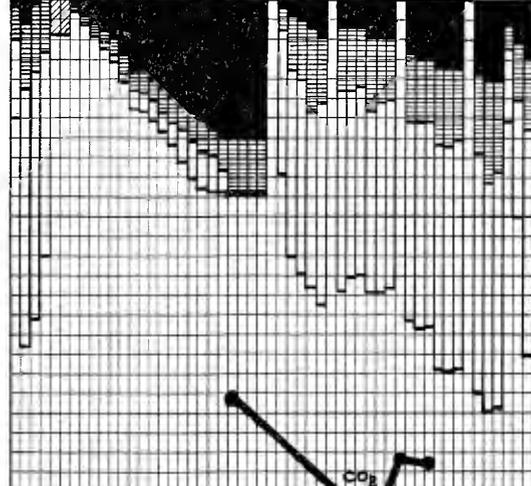
URINE { DEXTROSE
FeCl₃

19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15
NOVEMBER DECEMBER JANUARY 1915

1915
2nd ADMISSION

JUNE JULY
3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23

DIET
IN CALORIES



LOWER LIMIT OF
NORMAL PLASMA
COMBINING POWER
FOR CO₂

BODY WT. ON
ADMISSION

CC. N₂

3,500
3,000
2,500
2,000
1,500
1,000
500
0

URINE { DEXTROSE
FeCl₃

3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23
JUNE JULY

CASE NO. 2,243

NOVEMBER DECEMBER JANUARY 1915
 21 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15 17 19 21 23 25

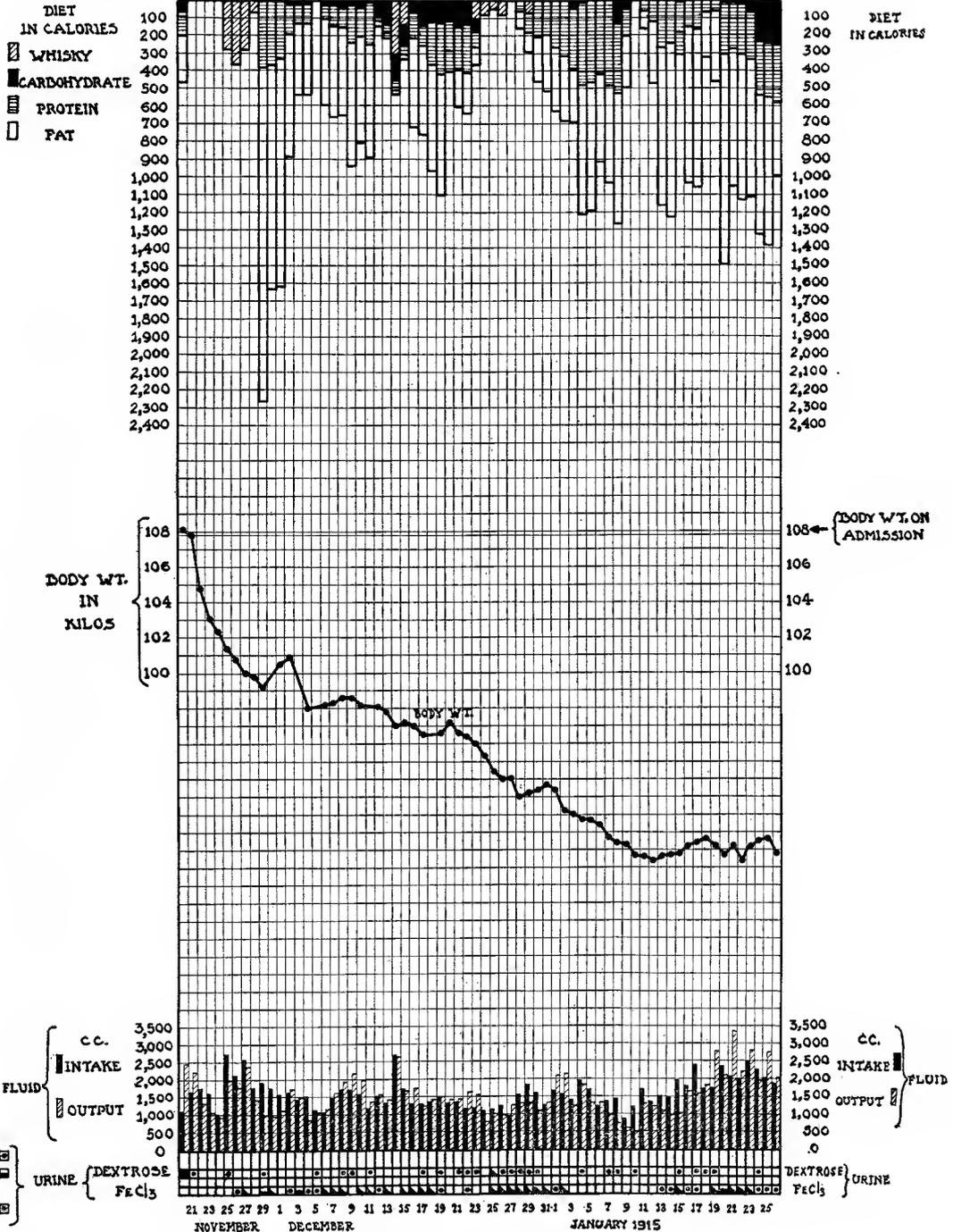
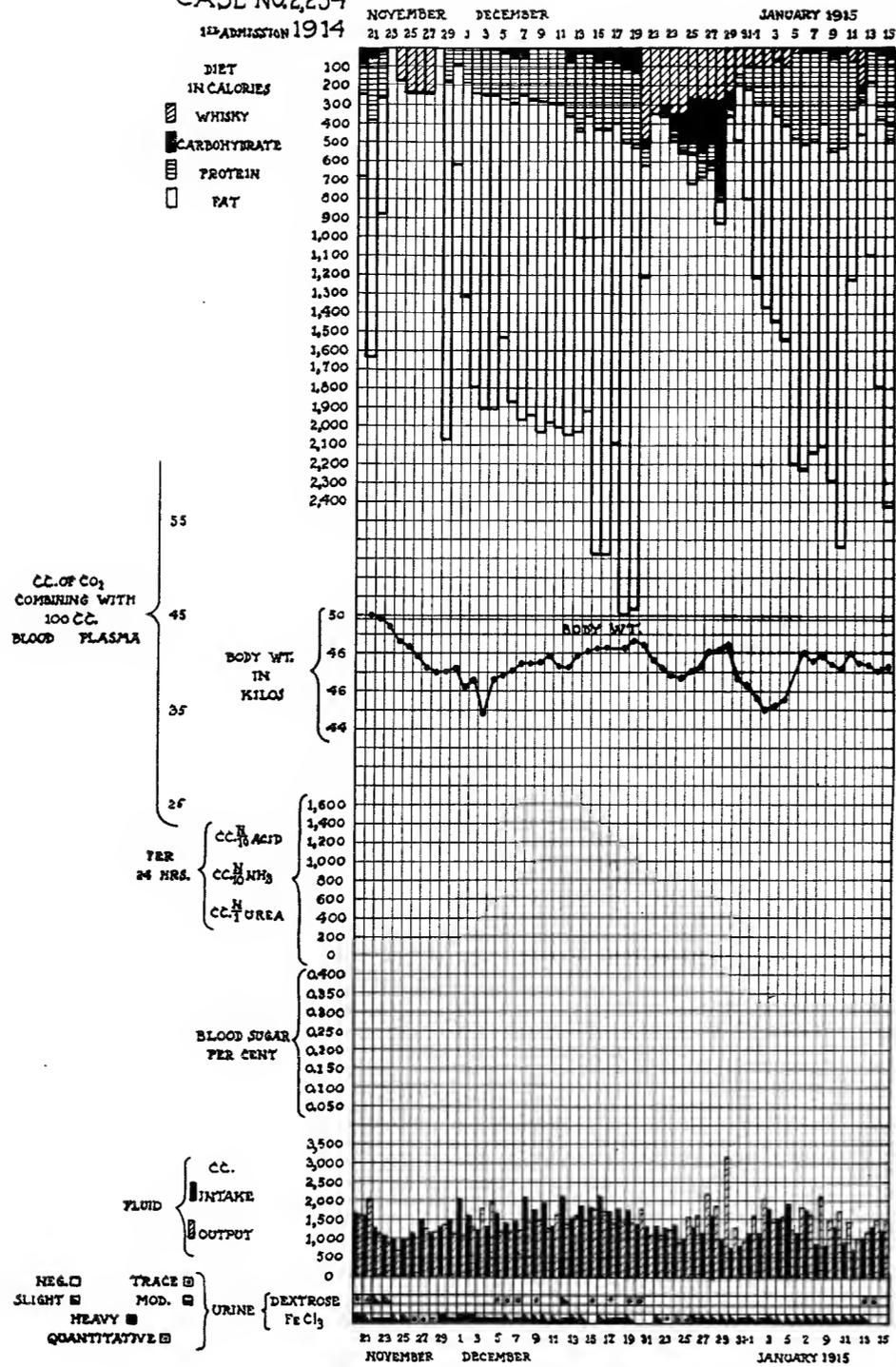


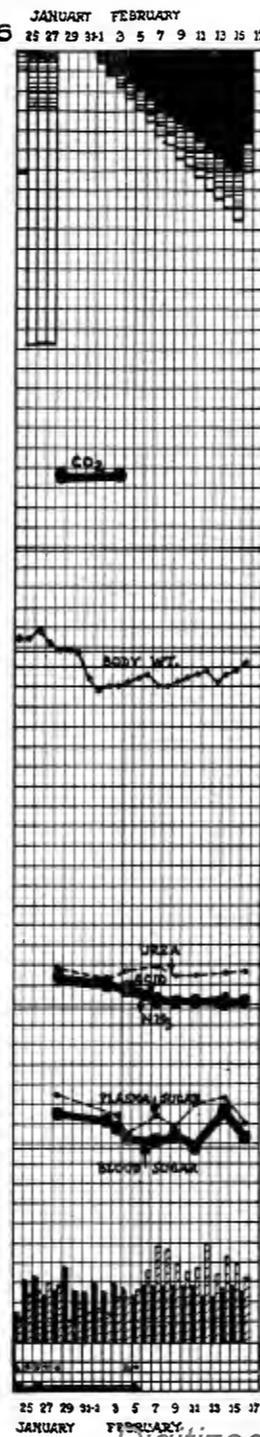
CHART 17. Case No. 21.

CASE NO. 2234

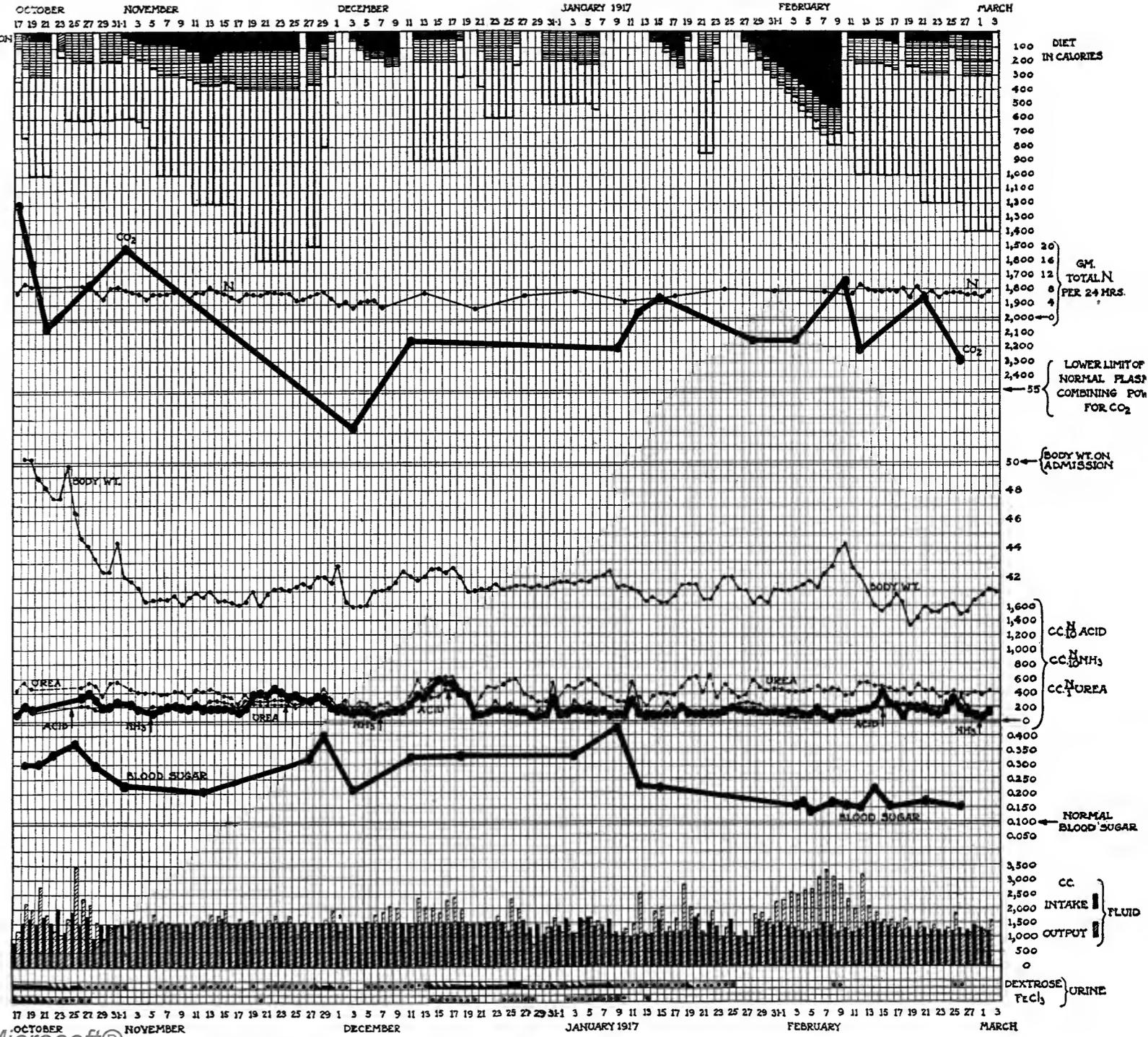
1st ADMISSION 1914



2nd ADMISSION 1916



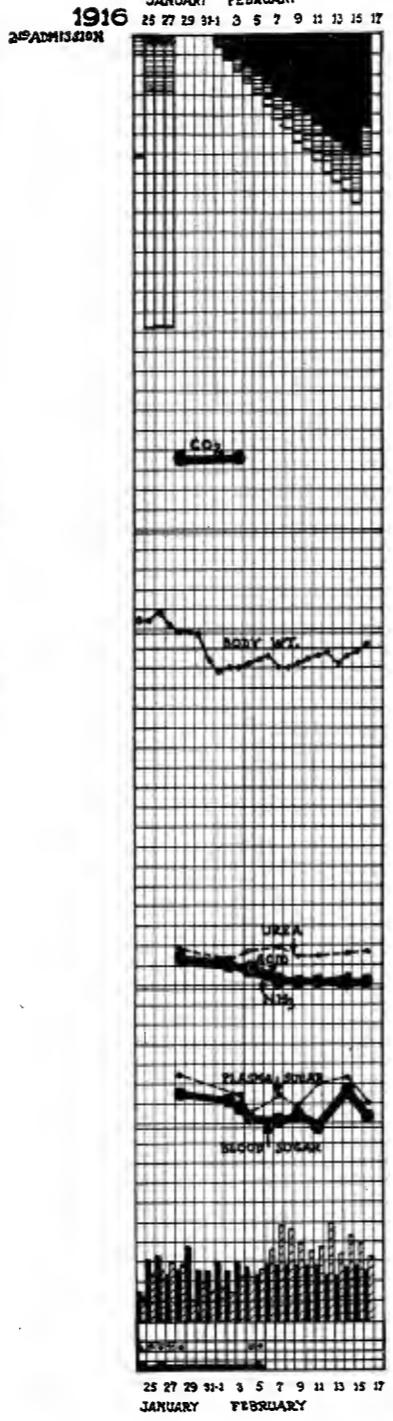
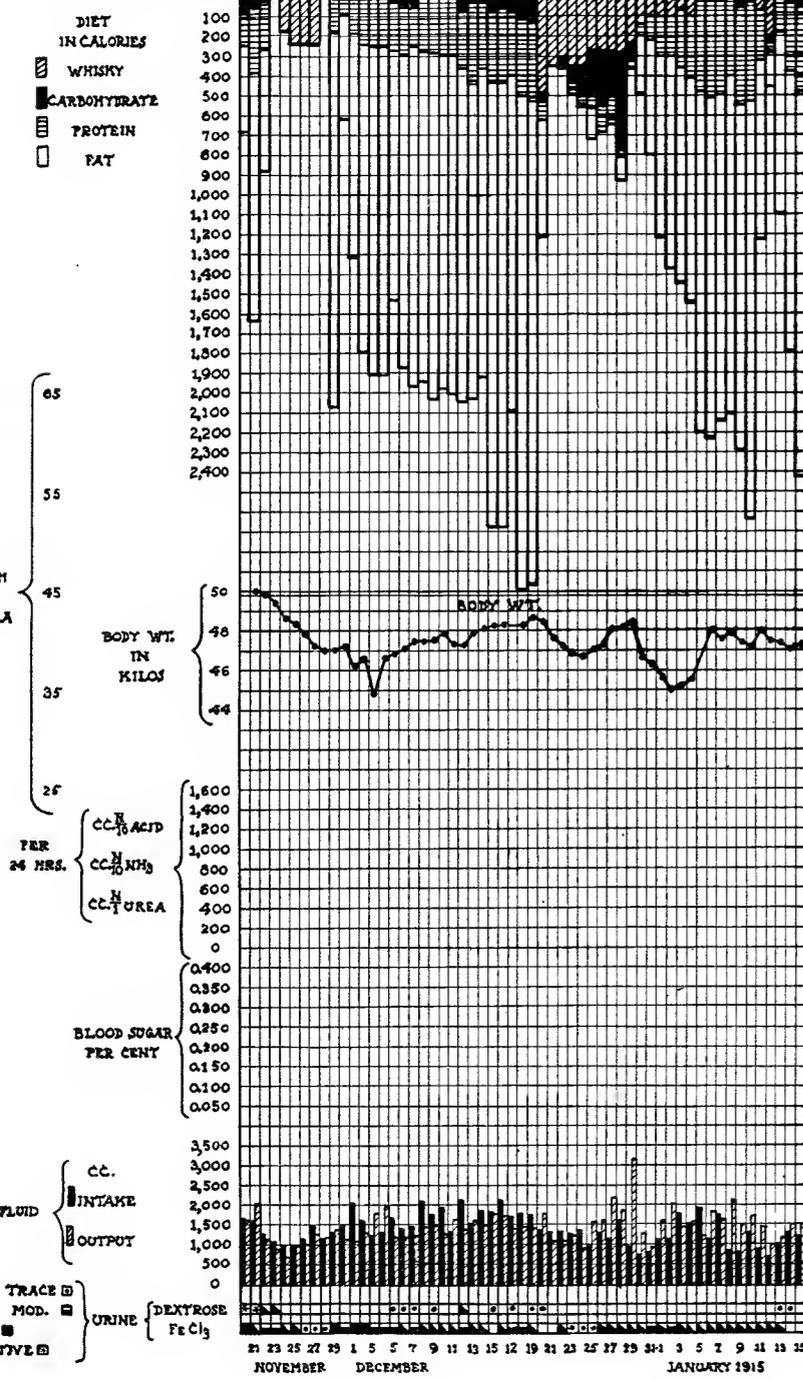
3rd ADMISSION 1916



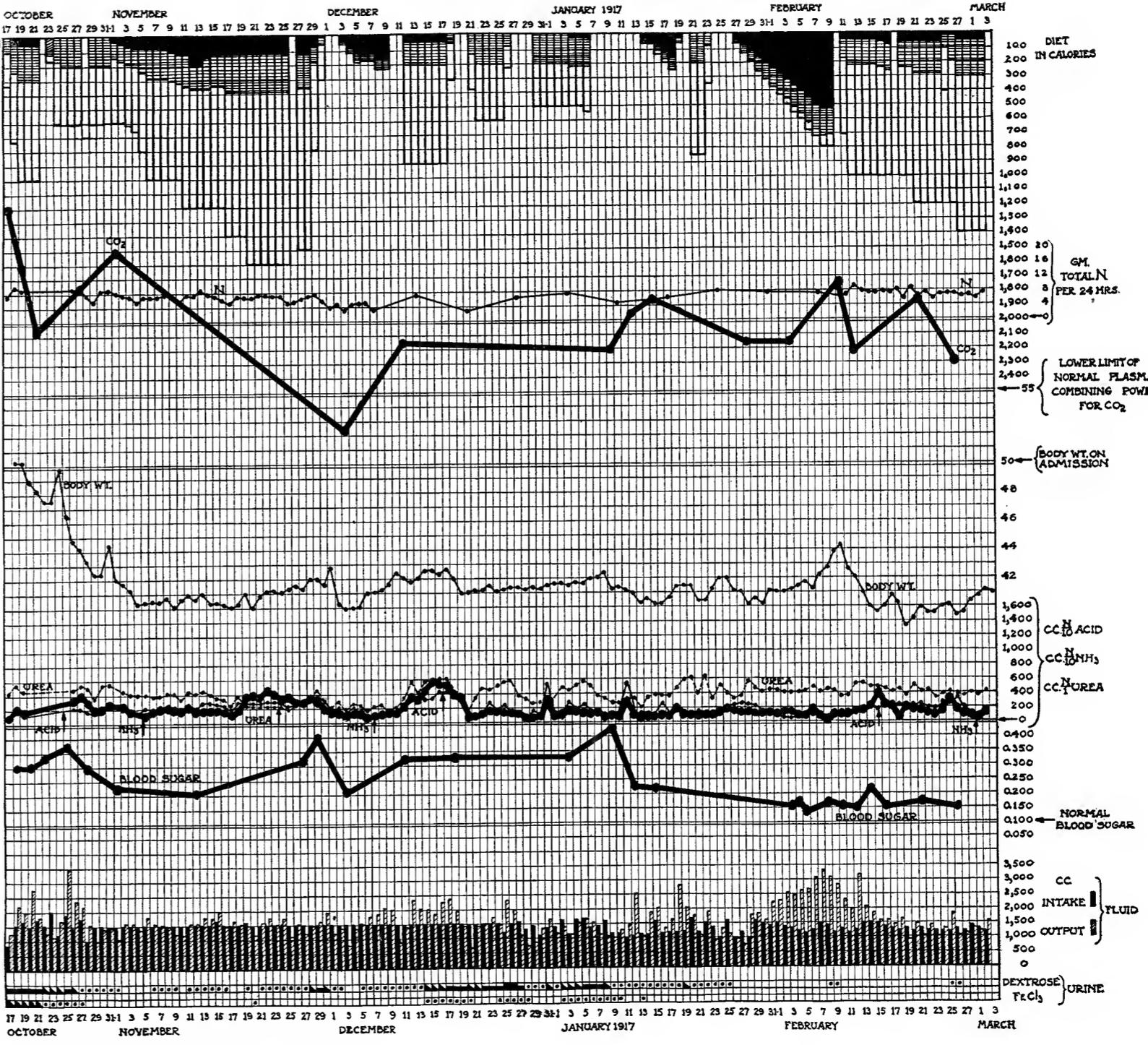
Digitized by Microsoft®
CHART 18. Case No. 22.

CASE NO. 2234

1st ADMISSION 1914



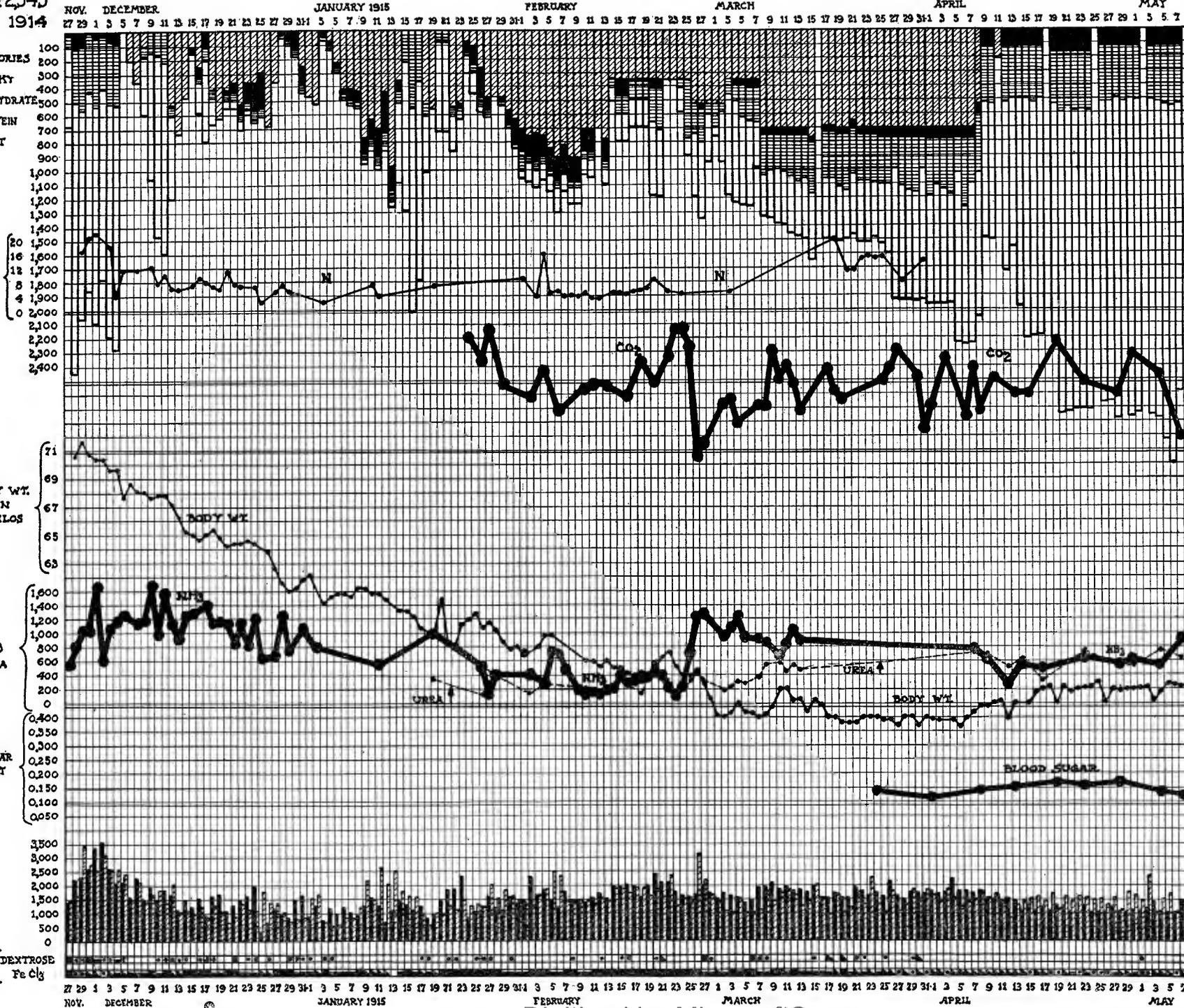
1916



Date.	Glucose excreted in 24 hrs.
1st admission.	
1914 Nov. 20	46.7*
" 21	13.9
2nd admission.	
1916 Jan. 25	3.2
" 27	2.5

* 12 hr. specimen.

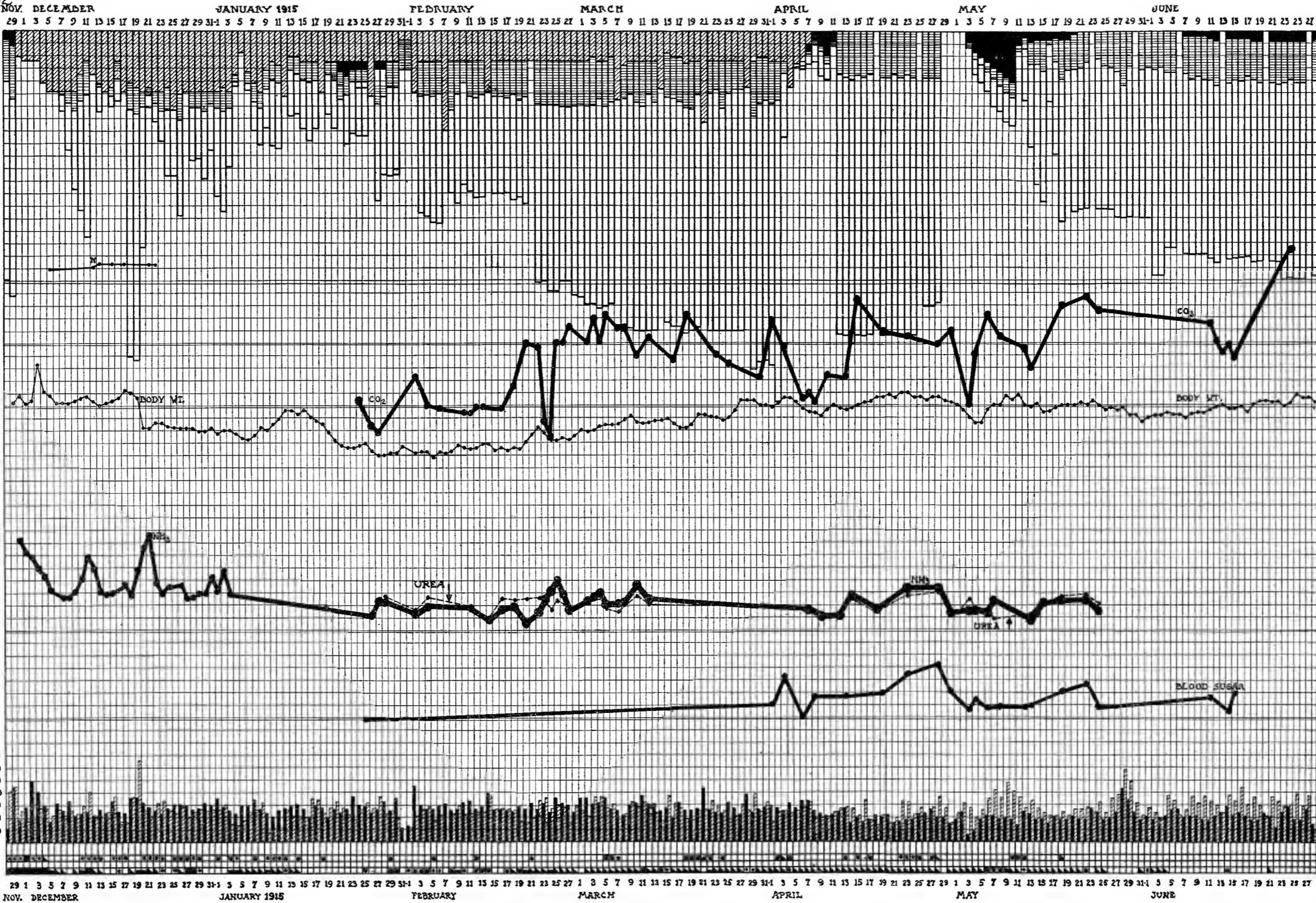
CASE NO. 2343



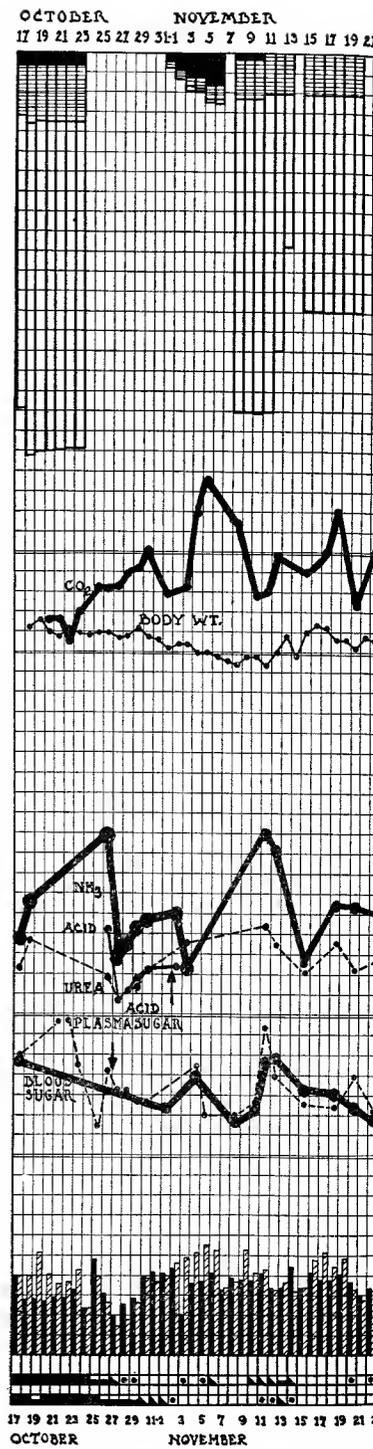
Date.	Glucose excreted in 24 hrs.
1914	
Nov. 28	29.2 gm.
" 29	17.0
Dec. 2	9.1
" 3	10.6
" 5	1.4
" 11	6.5
" 16	1.2
" 17	3.6
" 18	2.3
" 30	2.3
1915	
Jan. 26	1.5

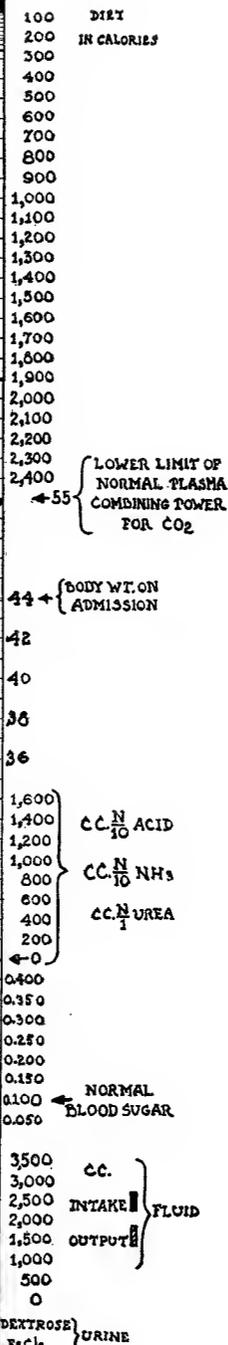
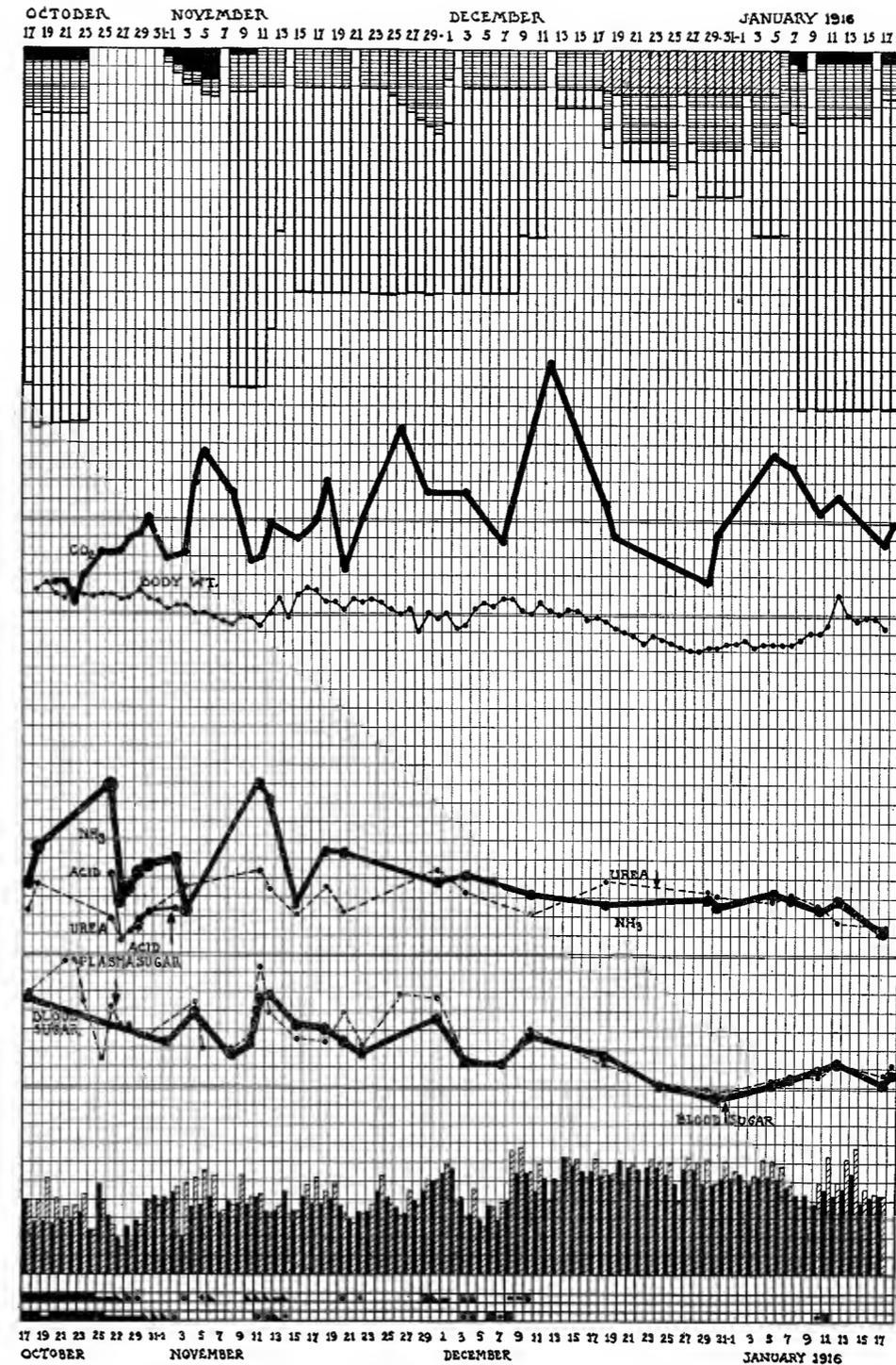
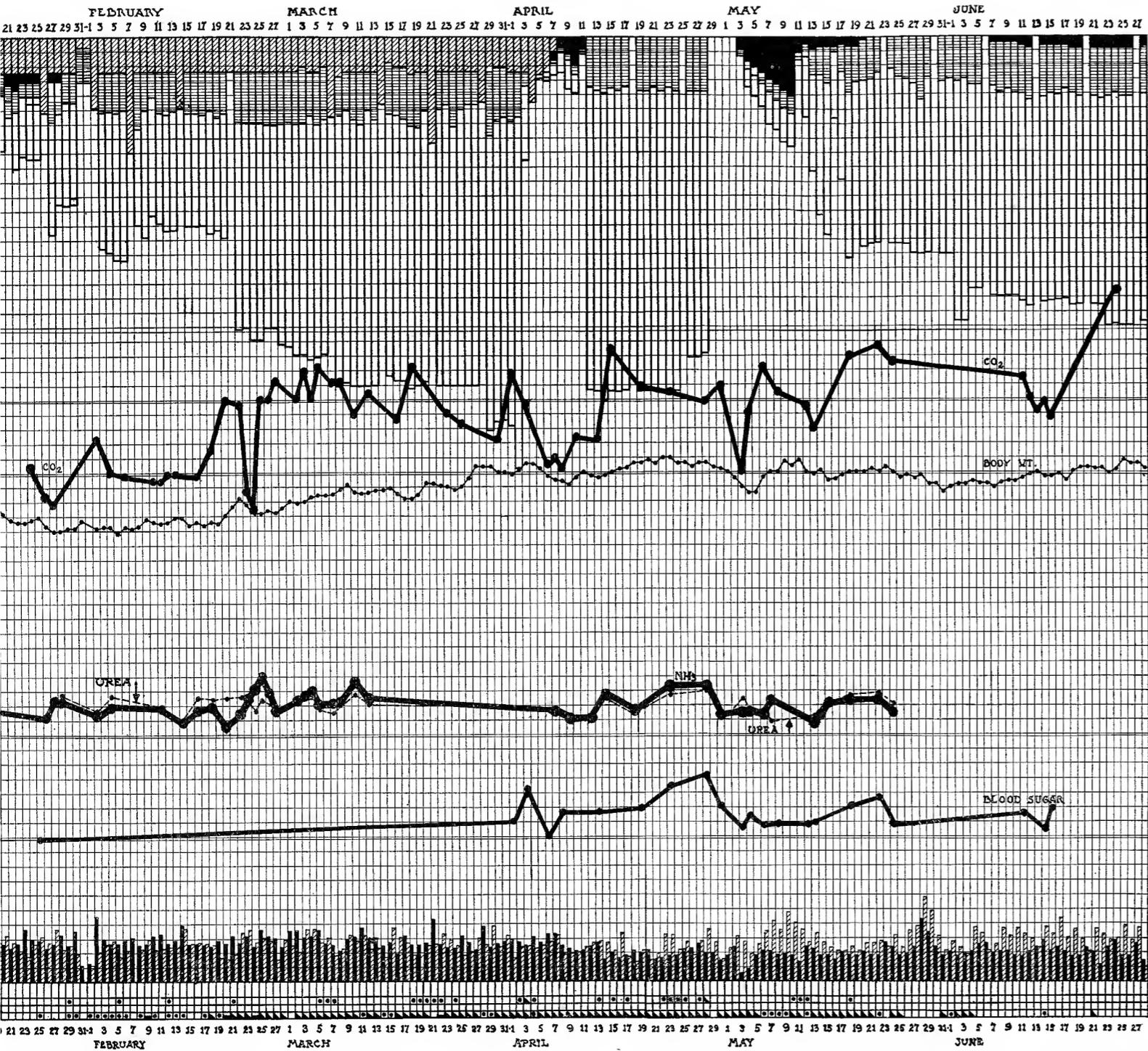
CASE NO. 2382

1st ADMISSION 1914



2nd ADMISSION





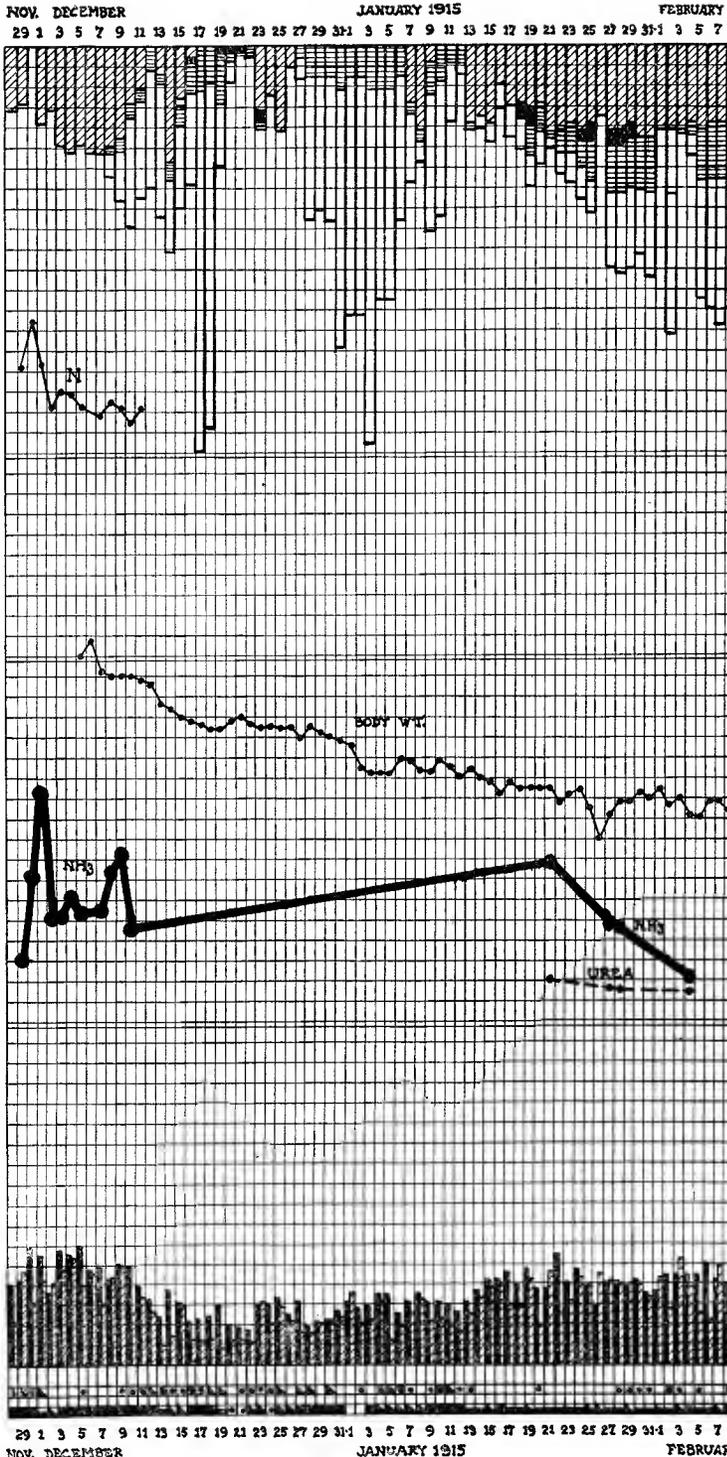
Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	gm.
Nov. 28	46.0*
" 29	45.0
" 30	20.5
Dec. 2	4.5
" 3	2.7
" 10	9.9
" 11	20.4
" 12	5.7
" 15	2.6
" 16	2.7
1915	
Jan. 10	0.7
Apr. 23	6.6
" 24	2.7

* 10 hr. specimen.

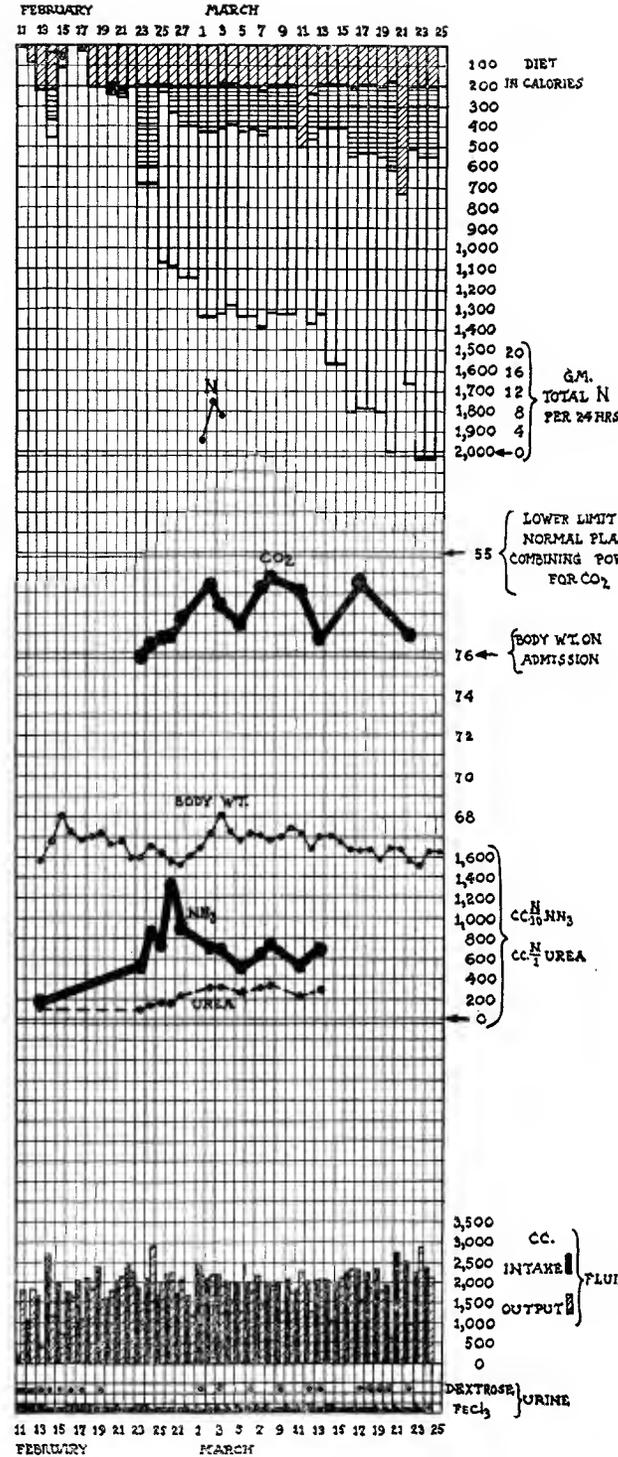
CHART 20. Case No. 24.

CASE NO. 2,255

1st ADMISSION 1914



2nd ADMISSION 1915

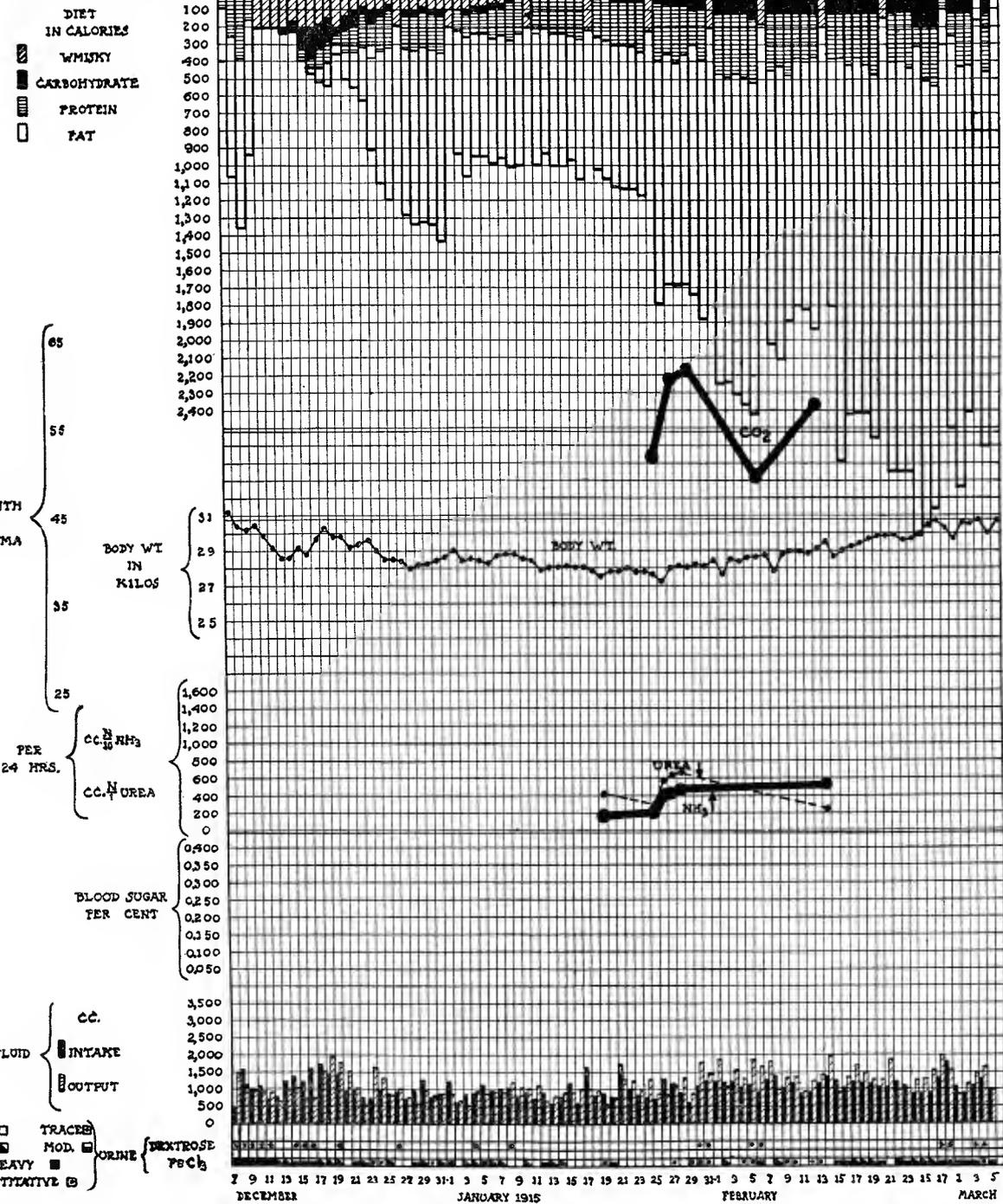


Date.	Glucose excreted in 24 hrs.
1st admission.	
1914	gm.
Nov. 28	10.0*
" 29	14.3
" 30	4.5
Dec. 13	2.2
" 16	1.2
" 17	1.1

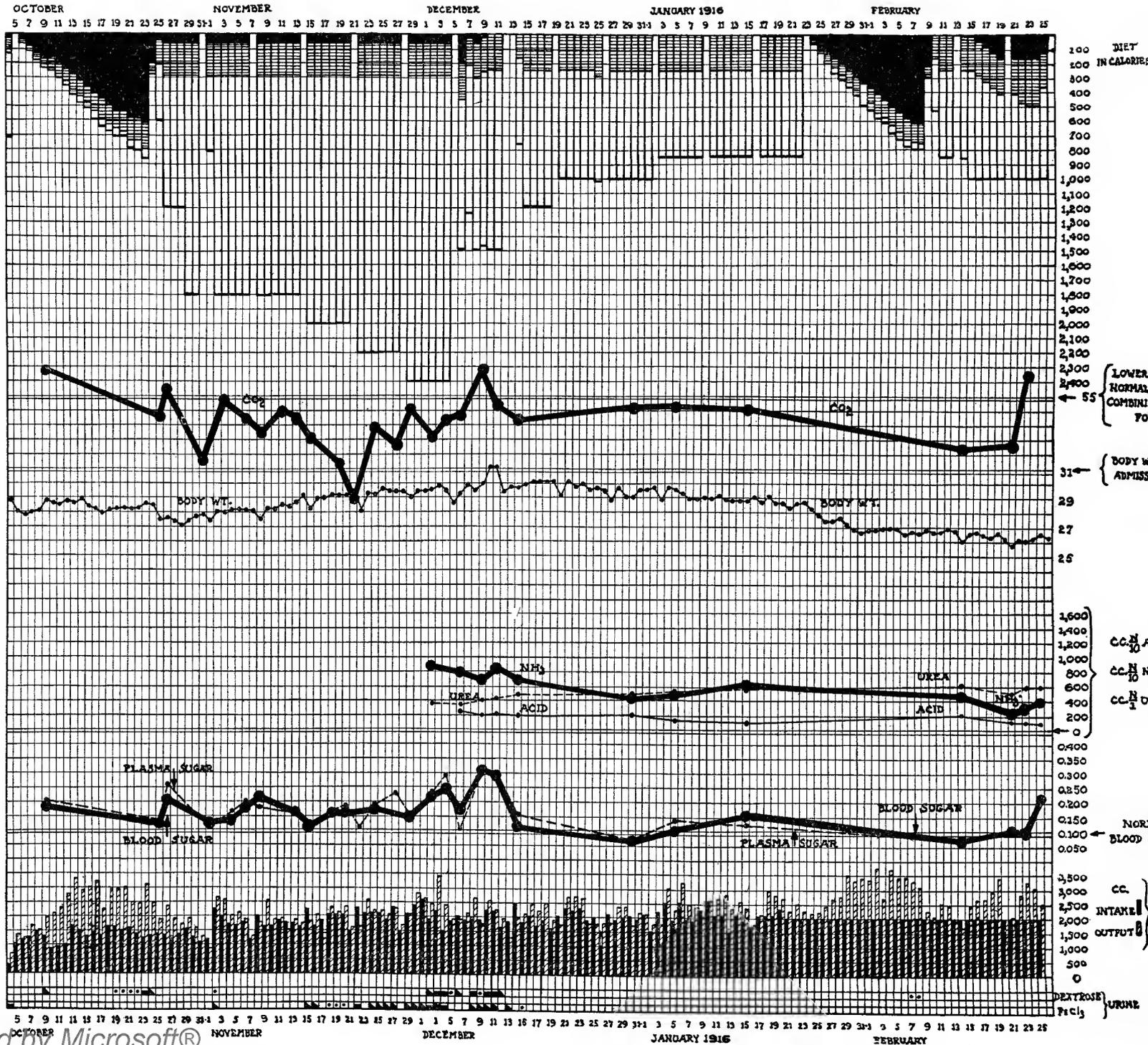
* 18 hr. specimen.

CASE NO. 2280

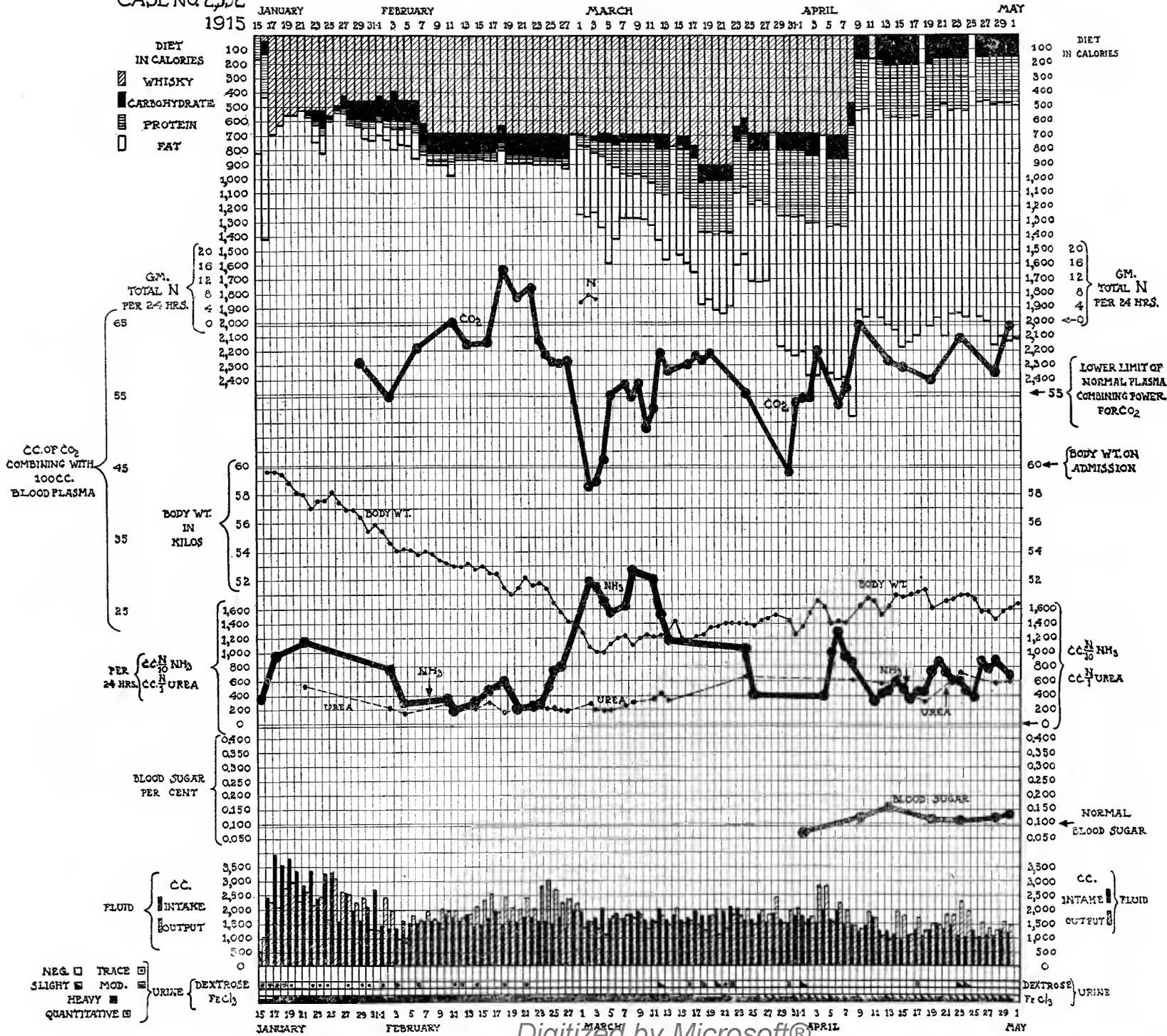
ADMISSION 1914 DECEMBER 7 9 11 13 15 17 19 21 23 25 27 29 31 JANUARY 1915 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 FEBRUARY 3 5 7 9 11 13 15 17 19 21 23 25 27 1 3 5 MARCH



1915
 2nd ADMISSION



CASE NO 2332
1915



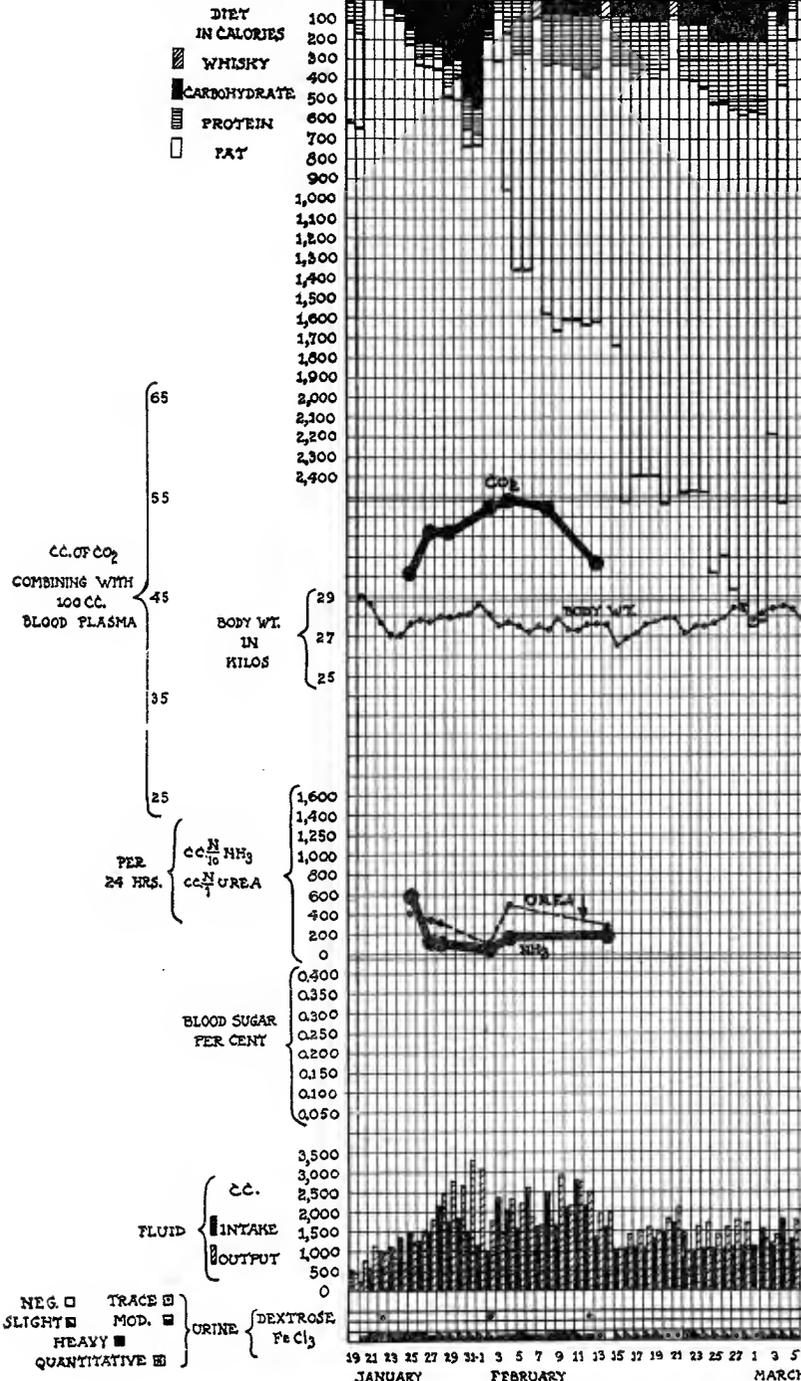
Date.	Glucose excreted in 24 hrs.
1915	gm.
Jan. 15	36.4*
" 16	32.4
" 17	9.7
" 18	6.6

* 12 hr. specimen.

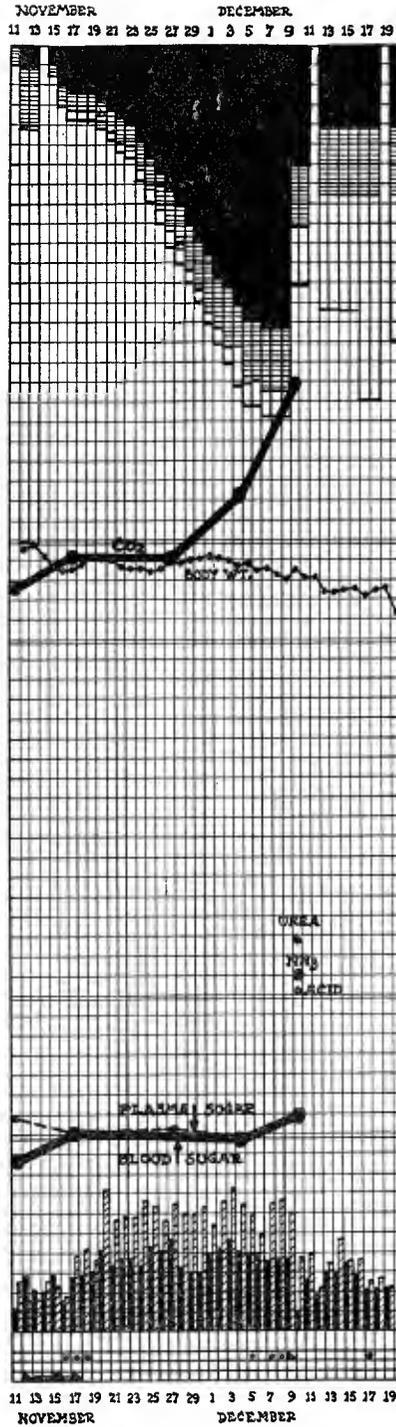
CASE NO. 2279

1st ADMISSION 1915

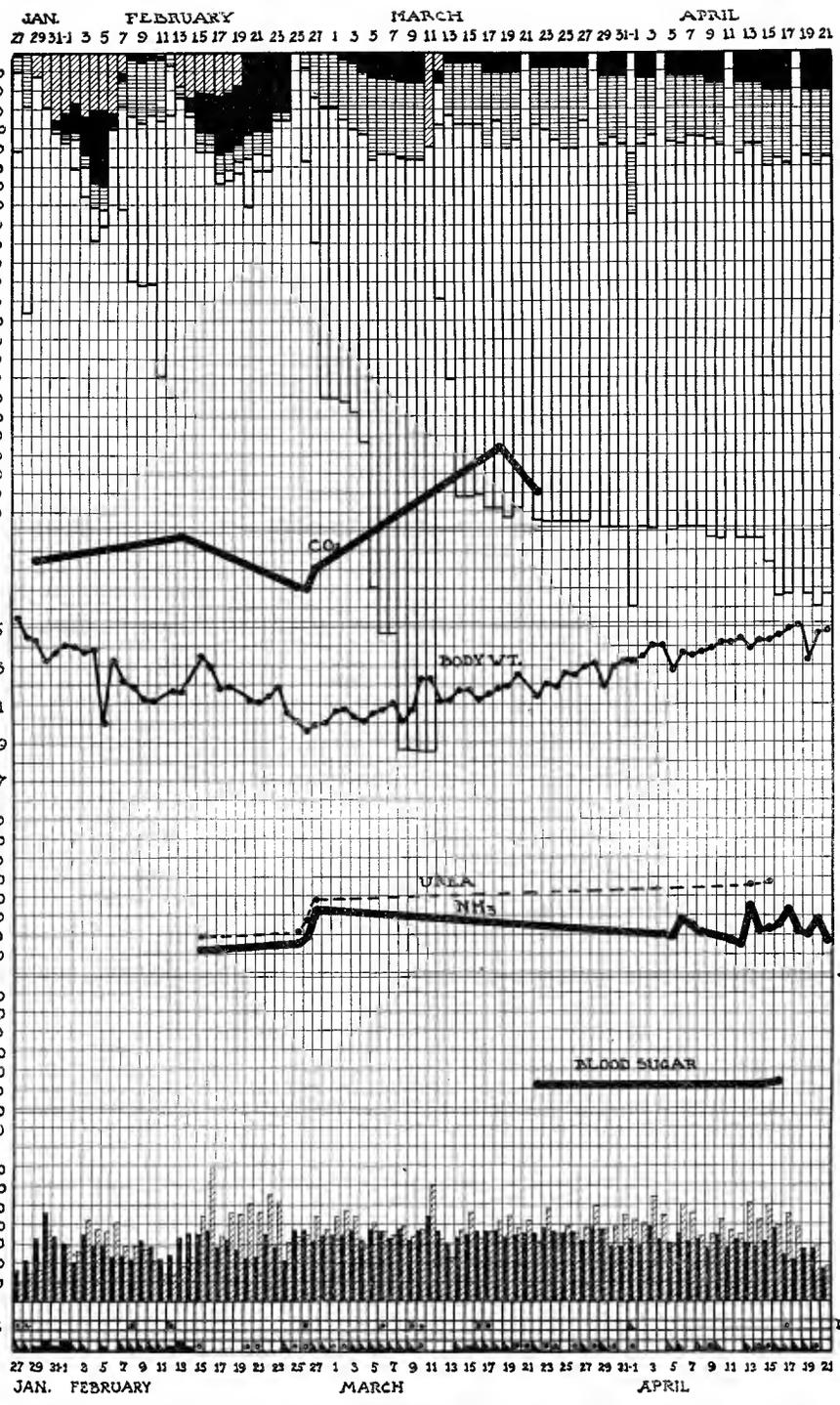
JANUARY FEBRUARY MARCH



1915
2nd ADMISSION



CASE NO. 2,324
1915



100 DIET IN CALORIES
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500
1,600
1,700
1,800
1,900
2,000
2,100
2,200
2,300
2,400

← 55 LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂

45 ← BODY WT. ON ADMISSION

1,600
1,400
1,200
1,000
800
600
400
200
← 0
0.400
0.350
0.300
0.250
0.200
0.150
← 0.100 NORMAL
0.050 BLOOD SUGAR

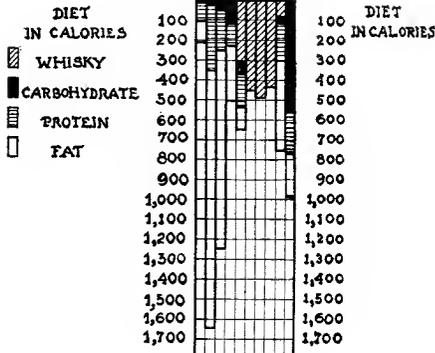
3,500 CC. FLUID
3,000 INTAKE
2,500
2,000
1,500 OUTPUT
1,000
500
0

DEXTROROSE URINE
FECES

Date.	Glucose excreted in 24 hrs.
1915	gm.
Jan. 27	7.5*
" 28	2.1

* 12 hr. specimen.

CASE NO. 2,257
 1915 JAN. 31 5 5 7 FEB.



Date.	Glucose excreted in 24 hrs.
1915	gm.
Feb. 3	5.5
" 7	10.1
" 8	*

* Incontinence of urine. Unable to collect specimen.

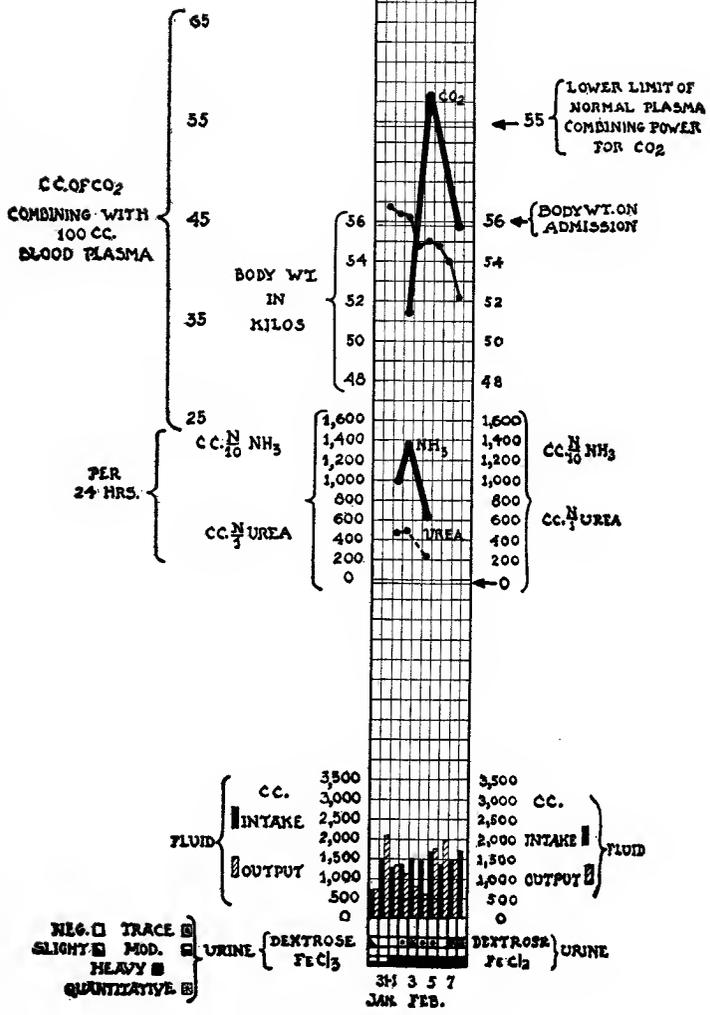
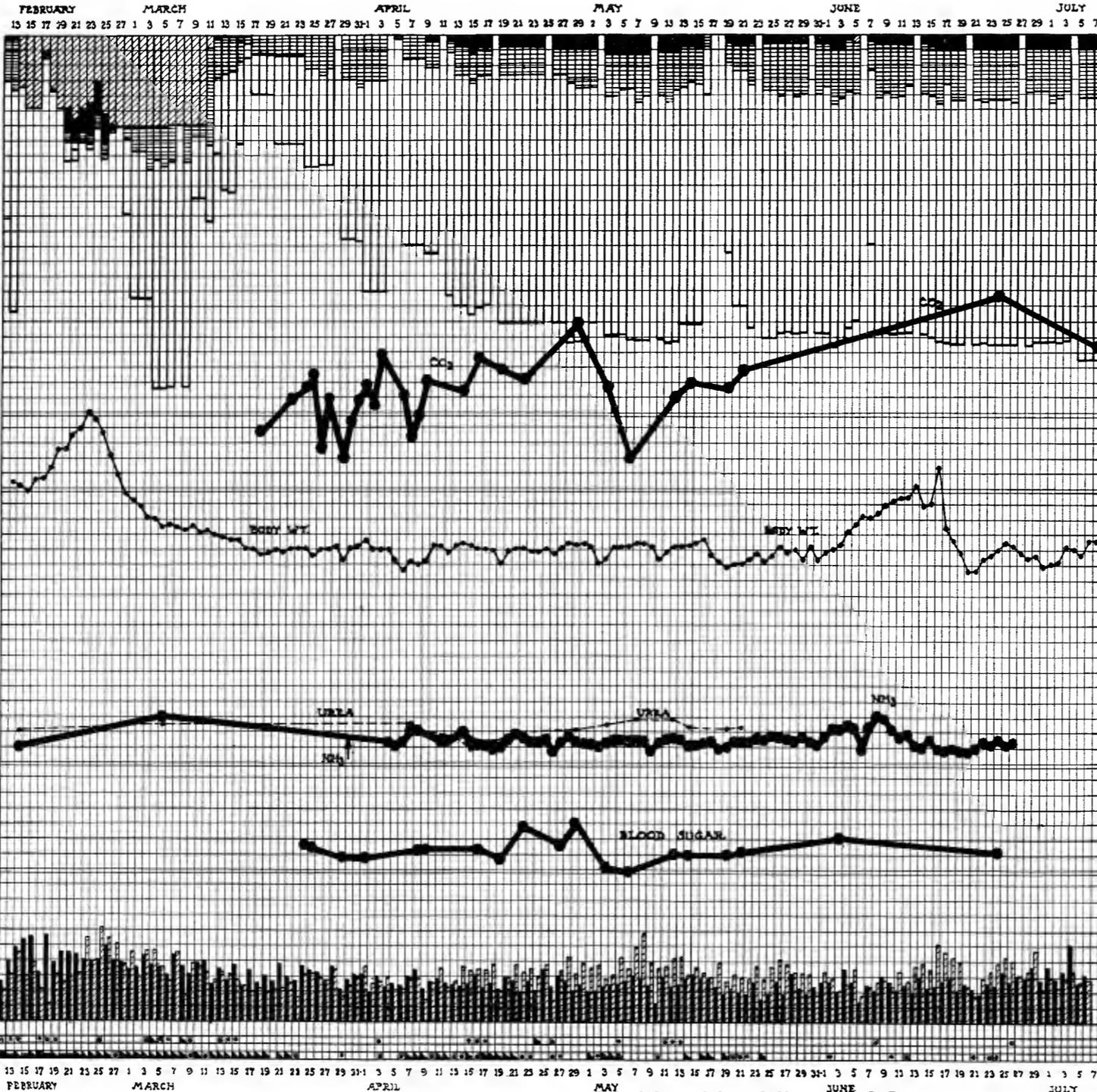


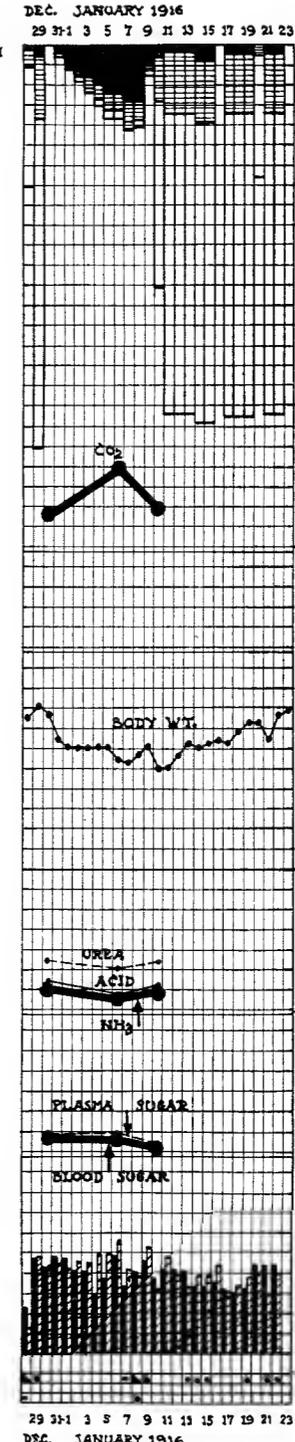
CHART 26. Case No. 30.

CASE NO. 2,389

1st ADMISSION 1915



2nd ADMISSION 1915

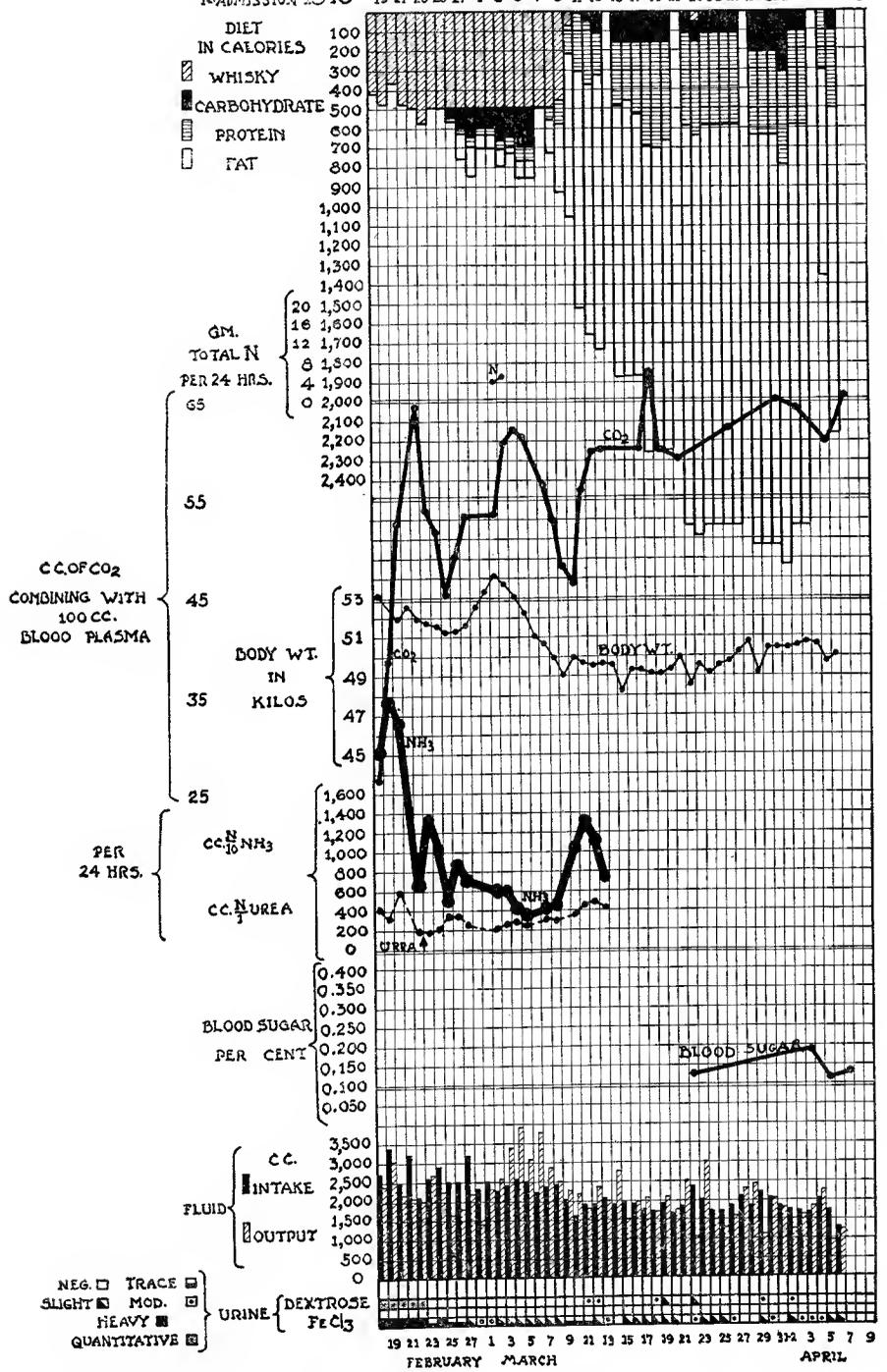


Date.	Glucose excreted in 24 hrs.
1st admission.	
1915	gm.
Feb. 12	48.6*
" 13	31.3
" 14	1.4
" 25	0.1
Mar. 5	0.5
" 13	5.3
" 14	2.3

* 18 hr. specimen.

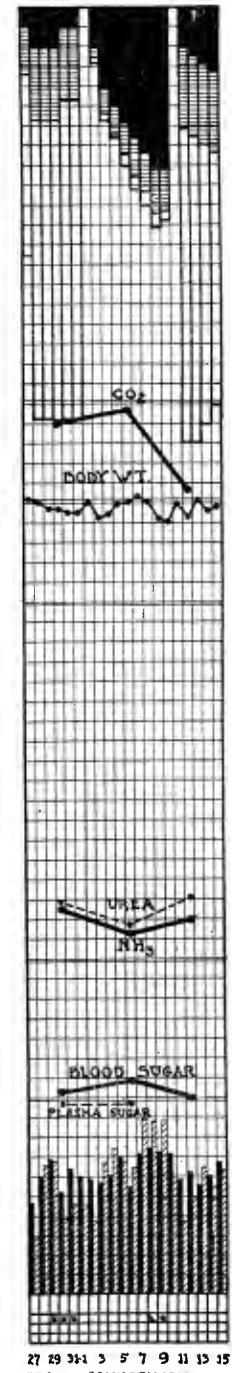
CASE NO. 2312

FEBRUARY MARCH APRIL
1915



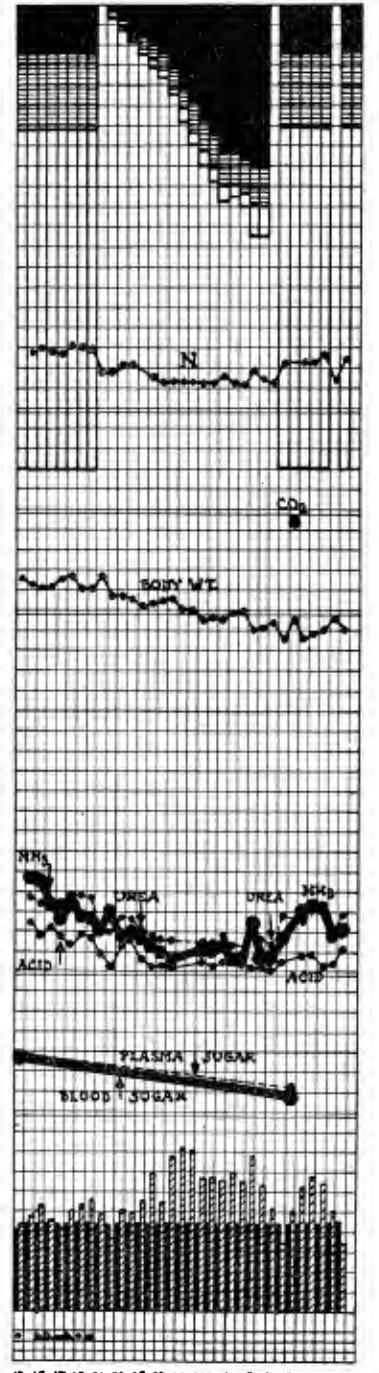
2nd ADMISSION

DEC. JANUARY 1916



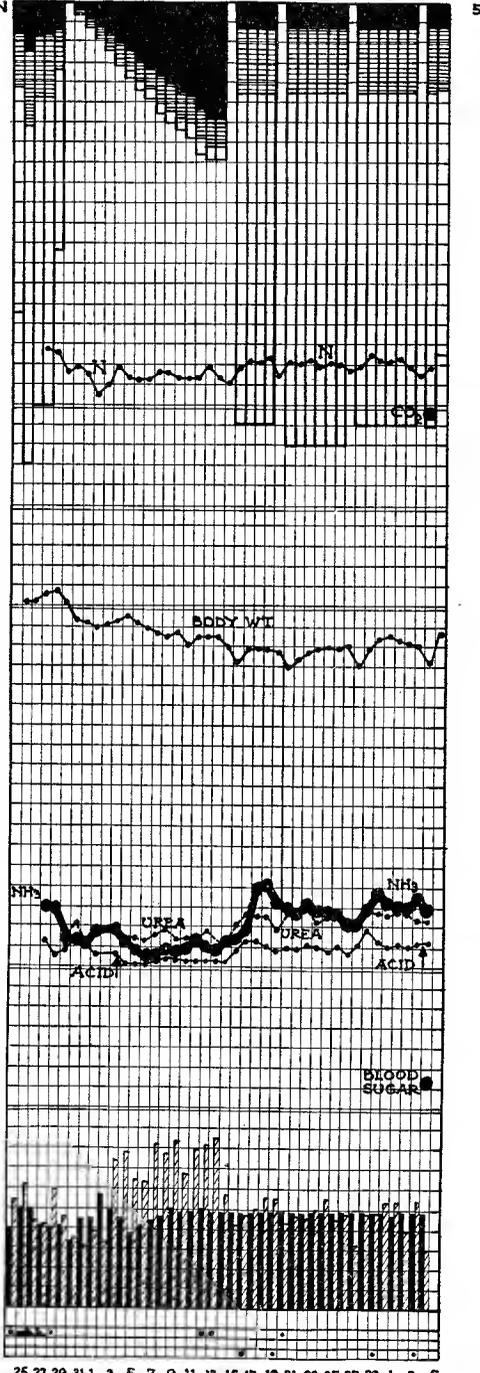
3rd ADMISSION

JULY AUGUST 1916



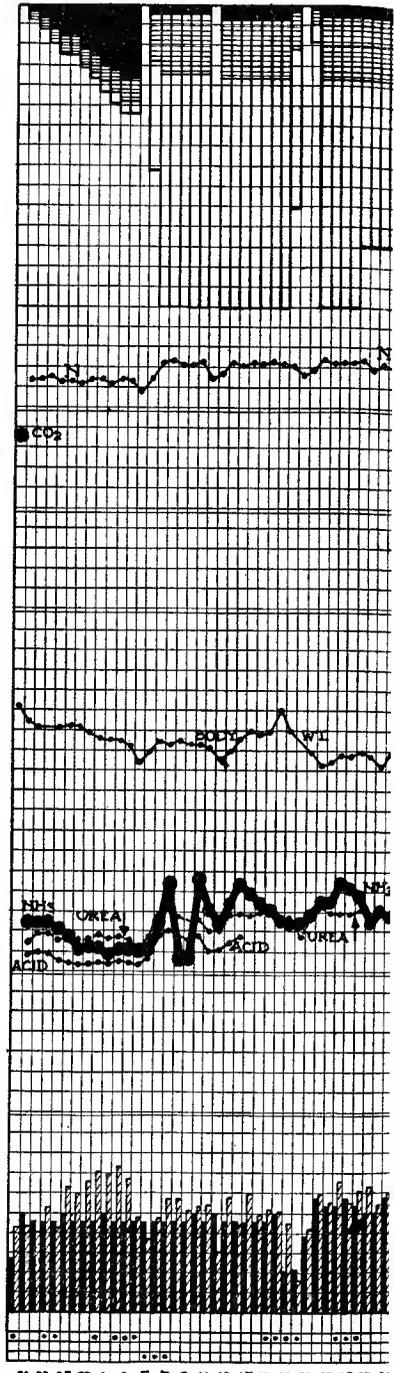
4th ADMISSION

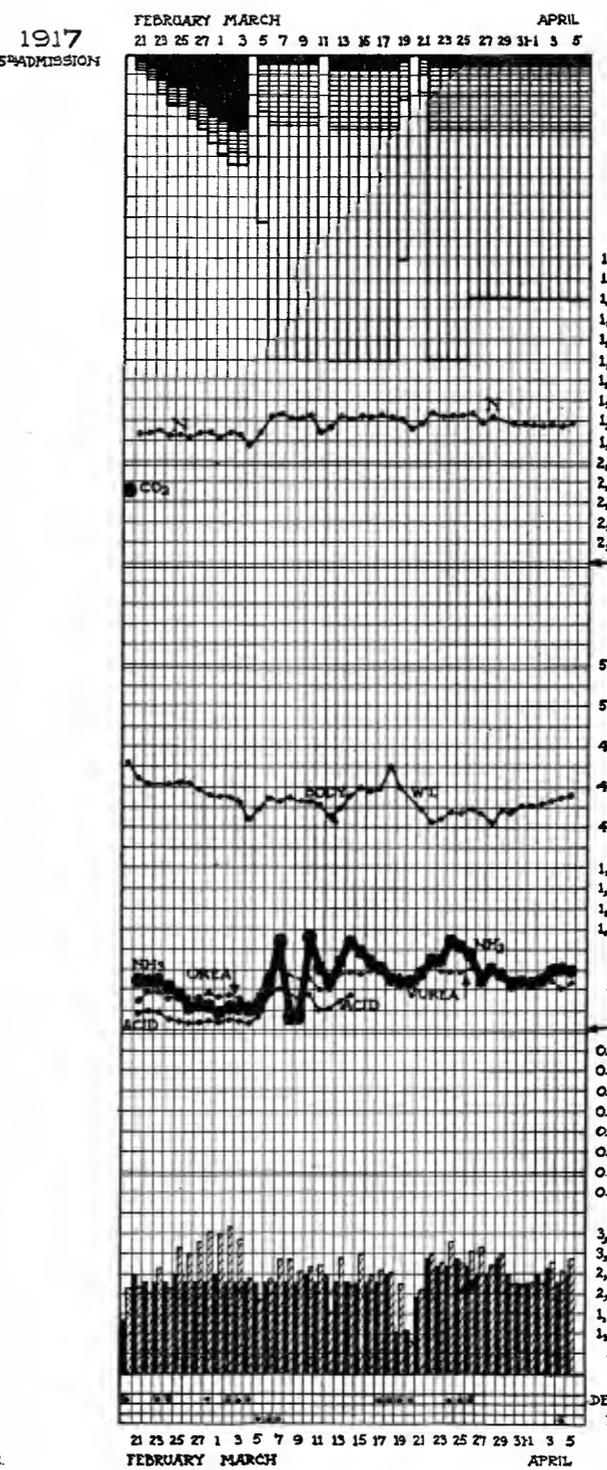
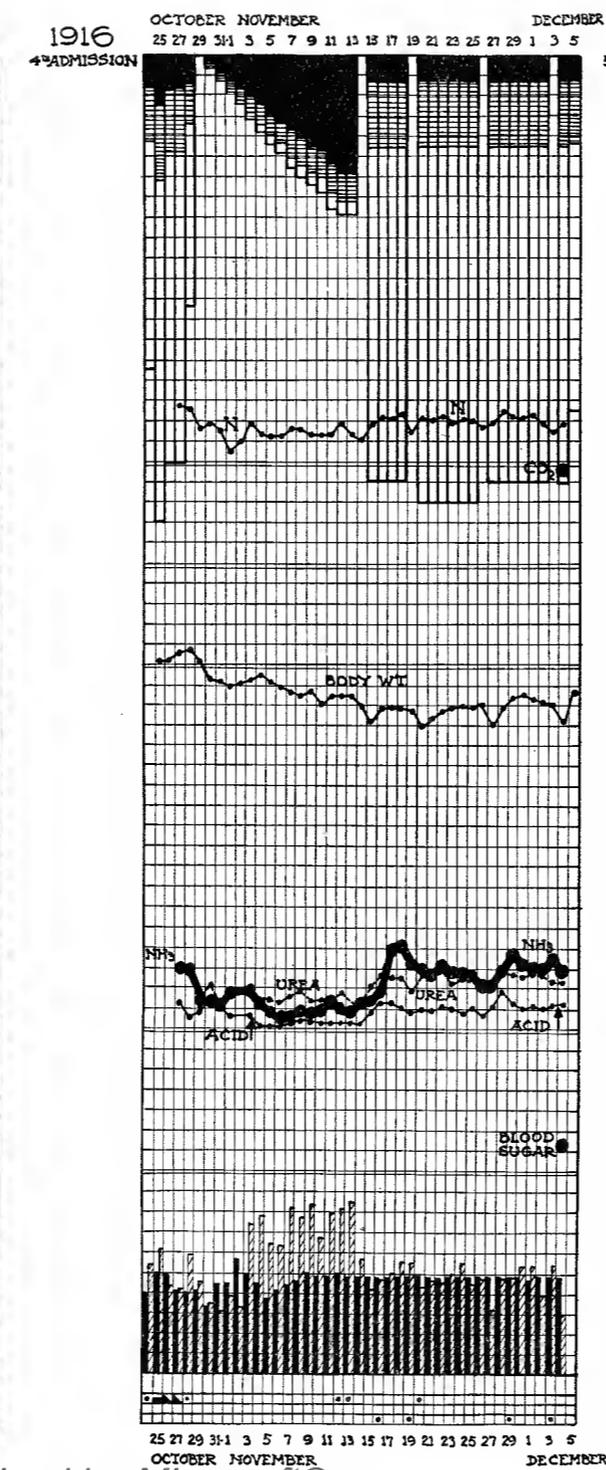
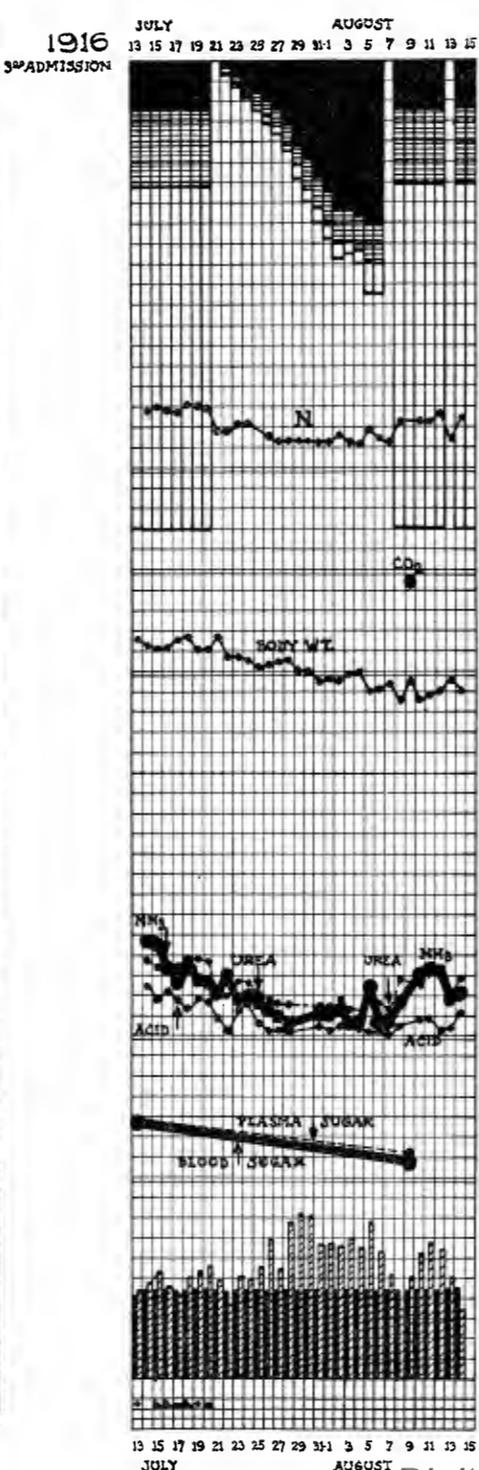
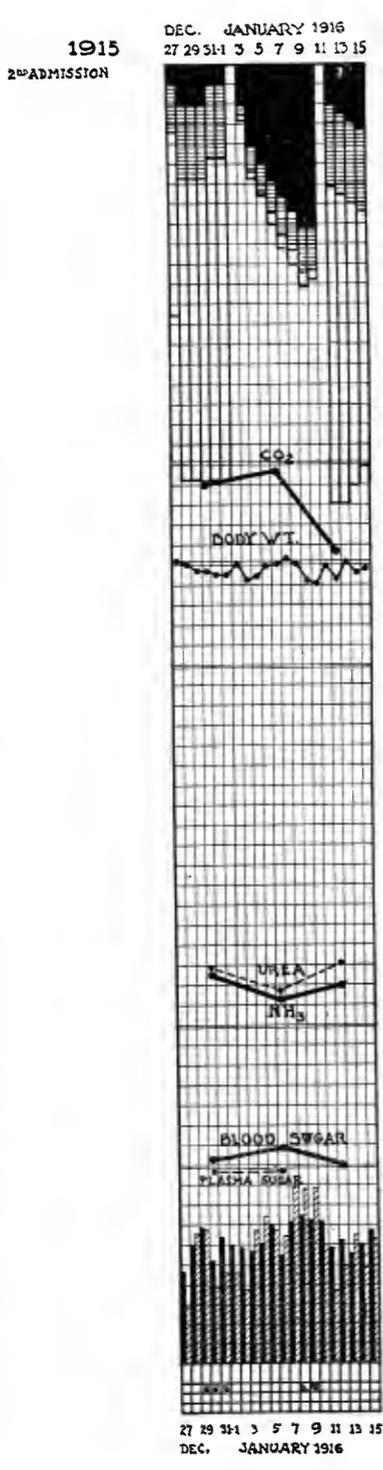
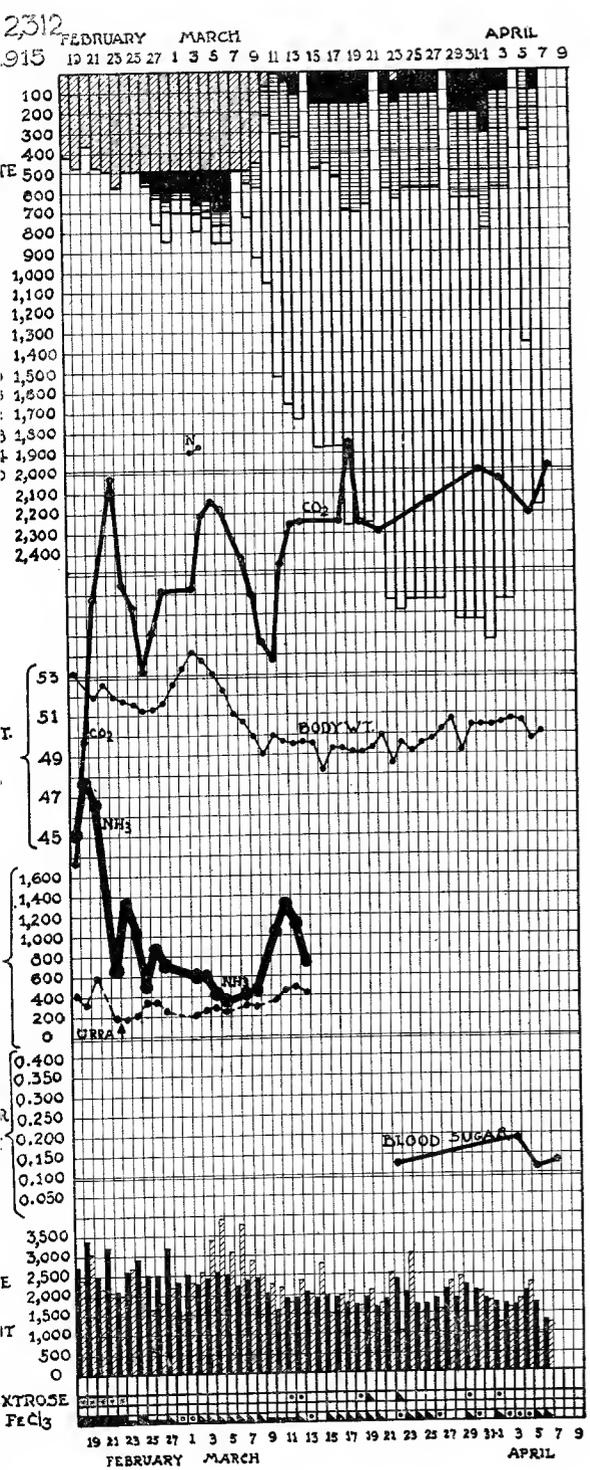
OCTOBER NOVEMBER DECEMBER 1916



5th ADMISSION

FEBRUARY MARCH 1917





DIET
INCALORIES

GM. TOTAL N
PER 24 HRS.

LOWER LIMIT OF
NORMAL PLASMA
COMBINING POWER
FOR CO₂

BODY WT ON
ADMISSION

CC. NH₃ ACID
CC. NH₃ NH₃
CC. NH₃ UREA

NORMAL
BLOOD SUGAR

CC. FLUID
INTAKE
OUTPUT

DEXTROSE
URINE
FeCl₃

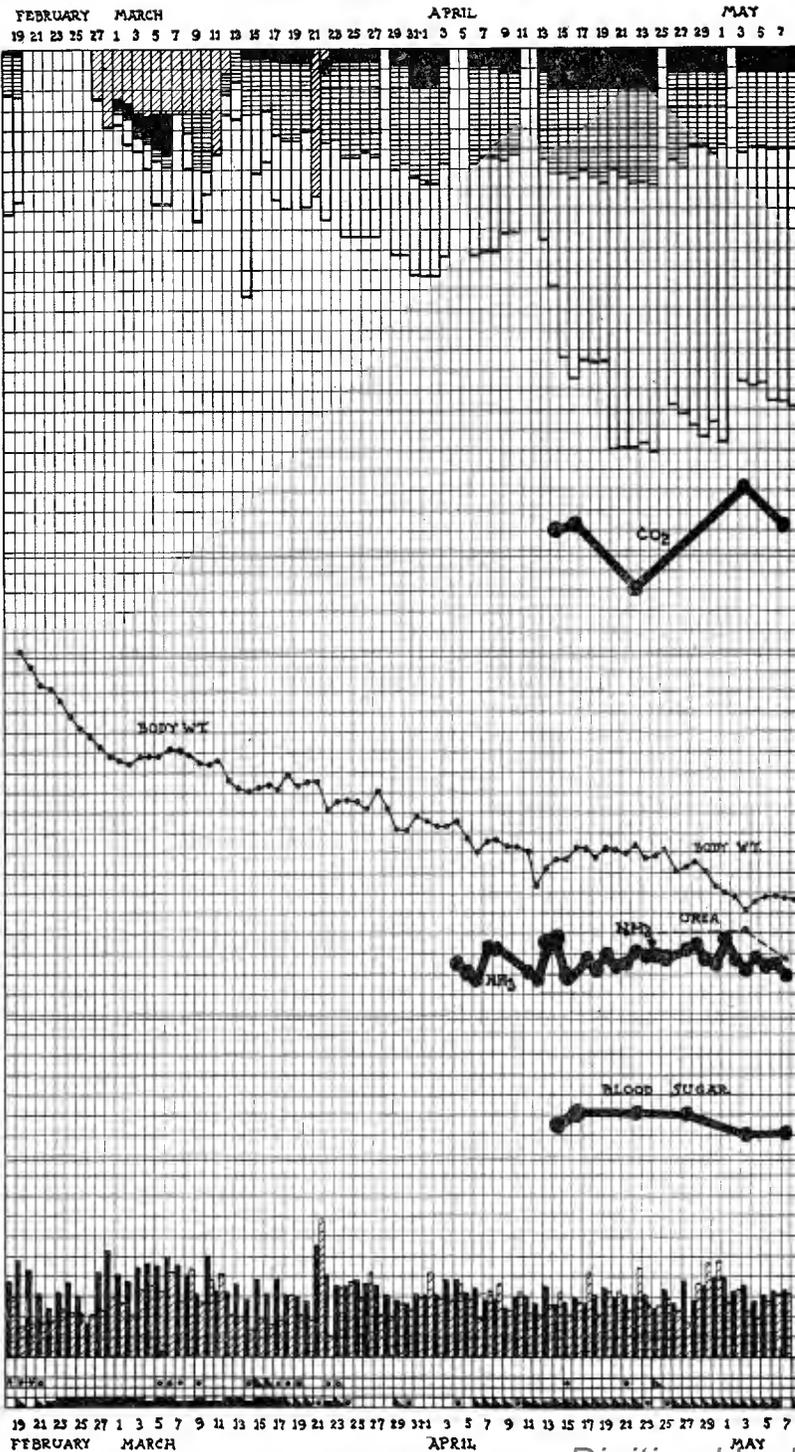
Date.	Glucose excreted in 24 hrs.
1st admission.	
1915	gm.
Feb. 18	39.6*
" 19	34.2
" 20	12.2
" 21	10.7
" 22	2.0

* 16 1/2 hr. specimen.

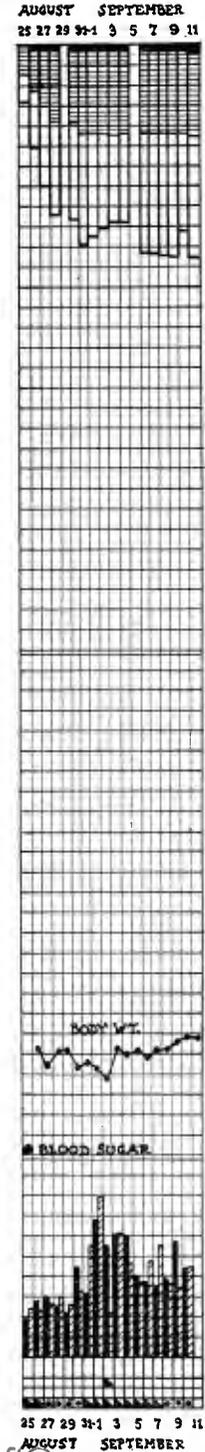
CHART 28. Case No. 32. Digitized by Microsoft®

CASE NO. 2341

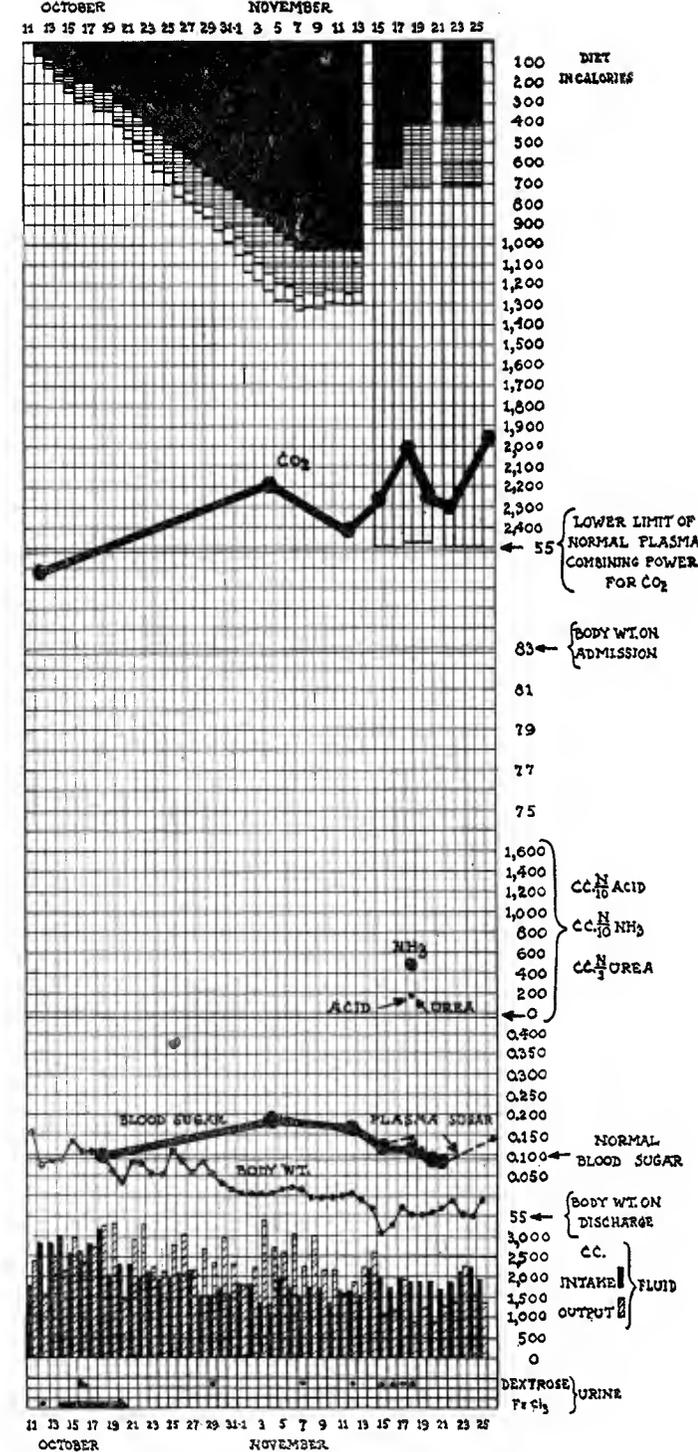
1st ADMISSION 1915



2nd ADMISSION



3rd ADMISSION



DIET IN CALORIES
 WHISKY
 CARBOHYDRATE
 PROTEIN
 FAT

CC. OF CO₂ COMBINING WITH 100CC. BLOOD PLASMA

BODY WT. IN KILOGS

PER 24 HRS. $\frac{CC. N}{10} NH_3$
 $\frac{CC. N}{1} UREA$

BLOOD SUGAR PER CENT

FLUID INTAKE OUTPUT

URINE DEXTROSE
 FeCl₃

NEG. □ TRACE □
 SLIGHT □ MOD. □
 HEAVY ■ QUANTITATIVE ■

100 DIET IN CALORIES
 200
 300
 400
 500
 600
 700
 800
 900
 1,000
 1,100
 1,200
 1,300
 1,400
 1,500
 1,600
 1,700
 1,800
 1,900
 2,000
 2,100
 2,200
 2,300
 2,400

← 55 LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂

83 ← BODY WT. ON ADMISSION

81
 79
 77
 75

1,600
 1,400
 1,200
 1,000
 800
 600
 400
 200
 0

CC. N/10 ACID
 CC. N/10 NH₃
 CC. N/1 UREA

← 0

0.400
 0.350
 0.300
 0.250
 0.200
 0.150
 0.100
 0.050

← 0.150 NORMAL BLOOD SUGAR

55 ← BODY WT. ON DISCHARGE

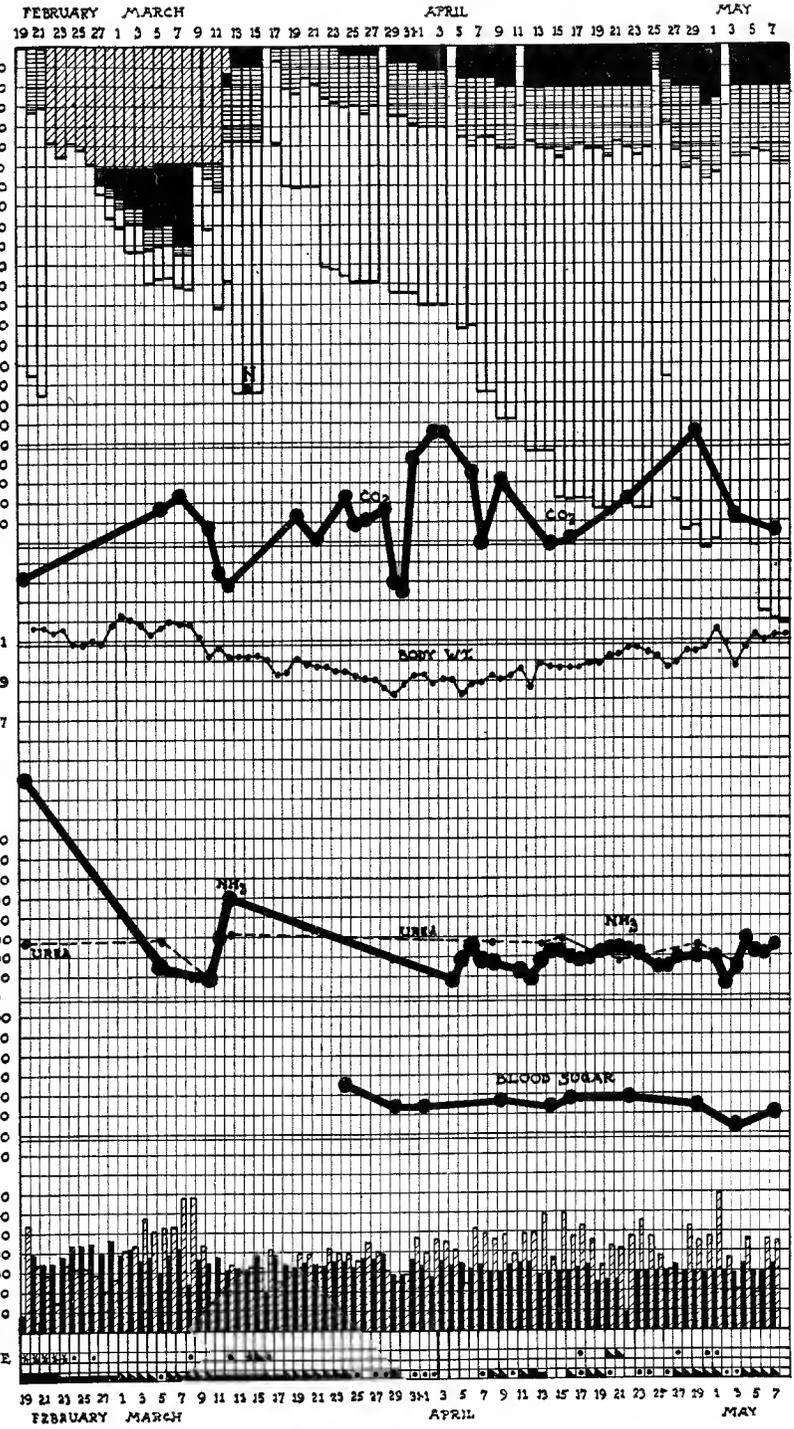
3,000
 2,500
 2,000
 1,500
 1,000
 500
 0

INTAKE OUTPUT

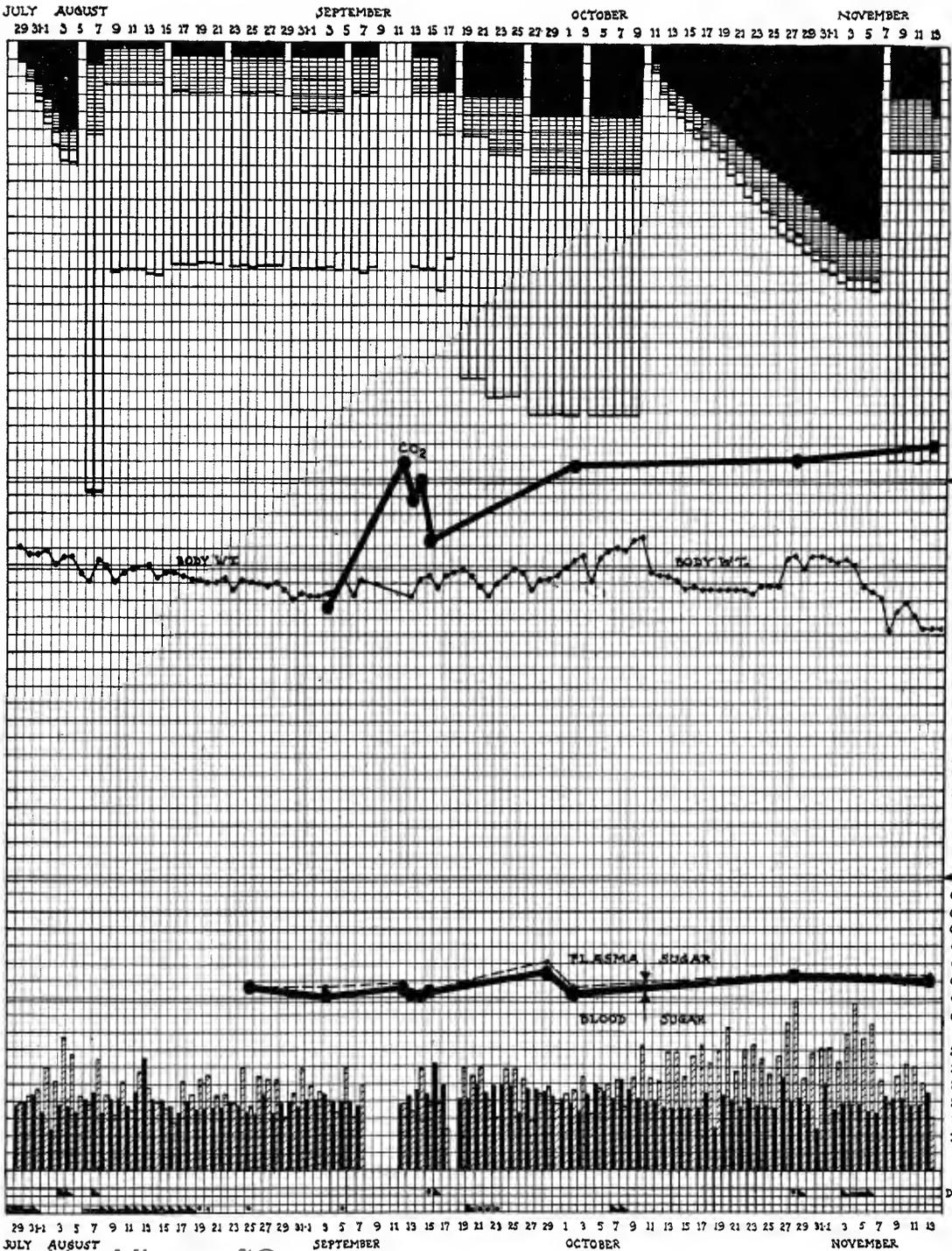
DEXTROSE URINE
 FeCl₃

CASE NO. 2,342

1st ADMISSION 1915



2nd ADMISSION



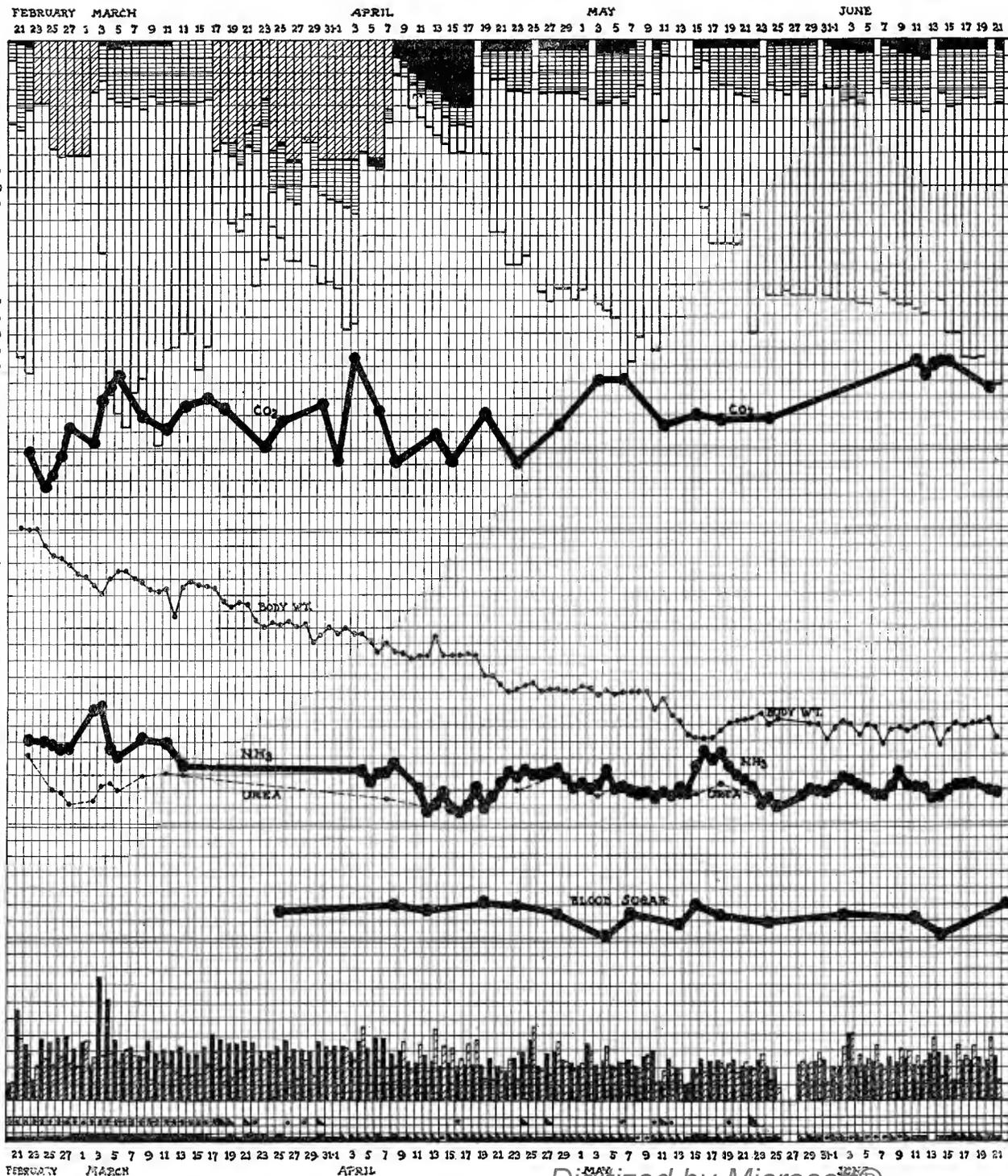
Date.	Glucose excreted in 24 hrs.
-------	-----------------------------

1st admission.	
1915	gm.
Feb. 19	150.0*
" 20	33.2
" 21	18.7
" 22	8.7
" 23	1.2
Mar. 14	2.0

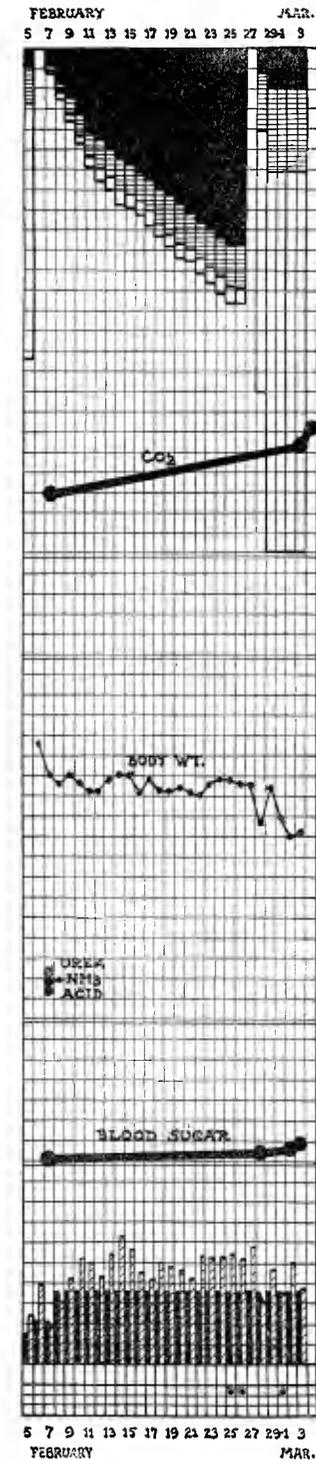
* 17 hr. specimen.

CASE NO. 2,374

1st ADMISSION 1915

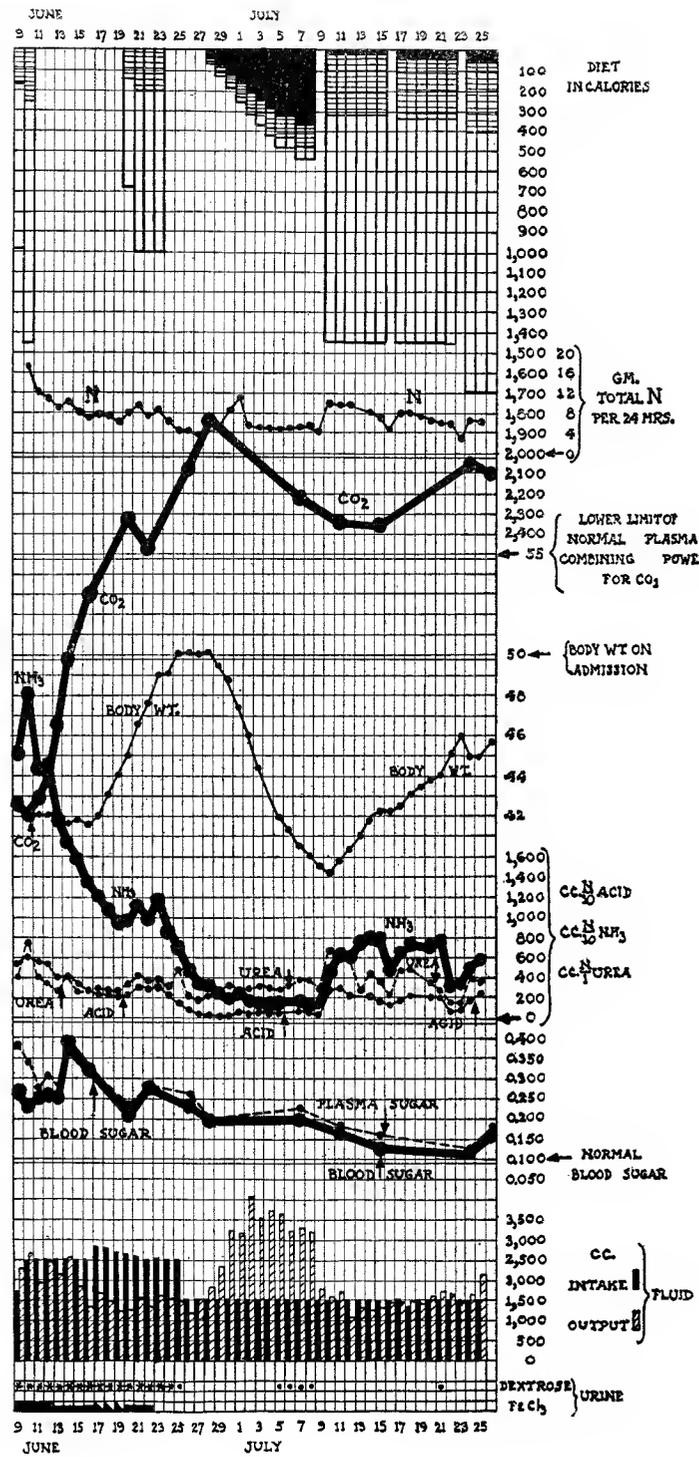
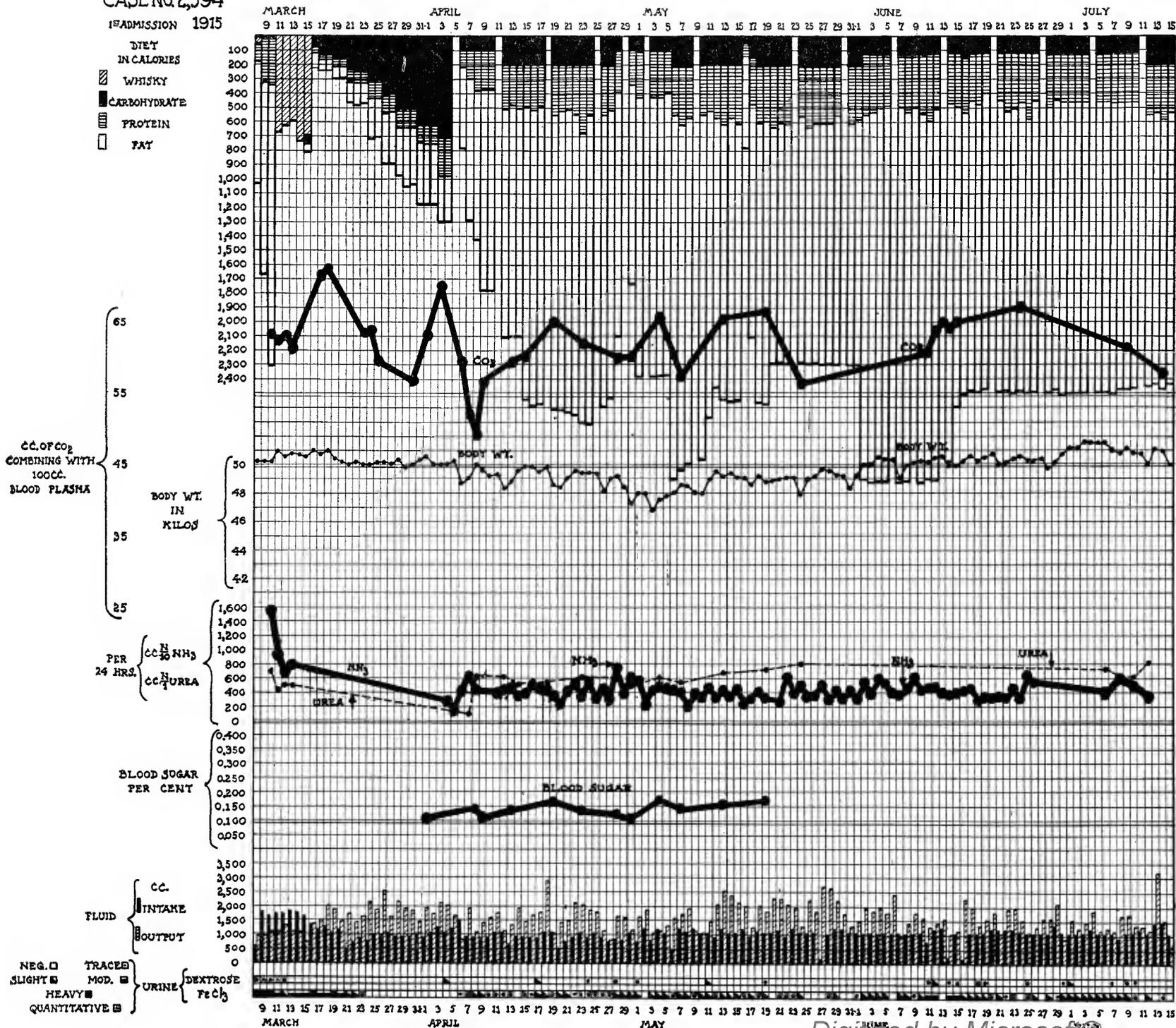


2nd ADMISSION



Date.	Glucose excreted in 24 hrs.
1 st admission.	
1915	gm.
Feb. 20	21.0*
" 21	25.0
" 22	22.0
" 23	14.2
" 24	5.7
" 25	2.8
" 26	2.0
" 28	1.5
Mar. 2	1.7
" 3	11.9
" 4	16.8
" 5	14.6
" 6	16.0
" 7	10.9
" 8	16.6
" 9	5.4
" 10	11.5
" 11	12.4
" 12	18.3
" 13	8.7
" 14	8.1
" 15	4.7
" 16	10.1
" 17	11.5

* 14 hr. specimen.



Date.	Glucose excreted in 24 hrs.
-------	-----------------------------

1st admission.

1915	gm.
Mar. 8	18.1*
" 9	10.4
" 10	14.6
" 11	2.5

2nd admission.

1916	gm.
June 9	57.2†
" 10	68.0
" 11	25.6
" 12	18.3
" 13	15.3
" 14	10.3
" 15	15.3
" 16	10.6
" 17	7.5
" 18	4.9
" 19	5.9
" 20	5.9
" 21	17.2
" 22	15.6
" 23	19.4
" 24	10.0

* 10 hr. specimen.
† 18 " "

CASE NO. 2414
1st ADMISSION 1915

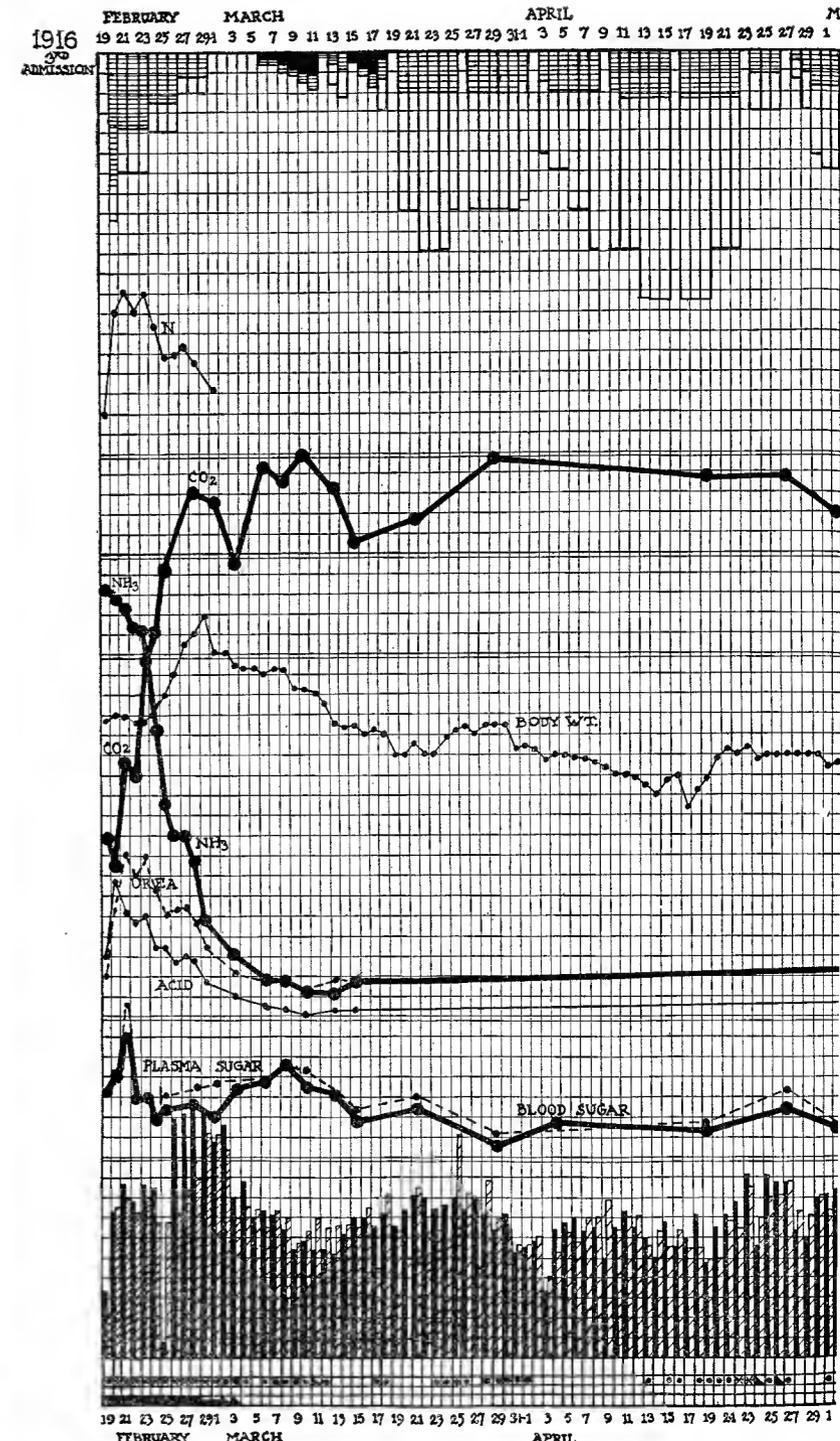
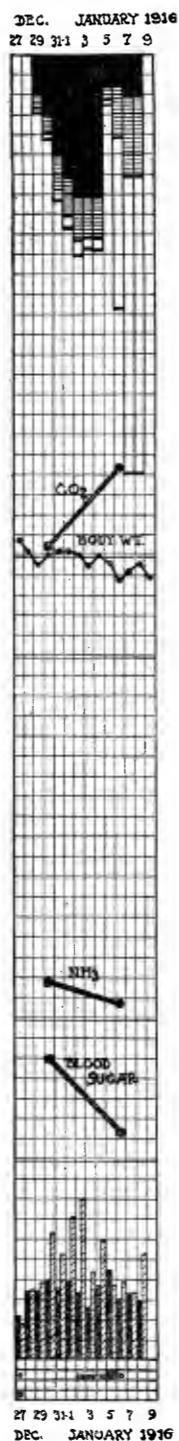
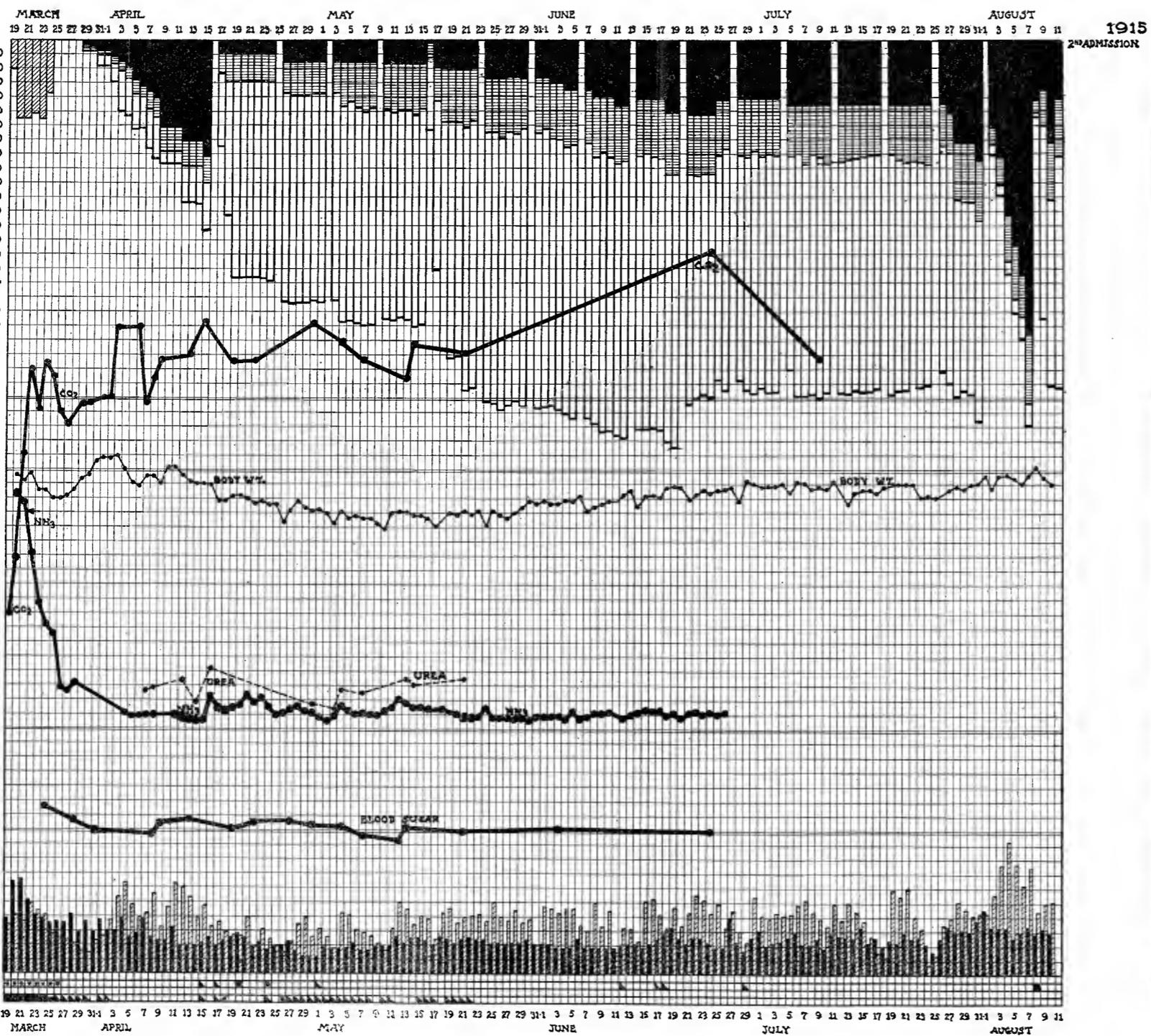
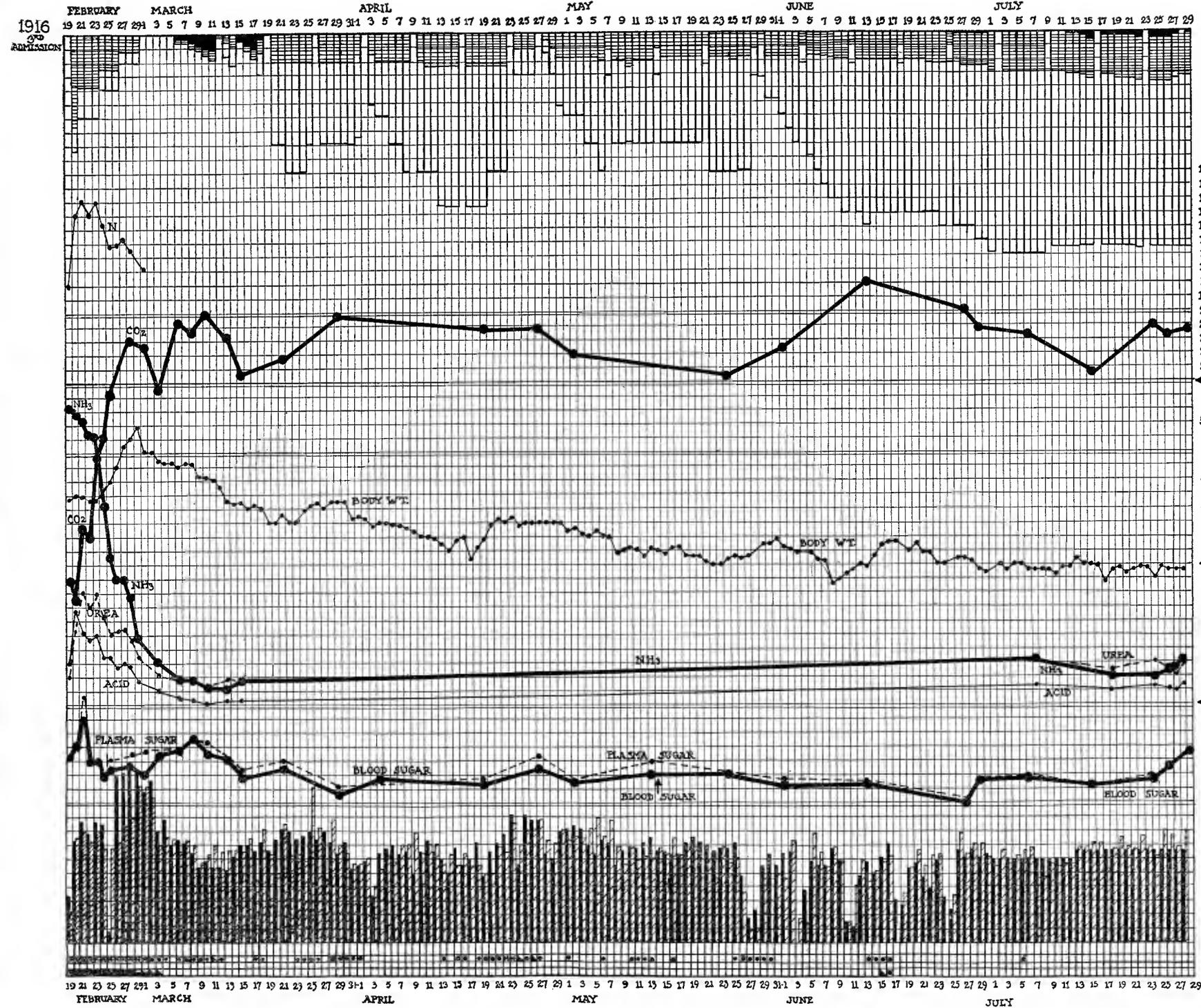
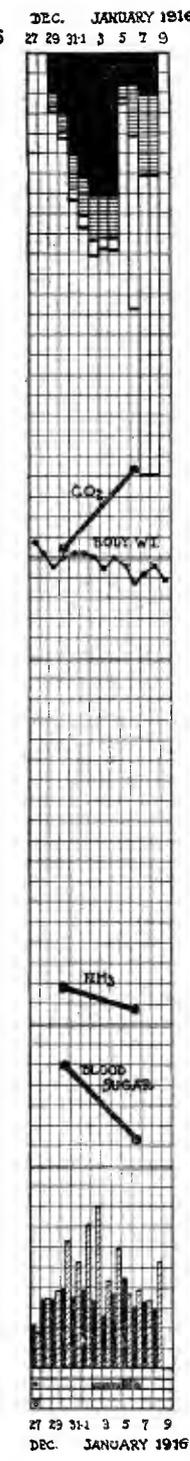
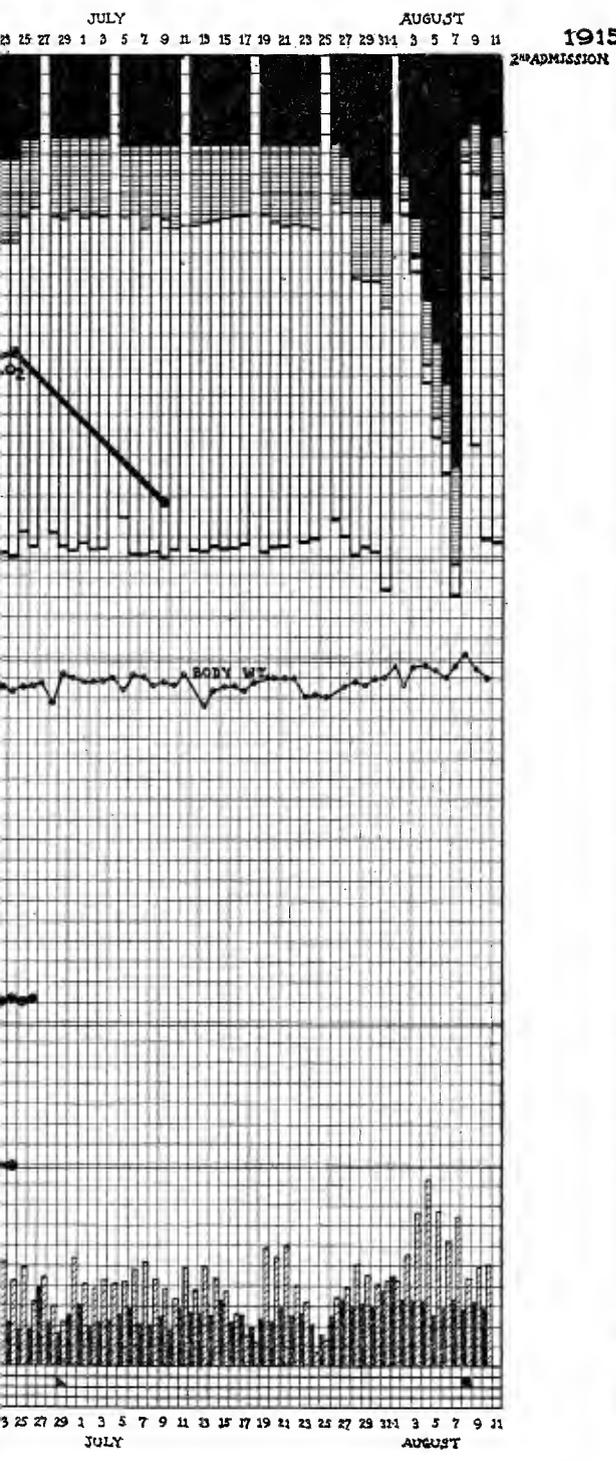


CHART 33. Case No. 37.



100
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500
1,600
1,700
1,800
1,900
2,000

20
16
12
8
4

55

50
48
46
44
42
40

1,600
1,400
1,200
1,000
800
600
400
200
0

0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050

3,500
3,000
2,500
2,000
1,500
1,000
500
0

Date.	Glucose excreted in 24 hrs.
1st admission.	
1915	gm.
Mar. 19	71.3*
" 20	52.6
" 21	36.2
" 22	23.7
" 23	9.0
" 24	11.9
" 25	2.6
3rd admission.	
1916	gm.
Feb. 19	20.3†
" 20	99.9
" 21	87.0
" 22	79.0
" 23	102.9
" 24	67.9
" 25	59.0
" 26	53.8
" 27	48.1
" 28	28.6
" 29	35.8
Mar. 1	23.9
Apr. 22	23.7
" 23	10.5

* 12 1/2 hr. specimen.
† 14 1/2 " "

CHART 33. Case No. 37.

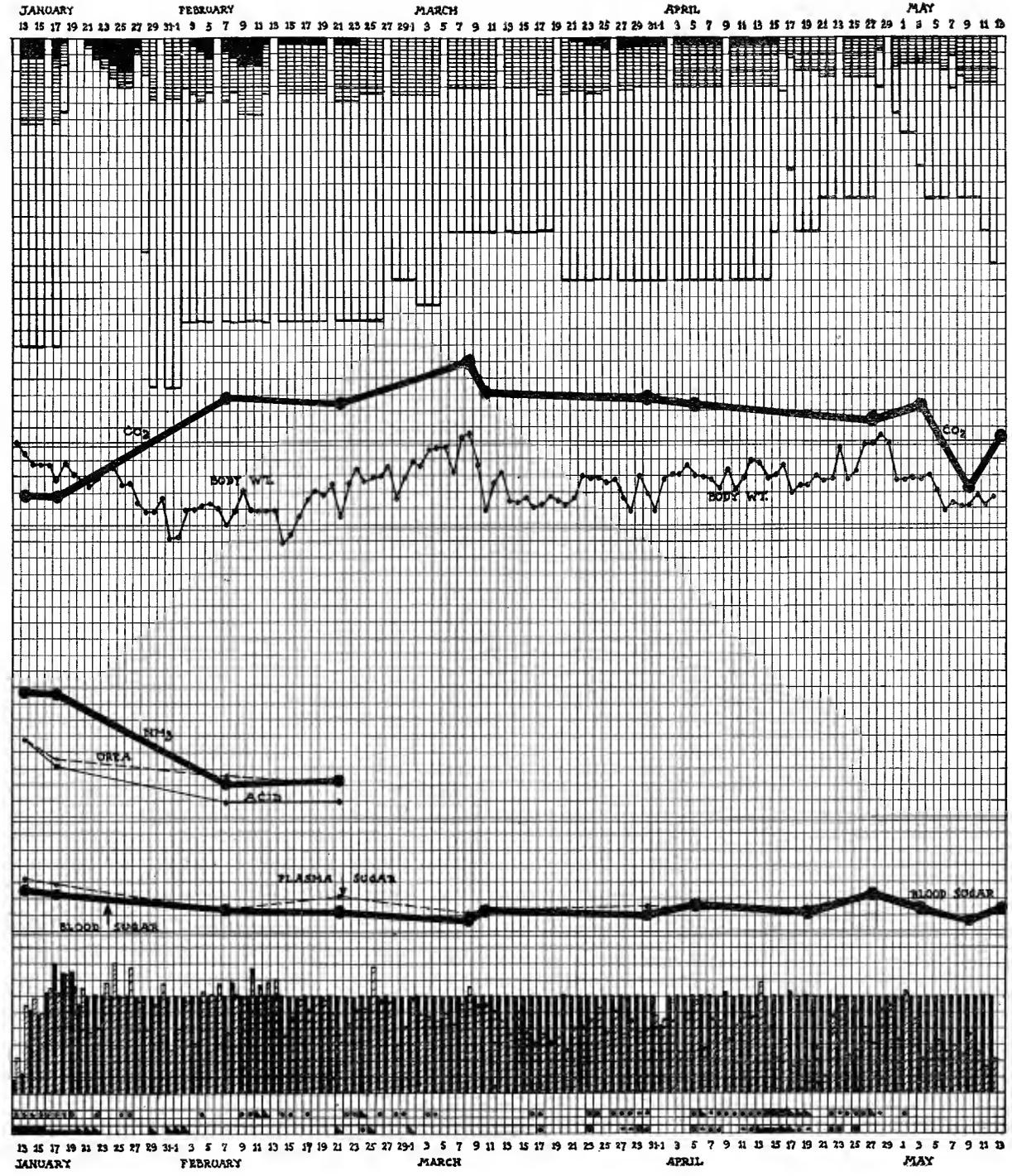
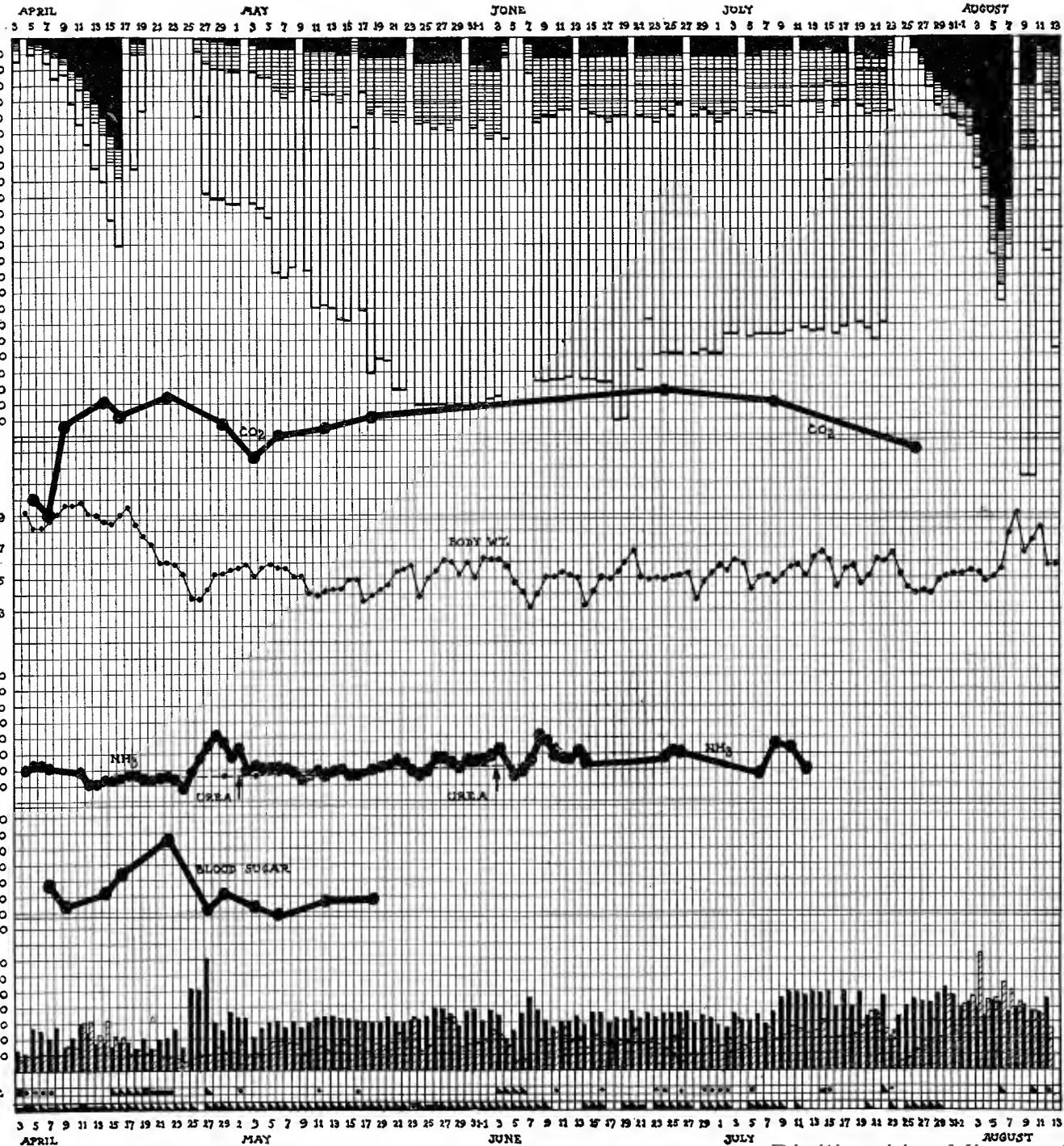
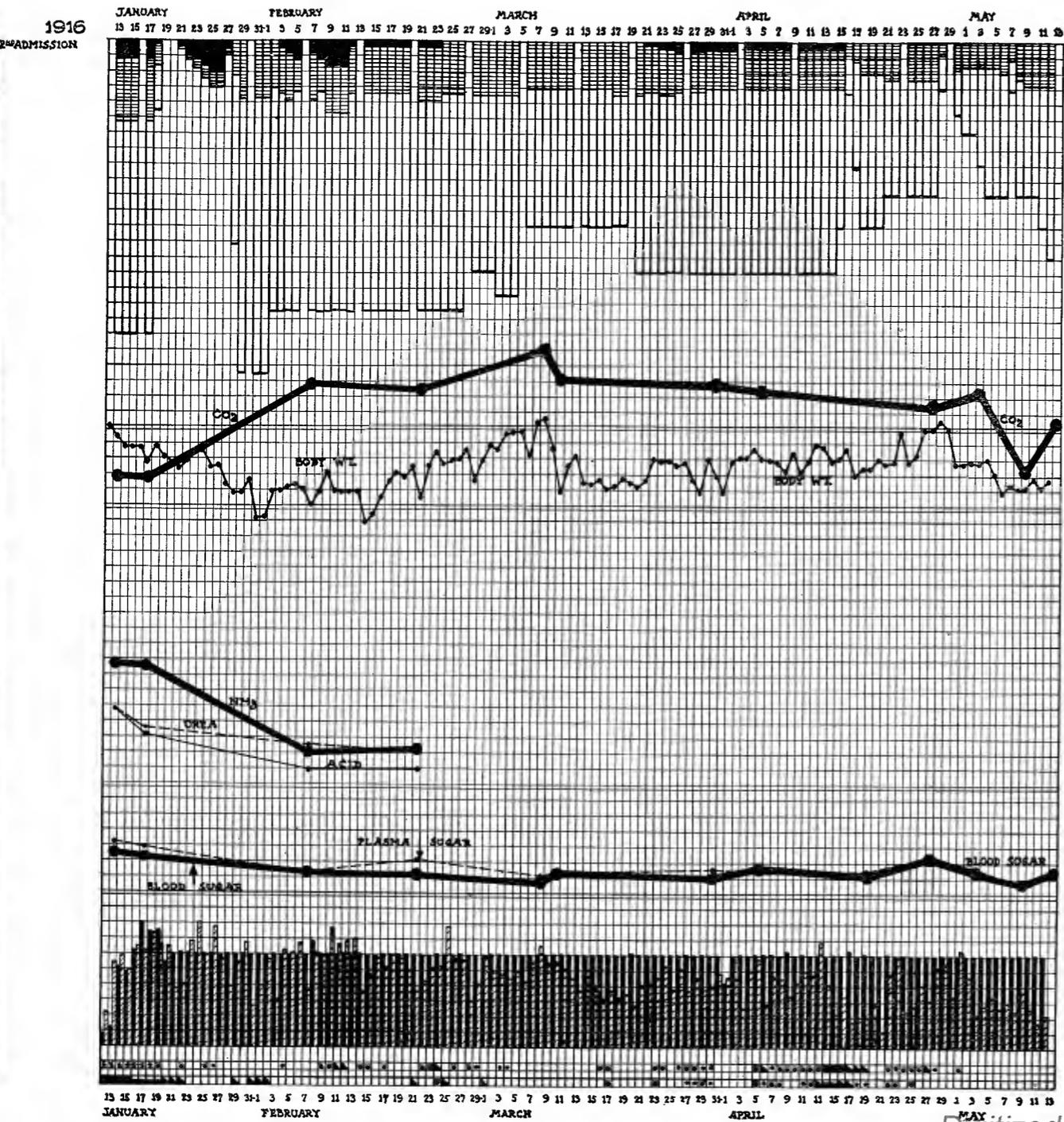
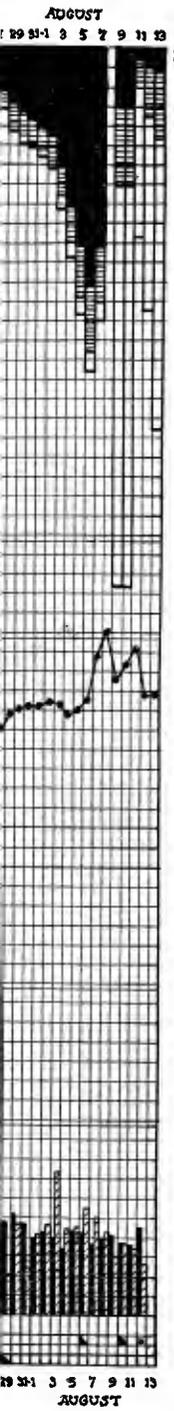
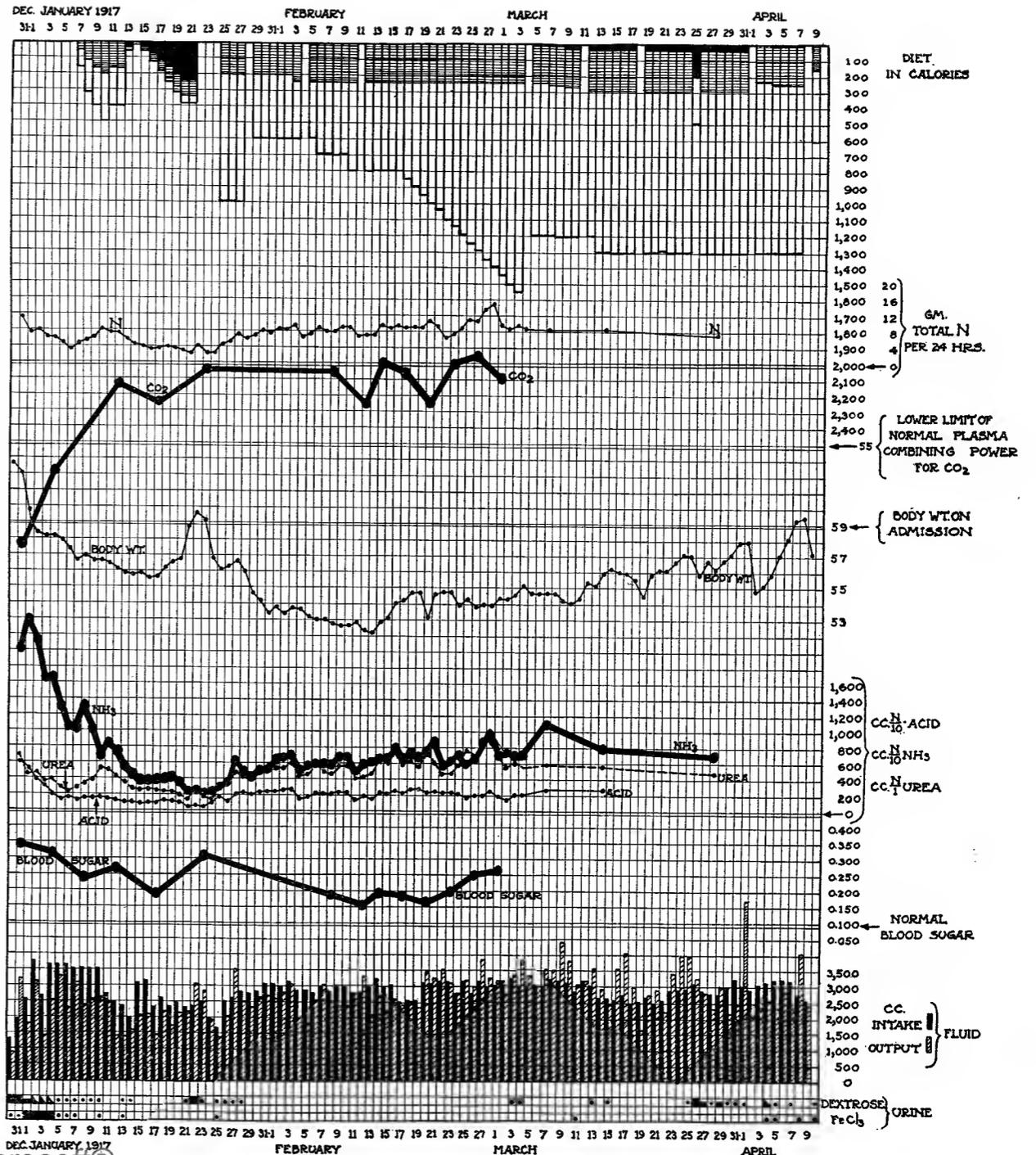


CHART 34. Case No. 39.



1916



DIET IN CALORIES

100
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500
1,600
1,700
1,800
1,900
2,000

20
16
12
8
4
0

GM. TOTAL N PER 24 HRS.

← 55 LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂

59 ← BODY WT. ON ADMISSION

57

53

1,600
1,400
1,200
1,000
800
600
400
200
0

CC. N₁₀ ACID
CC. N₁₀ NH₃
CC. N₁ UREA

0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050

NORMAL BLOOD SUGAR

3,500
3,000
2,500
2,000
1,500
1,000
500
0

CC. INTAKE } FLUID
CC. OUTPUT }

DEXTROSE } URINE
FeCl₃ }

Date.	Glucose excreted in 24 hrs.
2 nd admission.	
1916	gm.
Jan. 12	55.9*
" 13	56.5
" 14	38.9
" 15	45.1
" 16	9.1
" 17	30.8
" 18	9.0

* 16 hr. specimen.

CHART 34. Case No. 39.

CASE NO. 2409

1915 APRIL 17 19 21 23 25 27 29 1 MAY 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 JUNE 3 5 7 9 11 13 15 17 19 21 23 25 27 29 JULY 1 3 5 7 9 11 13 15 17 19 21 23

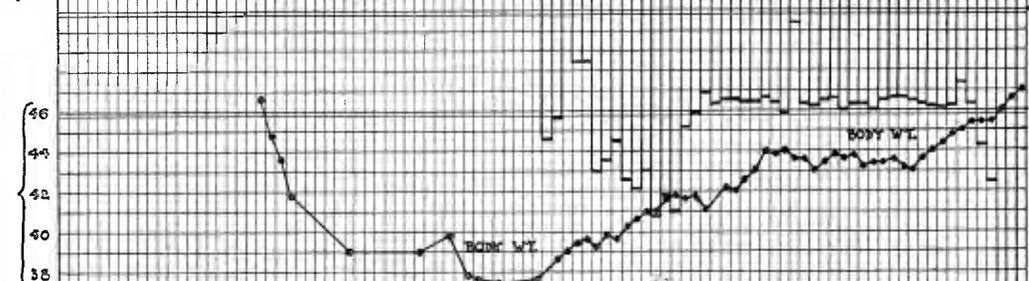
DIET
IN CALORIES
WHISKY
CARBOHYDRATE
PROTEIN
FAT

DIET
IN CALORIES



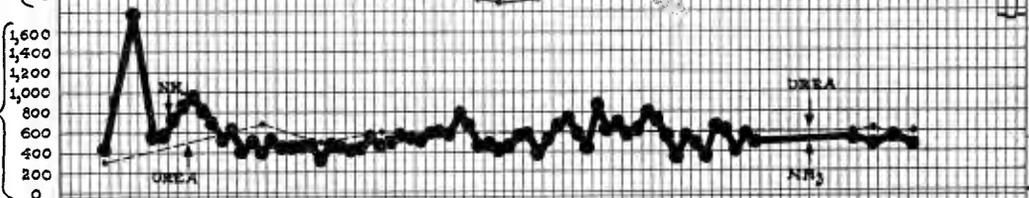
CC. OF CO₂
COMBINING WITH
100CC.
BLOOD PLASMA

LOWER LIMIT OF
NORMAL PLASMA
COMBINING POWER
FOR CO₂



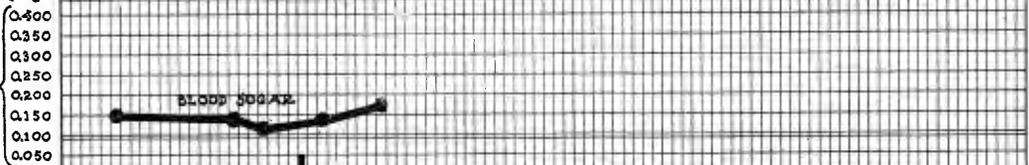
PER
24 HRS
CC. $\frac{N}{10}$ NH₃
CC. $\frac{N}{1}$ UREA

CC. $\frac{N}{10}$ NH₃
CC. $\frac{N}{1}$ UREA



BLOOD SUGAR
PER CENT

NORMAL
BLOOD SUGAR



FLUID
INTAKE
OUTPUT

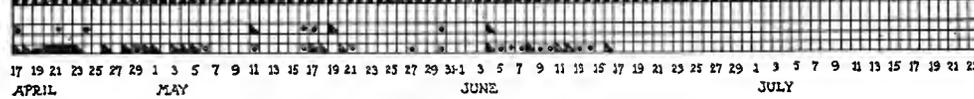
CC.
INTAKE
OUTPUT



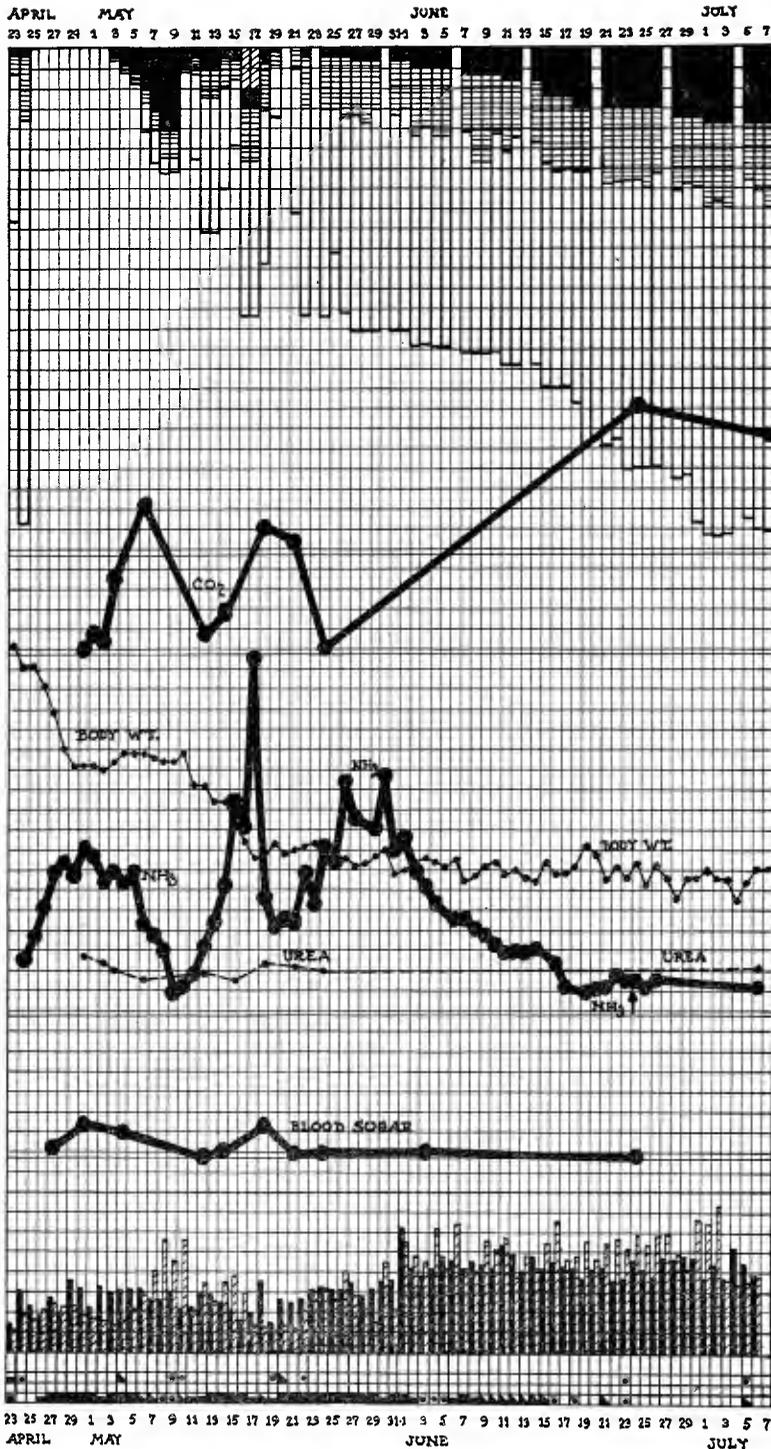
NEG. □ TRACE □
SLIGHT □ MOD. □
HEAVY ■ QUANTITATIVE ■

URINE
DEXTRORSE
FeCl₃

URINE
DEXTRORSE
FeCl₃

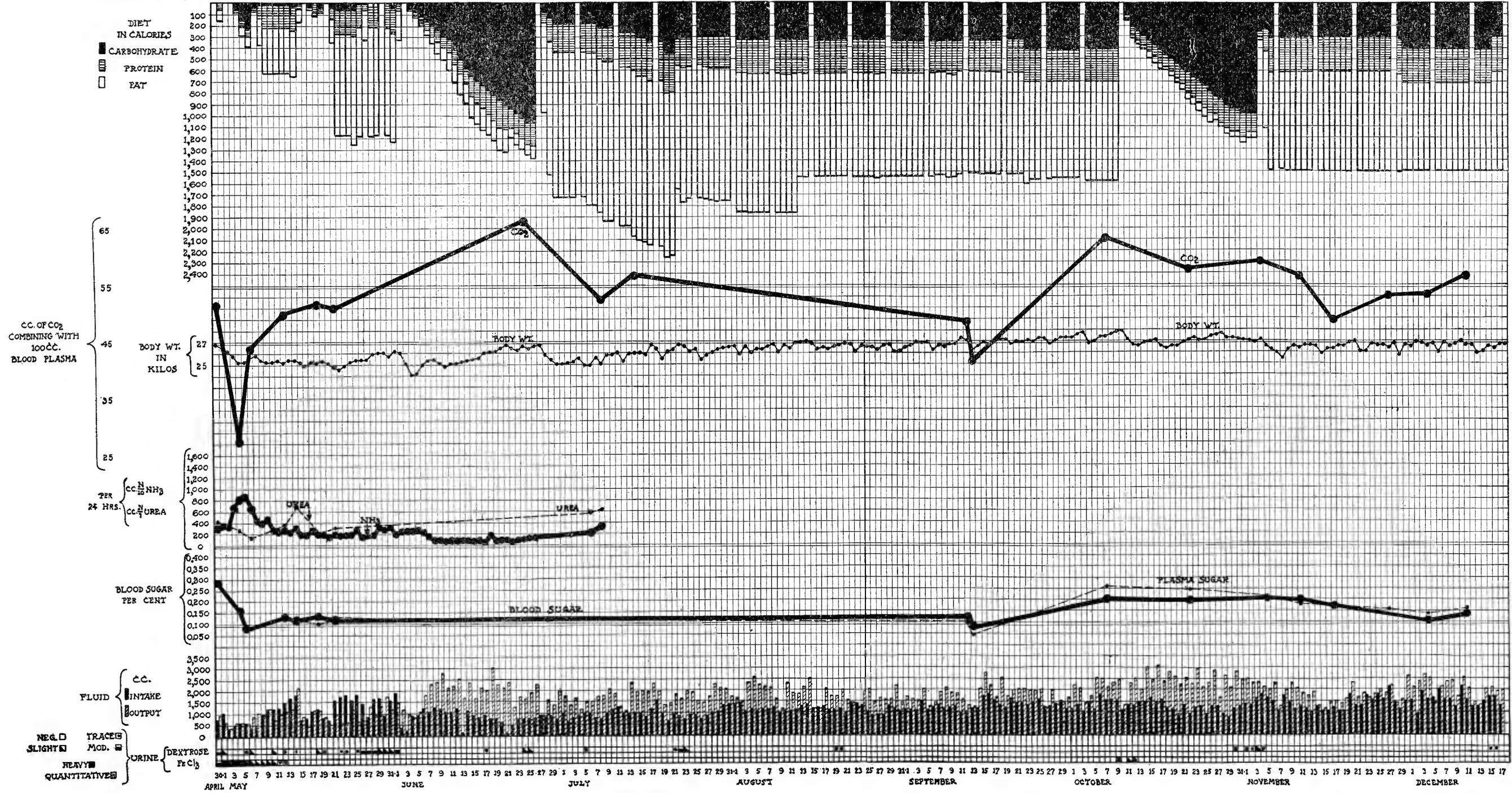


CASE NO. 2390
1915



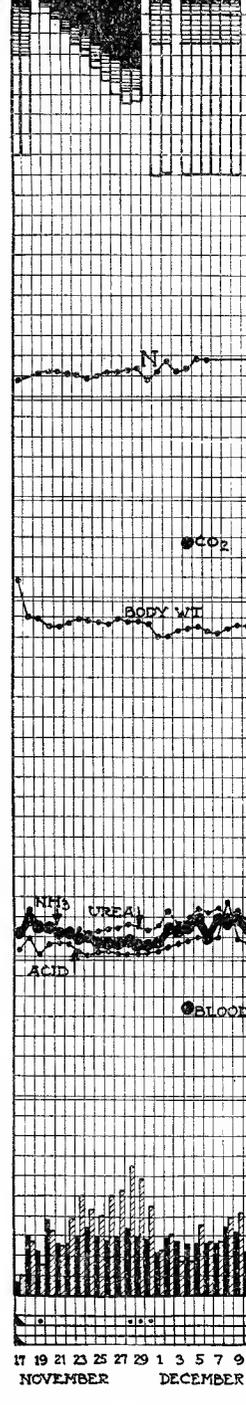
CASE NO. 2481

1st ADMISSION 1915



1916

2nd ADMISSION



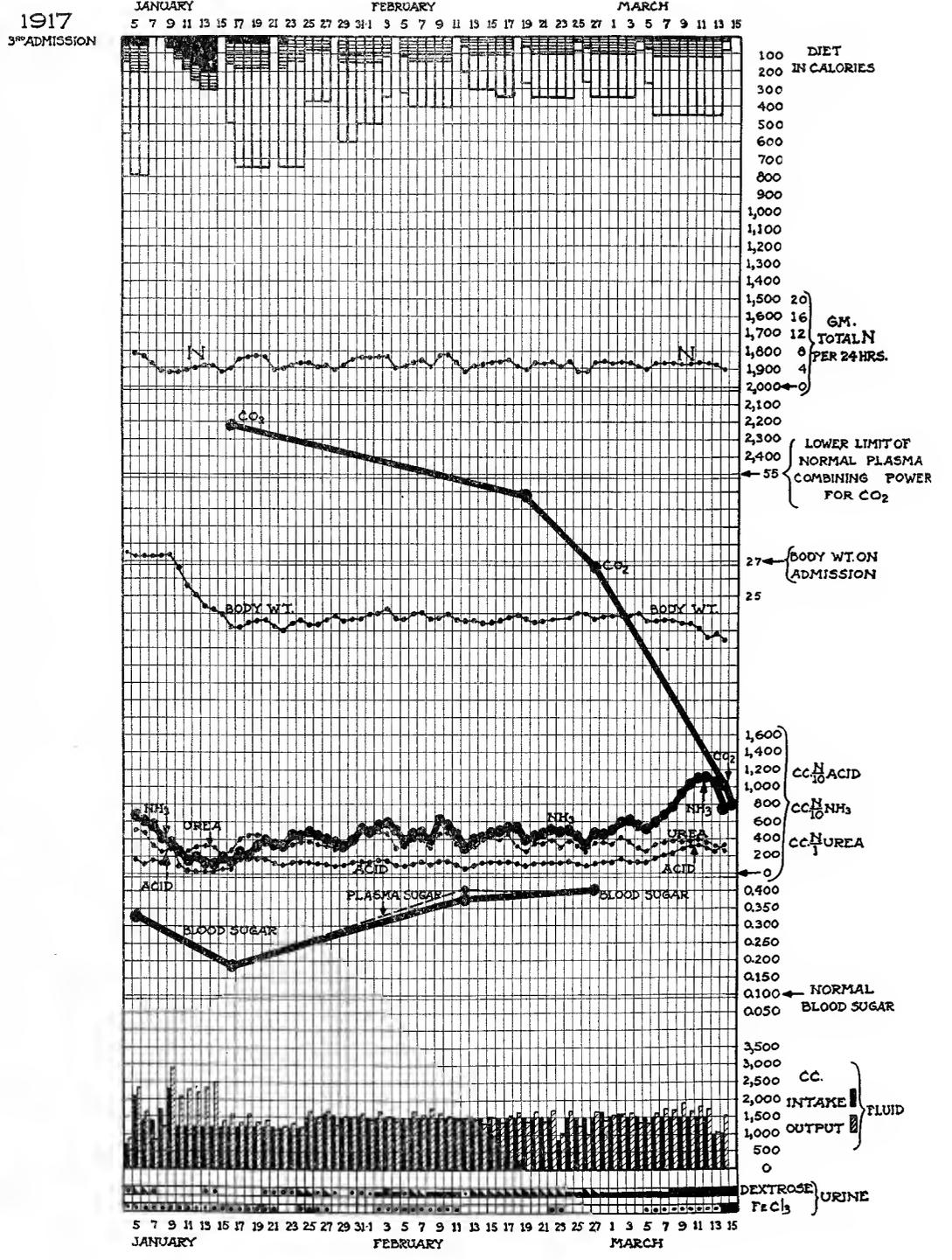
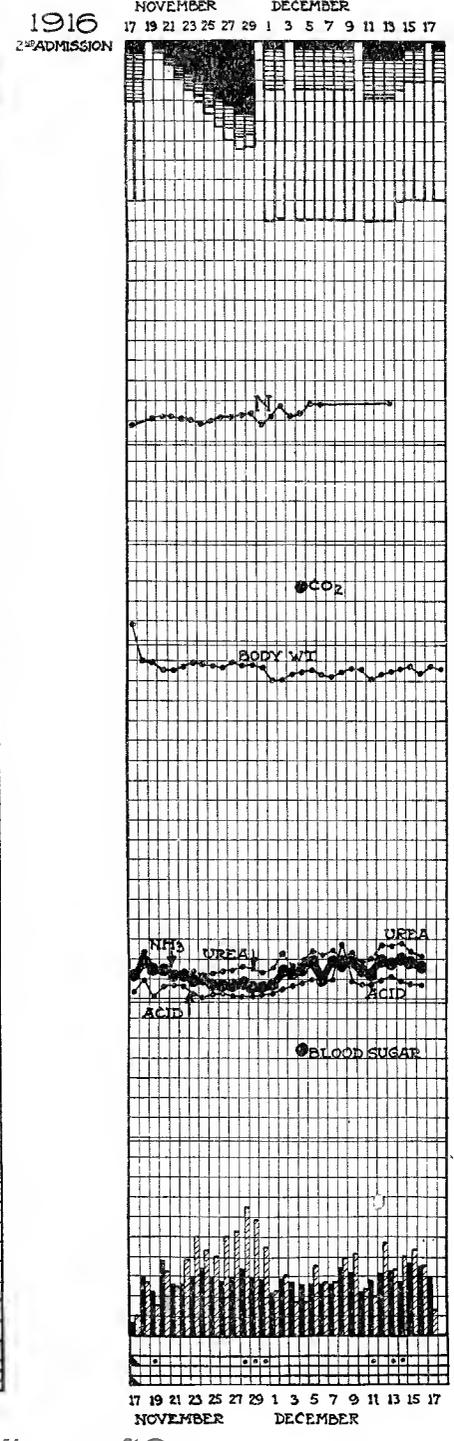
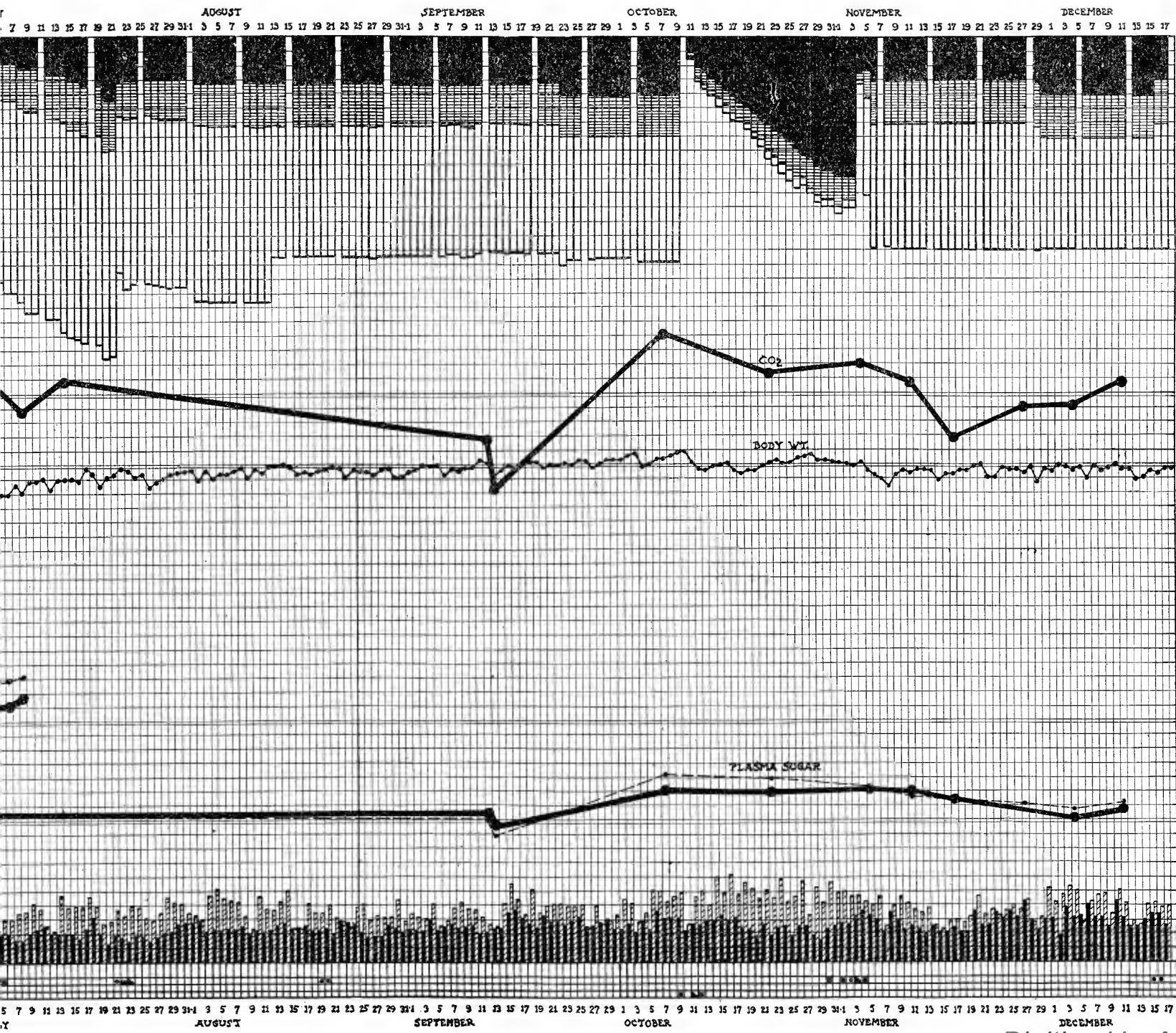


CHART 37. Case No. 42.

CASE NO. 2,492

1st ADMISSION 1915

MAY JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

1916

MARCH APRIL MAY

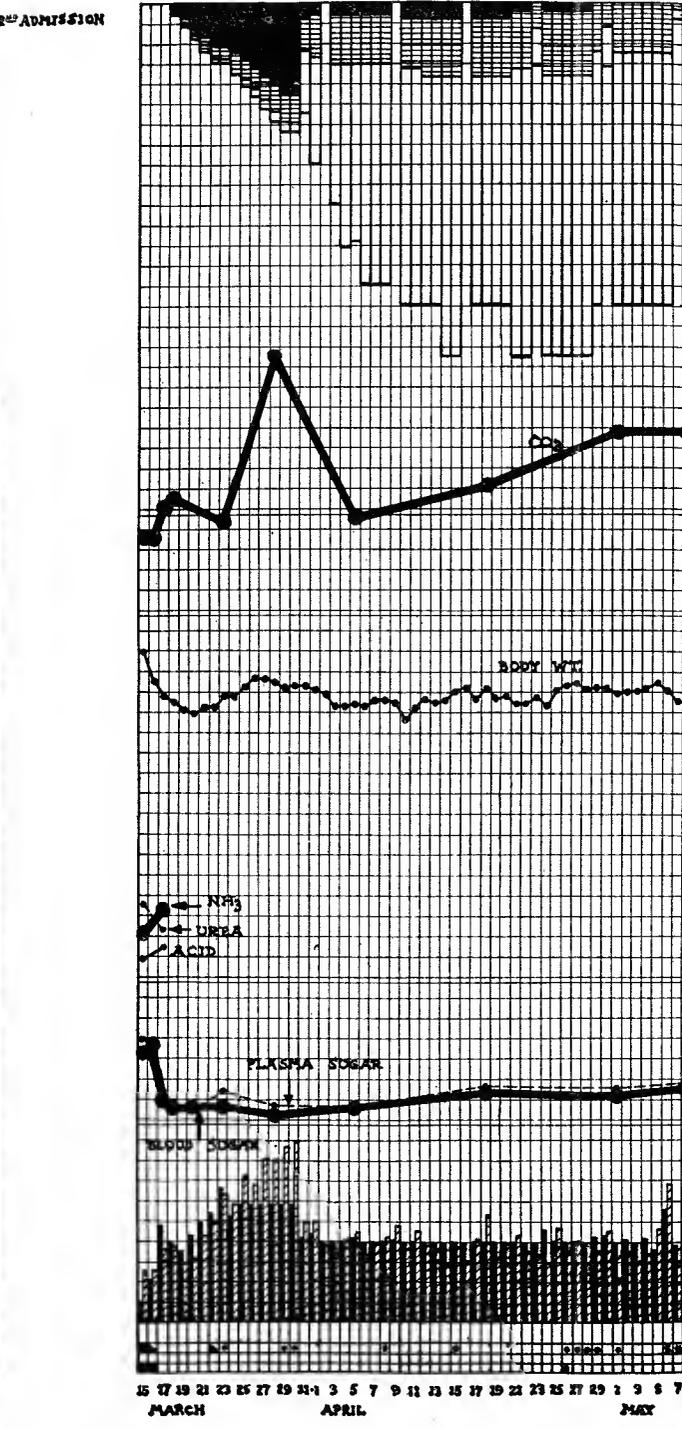
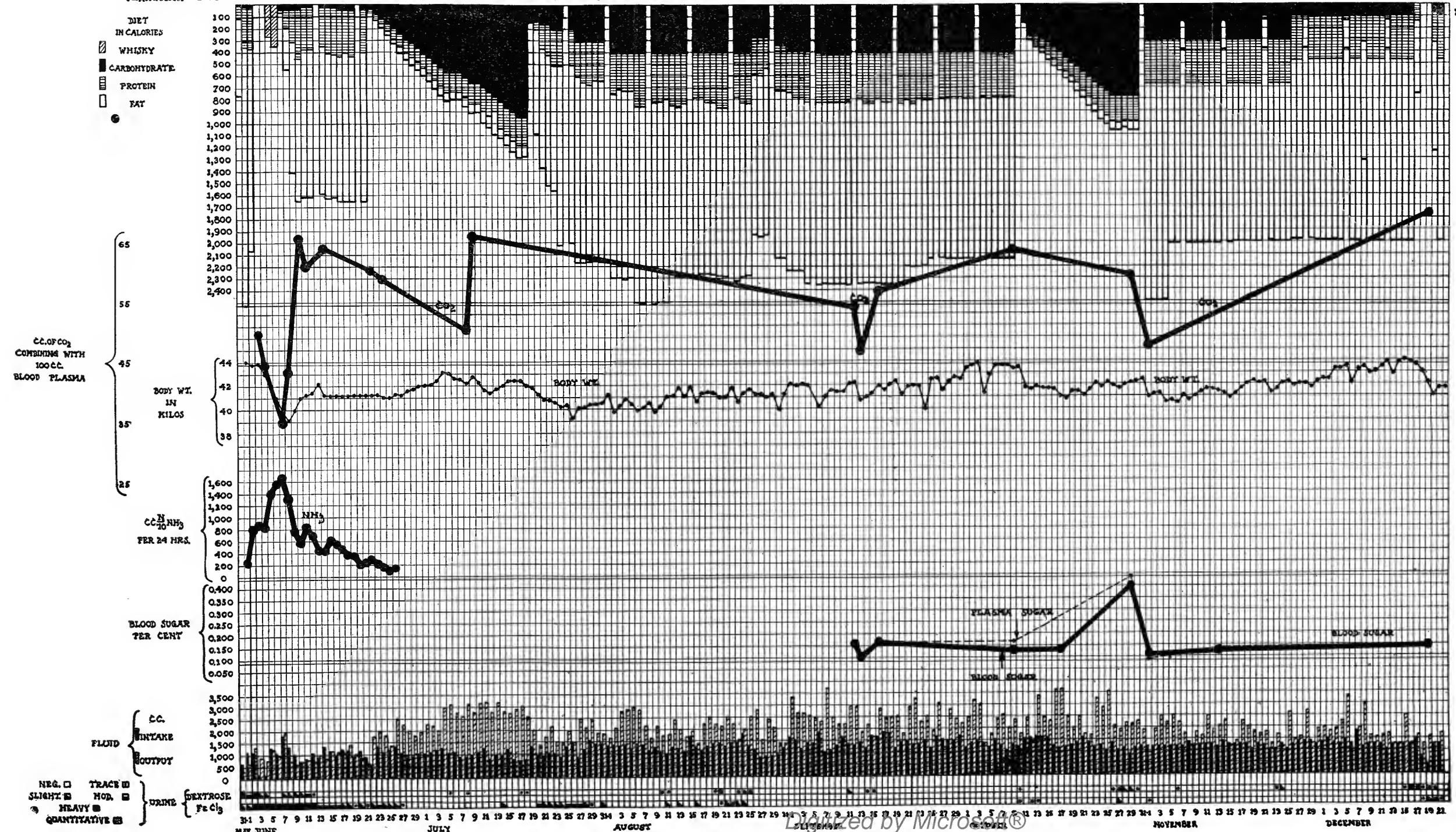
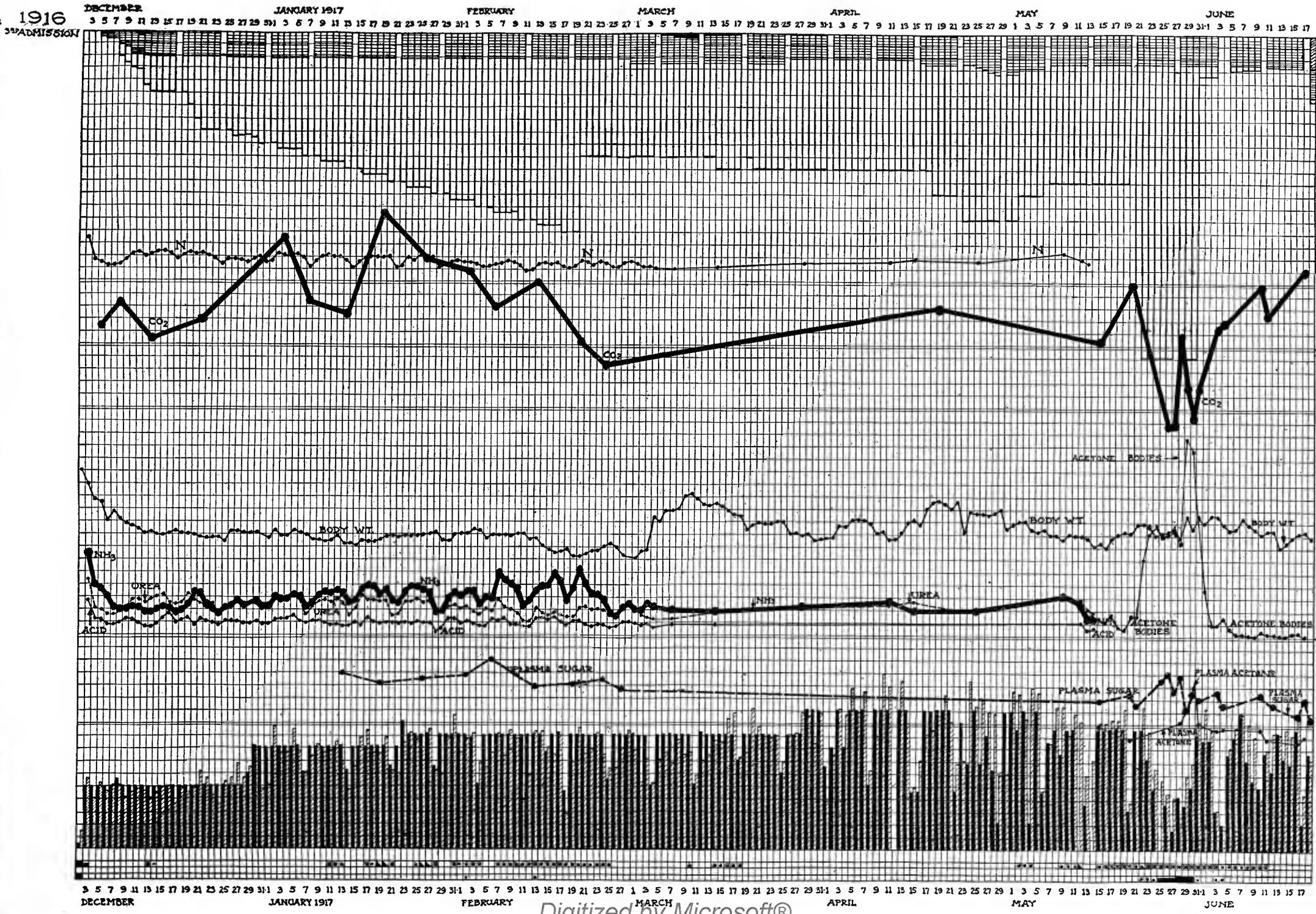
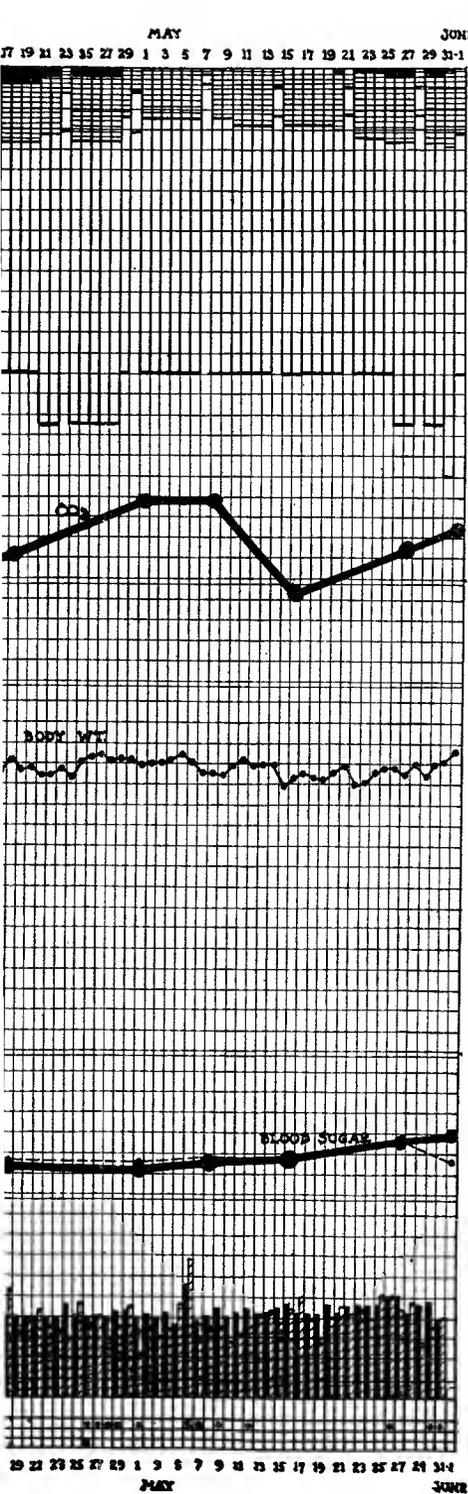


CHART 38. Case No. 43.



DIET IN CALORIES

100
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500

20
16
12
8
4
0

GM. TOTAL N PER 24 HRS.

2,000
1,800
1,600
1,400
1,200
1,000
800
600
400
200
0

55
50
45
44
42
40
38
36

LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂

44 ← BODY WT. ON ADMISSION

42
40
38
36

1,600
1,400
1,200
1,000
800
600
400
200
0

CC NH₄ ACID
CC NH₃
CC NH₂ UREA

0.400
0.350
0.300
0.250
0.200
0.150
0.100 ← NORMAL BLOOD SUGAR

3,500
3,000
2,500
2,000
1,500
1,000
500
0

CC FLUID INTAKE
CC FLUID OUTPUT

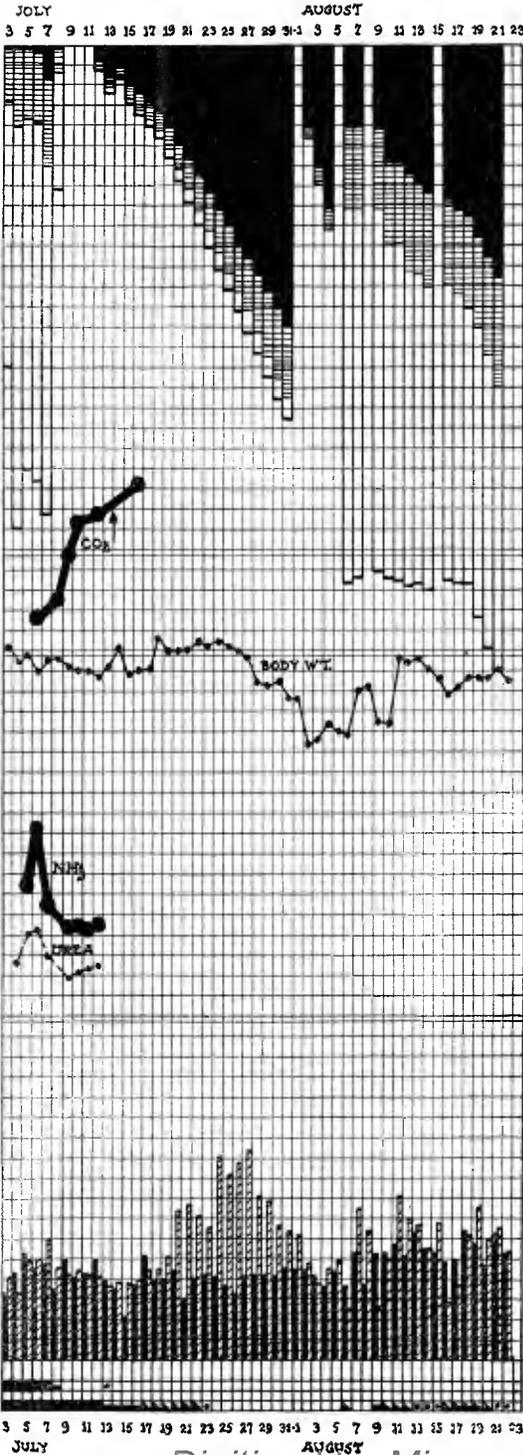
3,500
3,000
2,500
2,000
1,500
1,000
500
0

DEXTROSE URINE
FeCl₃

Date.	Glucose excreted in 24 hours.
1st admission.	
1915	gm.
Oct. 27	6.5
Dec. 17	6.7
2nd admission.	
1916	
May 6	11.5
" 7	2.7
3rd admission.	
May 16	5.0
" 17	10.9
" 18	10.4
" 19	10.9
" 20	7.2
" 23	18.0
" 24	19.0
" 25	18.5
" 26	13.8
" 27	35.6
" 28	5.7
" 29	24.1
" 30	24.8
" 31	45.7
June 1	31.9
" 2	24.2
" 3	8.8

CASE NO. 2,419

1st ADMISSION 1915



1917

2nd ADMISSION

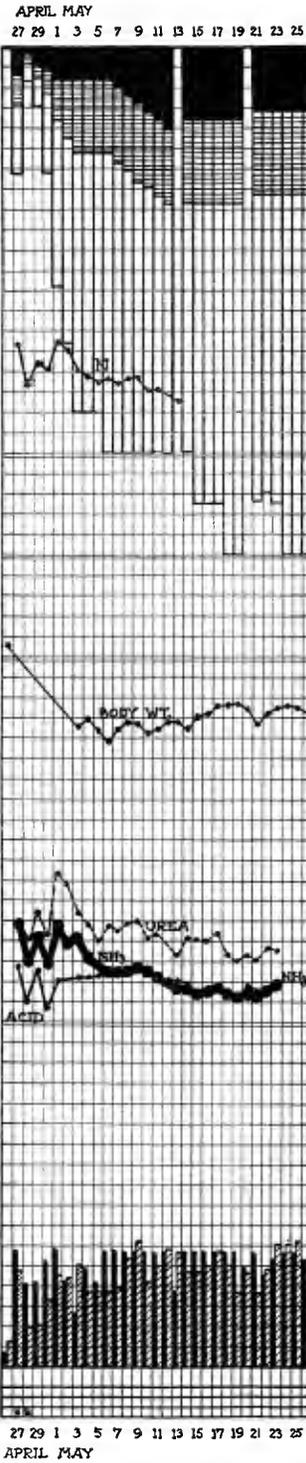


TABLE XIII.

Date.	Body weight.	Temperature.	Diet.				Treatment.		Fluid intake.	Urine.					Acetone bodies.			Blood.						Remarks.				
			Total calories.	Protein.	Fat.	Carbohydrate.	Whisky.	Calcium carbonate.		Sodium bicarbonate.	Volume.	Reaction.	Total nitrogen.	NH ₃ -N	Sugar.	D: N ratio.	Acetone and diacetic (as β-oxobutyric).	β-oxobutyric acid.	Total (as β-oxobutyric).	Sugar.	Plasma sugar.	Corpuscle sugar.	Plasma CO ₂ .		Hemoglobin.	Corpuscles.	Lipemia.	
	kg.	°F.		gm.	gm.	gm.	cc.	gm.	gm.	cc.	cc.		gm.	gm.	gm.		gm.	gm.	gm.	per cent	per cent	per cent	vol. per cent	per cent	per cent			
1915 Sept. 1	19.4	98.5 96.3	28	—	—	—	8	15	15	1094	1185	Acid.	4.74	0.14	12.9	2.72	1.61	9.19	10.80	0.333	0.400	0.263 (calc. 0.166)	73.5	90	30.2	++++	Urine from 4:50 p.m. Sept. 1 to 7 a.m. Sept. 2.	
" 2	22.0	97.4 96.2	56	—	—	—	16	20	20	3850	1405	Alkaline.	4.08	0.26	6.3	1.55	0.91	3.46	4.37	—	—	—	—	—	—	—	—	
" 3	21.3	98.8 96.9	42	—	—	—	12	—	—	801	1345	Acid.	—	—	++	—	+++	—	—	—	—	—	—	—	—	—	—	
" 4	20.2	99.0 96.4	7	—	—	—	2	—	—	476	1345	"	2.96	0.21	+	—	1.07	0.11	1.18	—	—	—	—	—	—	—	—	
" 5	20.0	97.4 96.2	—	—	—	—	—	—	—	190	1260	Neutral.	2.15	0.11	0	—	0.56	0.04	0.60	—	—	—	—	—	—	—	—	
" 6	—	96.8 95.4	196.9	1.0	—	53.3	15	—	5	972	945+	"	—	—	0	—	—	—	—	—	—	—	—	—	—	—	5 a.m. 10 gm. levulose in 100 cc. water by stomach tube. 10 gm. levulose in 100 cc. saline, subcutaneously. 6:50 a.m. 20 gm. levulose in 250 cc. saline, subcutaneously.	
" 7	17.6	100.8 98.8	946	48.7	73.0	—	19	—	5	1029	1418	" Alkaline.	—	—	0	—	—	—	—	—	—	—	—	—	—	—	—	Ferric chloride reaction negative.
" 8	17.2	101.1 99.8	994	44.7	81.2	—	16	—	—	908	625	Acid.	8.86	0.56	++	—	0.12	1.15	1.27	—	—	—	—	—	—	—	—	
" 9	—	102.2 99.6	613	24.5	31.3	40.5	16	—	5	958	788+	"	7.43	0.60	11.32	—	0.45	3.03	3.48	0.286	0.286	0.25 (calc. 0.286)	67.8	80	34.0	++++	11 a.m. Blood taken. Oatmeal 60 gm. between noon and 5 p.m.	
																				0.287	0.308	0.227 (calc. 0.217)	84.9	82	27.5	+++	9 p.m. Blood taken before transfusion.	
																				0.222	0.27	0.164 (calc. 0.151)	85.9	95	39.8	+	9 " Injection 225 cc. citrated blood. 12 m. Blood taken.	
" 10	—	98.4 97.0	126	—	—	—	36	—	—	518	409+	" Alkaline.	—	0.32	0	—	—	—	—	—	—	—	—	—	—	—	—	
" 11	—	102.0 98.4	443	39.8	22.4	20	16	—	—	1456	860+	"	3.16	0.15	0	—	+	—	—	—	—	—	—	—	—	—	—	7:30 to 8:45. a.m. 150 cc. citrated blood injected. By mistake blood not taken before transfusion. 8:45 a.m. Blood taken at end of transfusion.
																				0.066	0.059	0.064 (calc. 0.075)	71.5	94	38.5	Plasma clear.		

CASE NO. 2,455

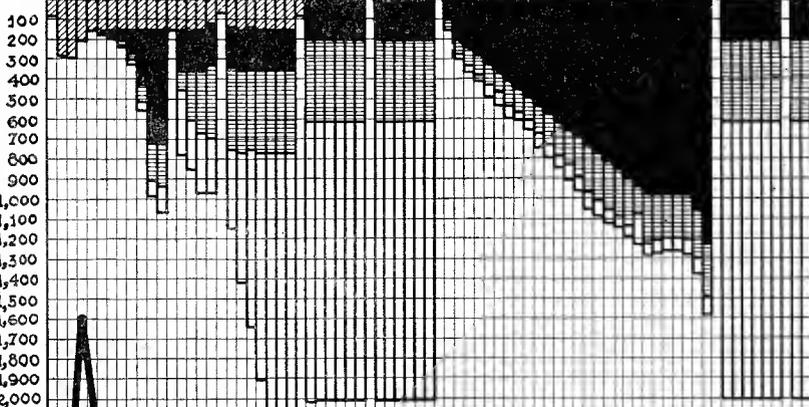
SEPTEMBER

OCTOBER

NOVEMBER

1915 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15

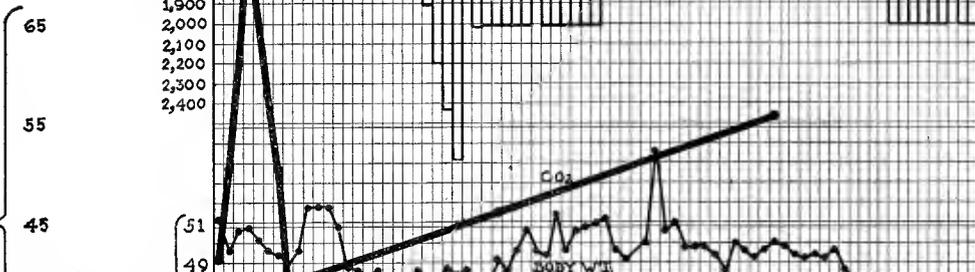
DIET
IN CALORIES
WHISKY
CARBOHYDRATE
PROTEIN
FAT



DIET
IN CALORIES

Date.	Glucose excreted in 24 hrs.
1915	gm.
Sept. 24	27.75
" 25	2.77

CC. OF CO₂
COMBINING WITH
100 CC.
BLOOD PLASMA



← 55 LOWER LIMIT OF
NORMAL PLASMA
COMBINING POWER
FOR CO₂

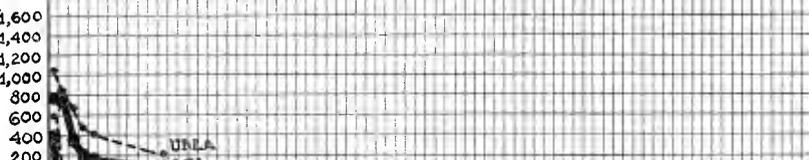
51 ← BODY WT. ON
ADMISSION

BODY WT.
IN
KILOGS



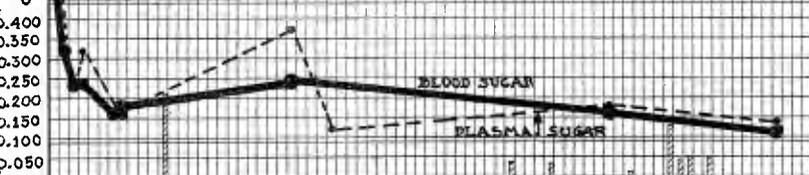
43

PER
24 HRS.
CC. $\frac{N}{10}$ NH₃
CC. $\frac{N}{10}$ UREA



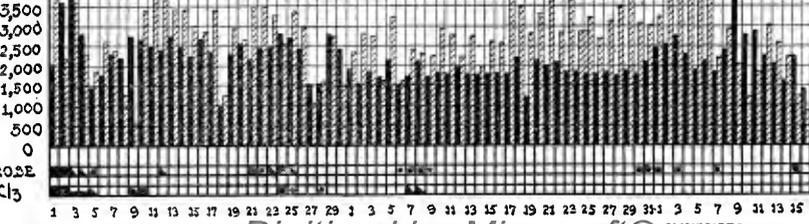
1,600
1,400
1,200
1,000
800
600
400
200
← 0
CC. $\frac{N}{10}$ NH₃
CC. $\frac{N}{10}$ UREA

BLOOD SUGAR
PER CENT



0.400
0.350
0.300
0.250
0.200
0.150
0.100
← 0.100 NORMAL
BLOOD SUGAR
0.050

FLUID
CC.
INTAKE
OUTPUT



3,500
3,000
2,500
2,000
1,500
1,000
500
0
CC.
INTAKE
OUTPUT
FLUID

NEG. □ TRACE □
SLIGHT □ MOD. □
HEAVY □
QUANTITATIVE □
URINE { DEXTROSE
FeCl₃ }

URINE { DEXTROSE
FeCl₃ }

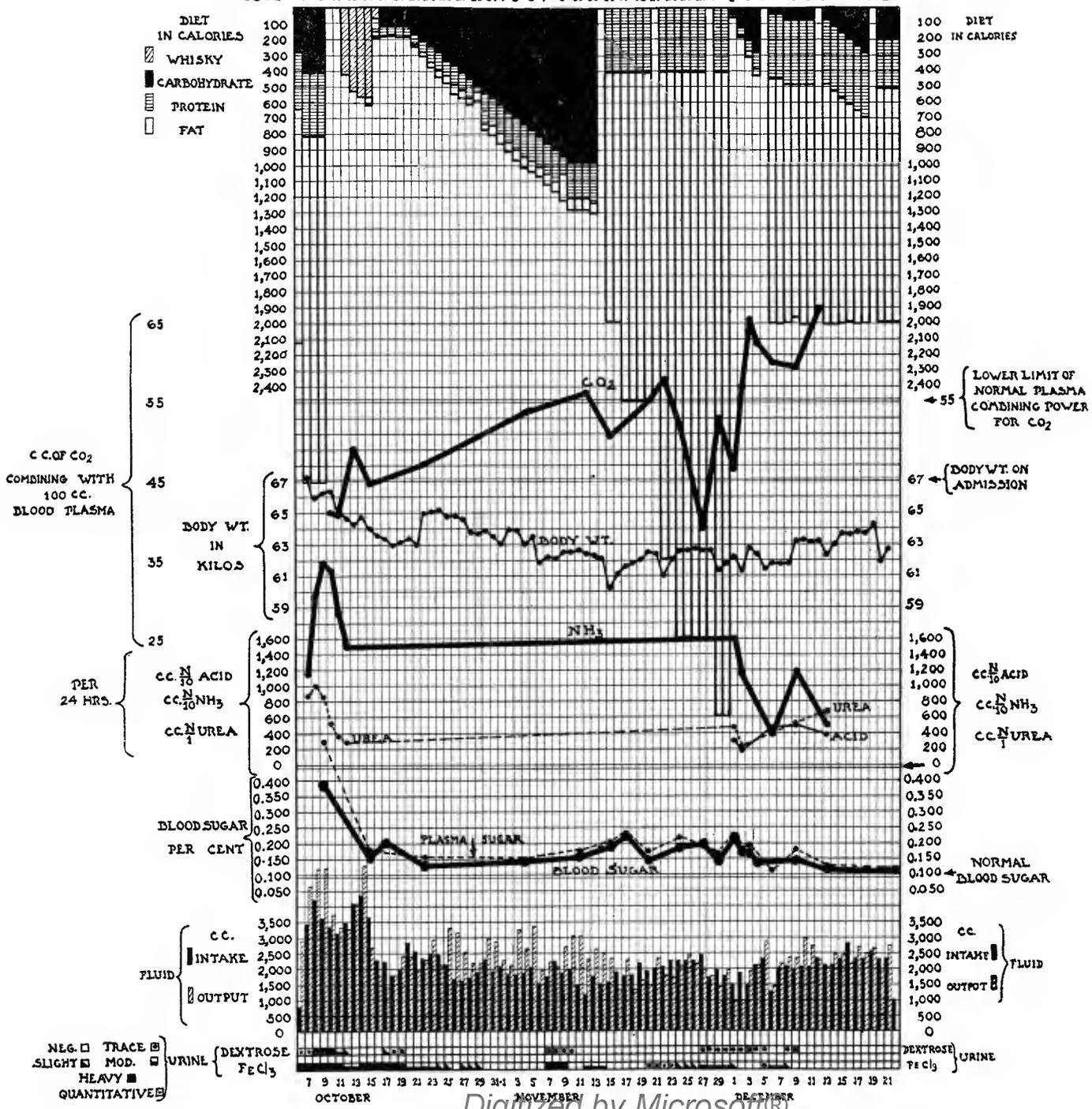
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15

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CHART 40. Case No. 46.

CASE NO. 2,491

1915 OCTOBER NOVEMBER DECEMBER



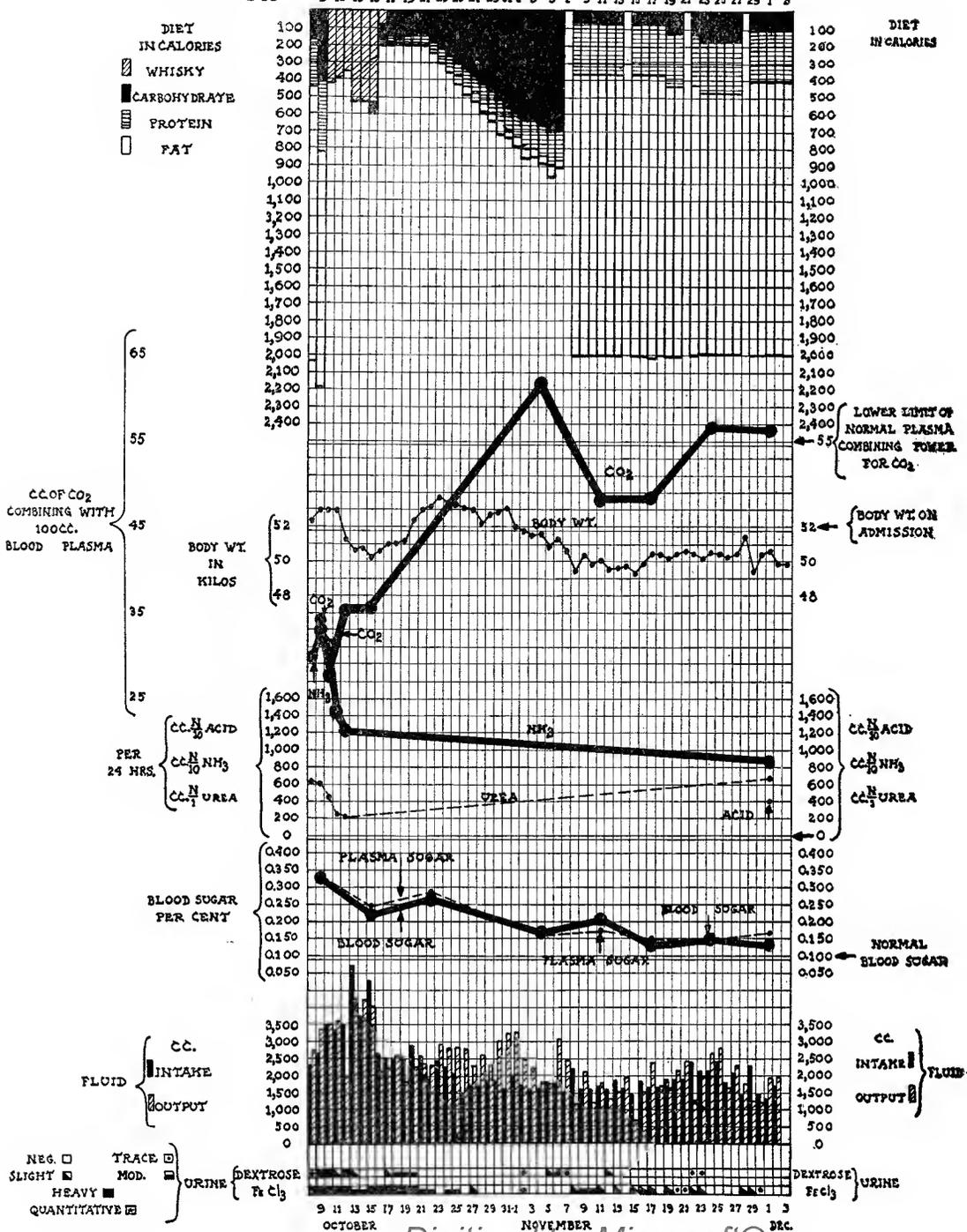
Date.	Glucose excreted in 24 hrs.
1915	gm.
Oct. 6	66.2*
" 7	61.7

* 19½ hr. specimen.

CASE NO. 2,469
1915

OCTOBER NOVEMBER DEC.

9 11 13 15 17 19 21 23 25 27 29 31 3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3

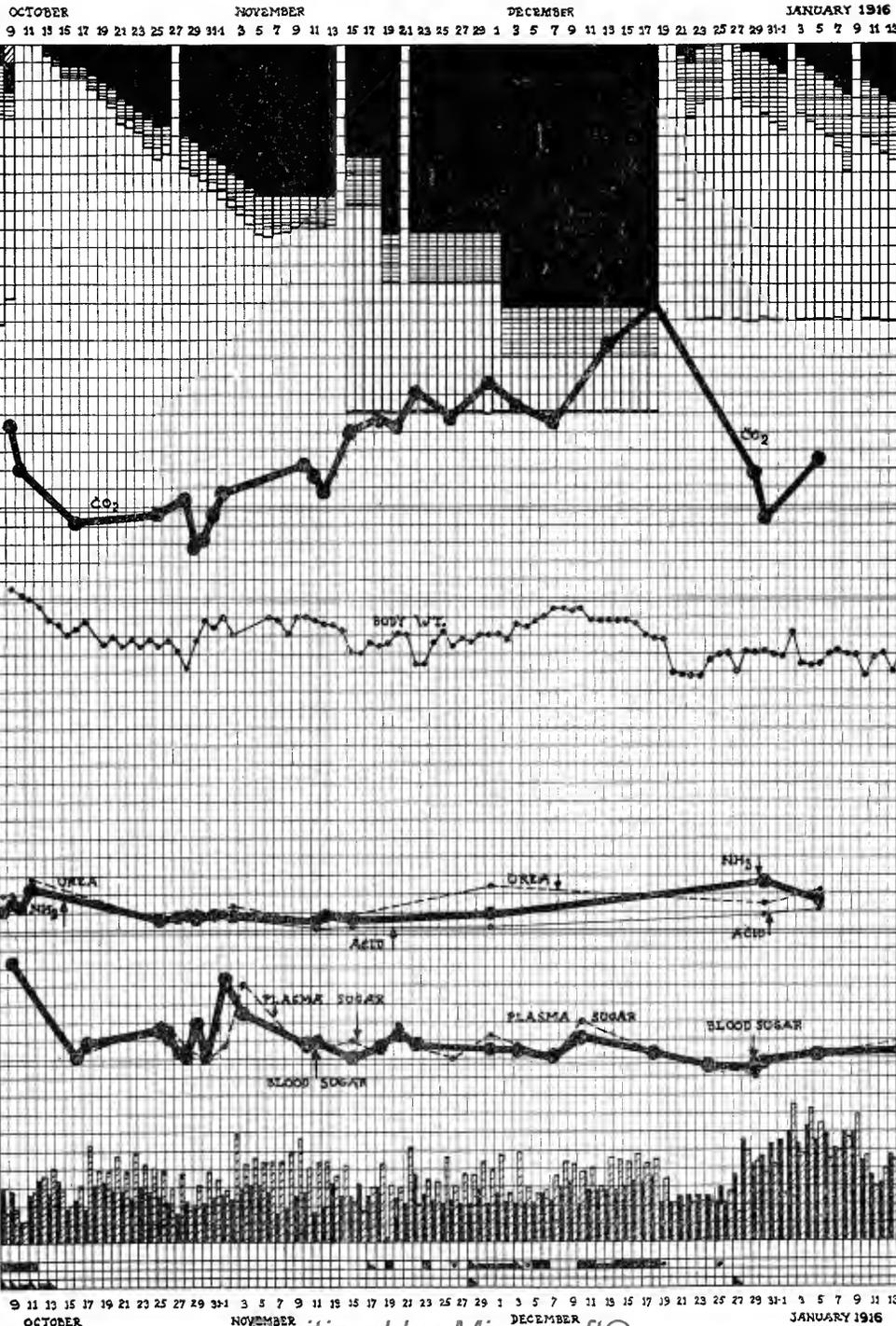


Date.	Glucose excreted in 24 hrs.
1915	gm.
Oct. 8	118.2*

* 19 hr. specimen.

CASE NO. 2,525

1st ADMISSION 1915

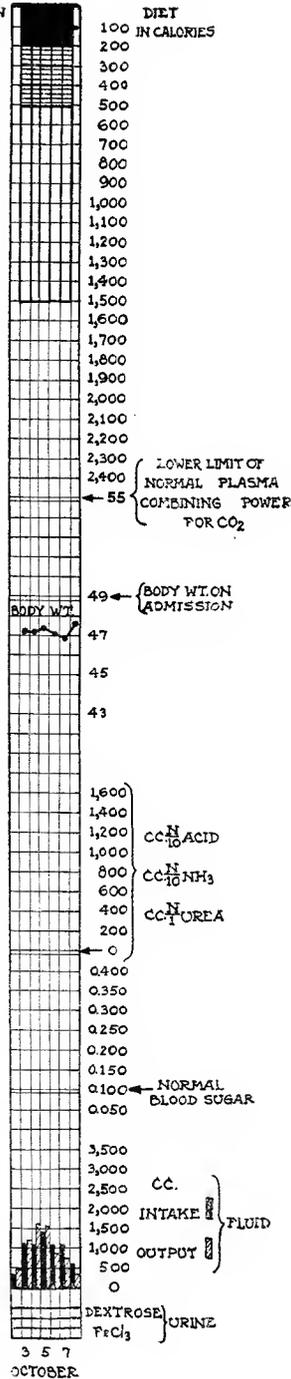


1916

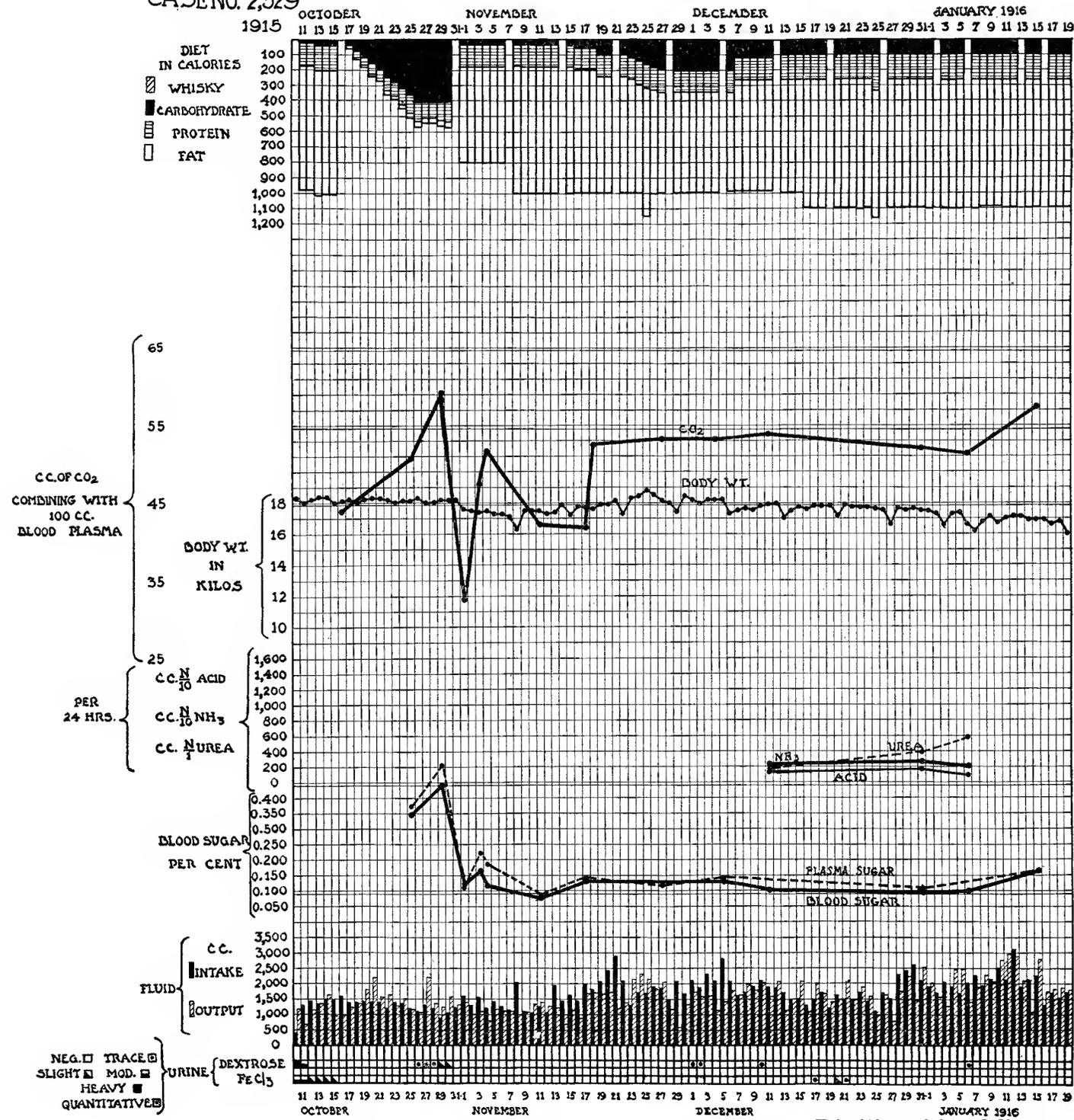
OCTOBER

2nd ADMISSION

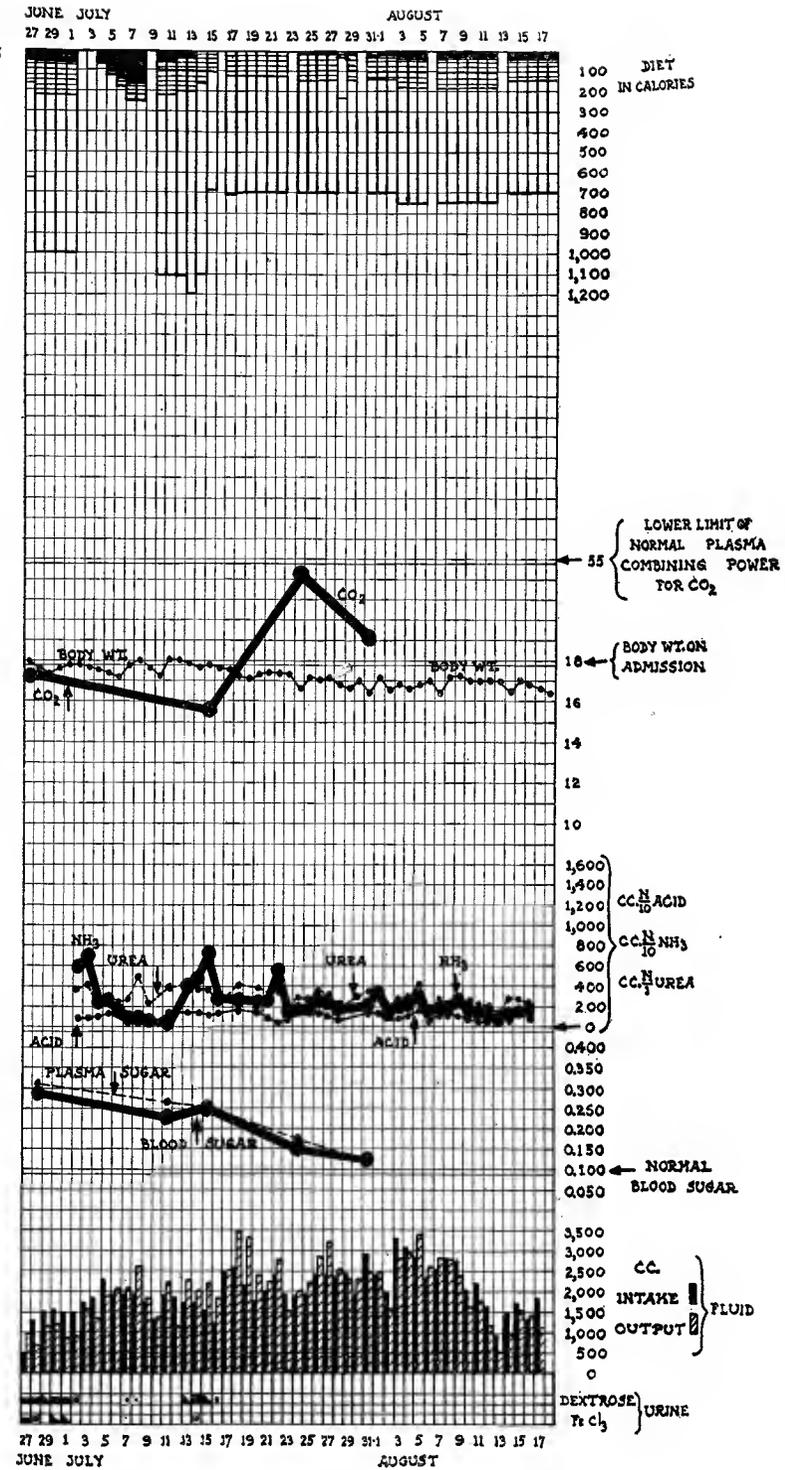
3 5 7



CASE NO. 2,529

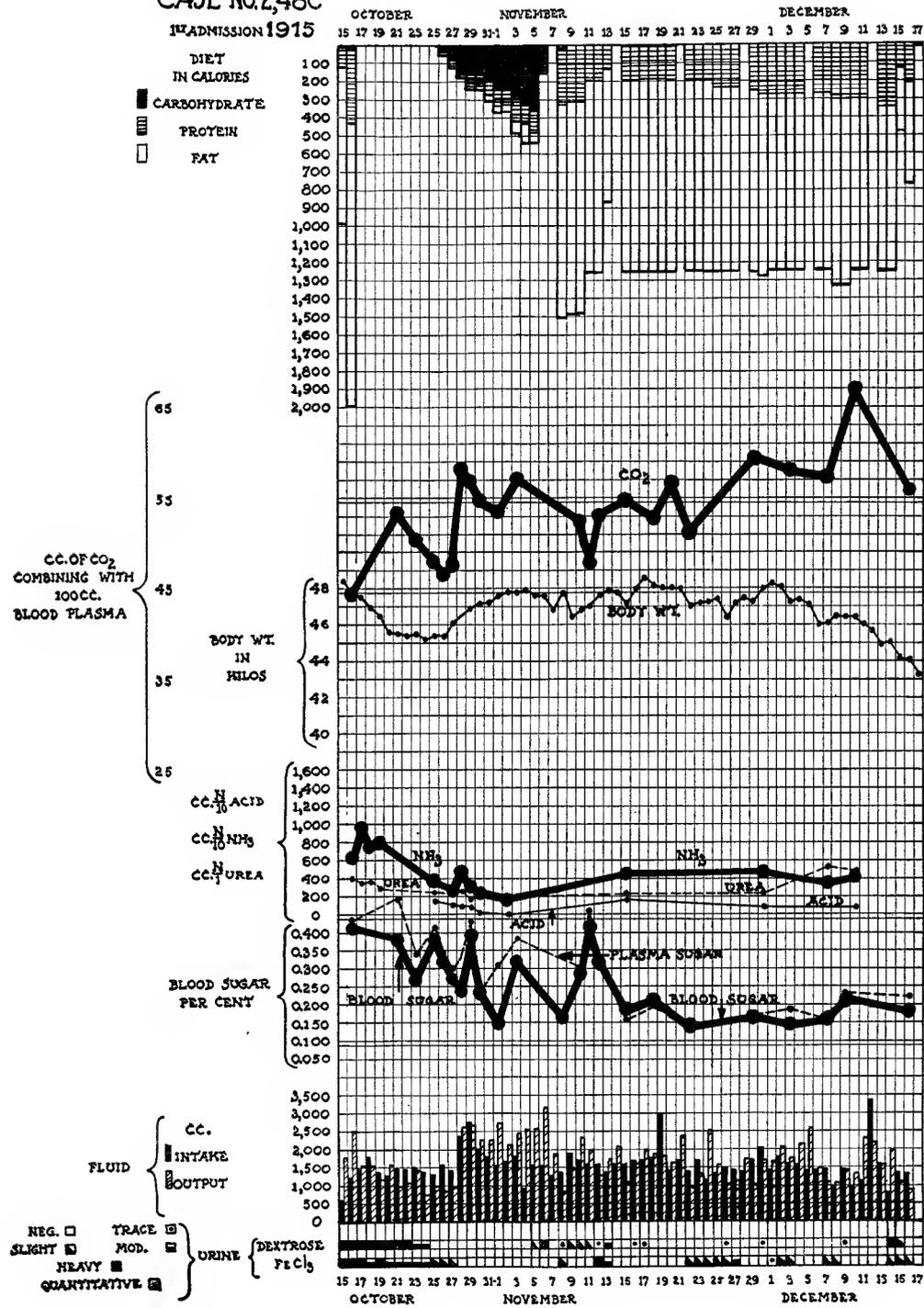


1916
2nd ADMISSION



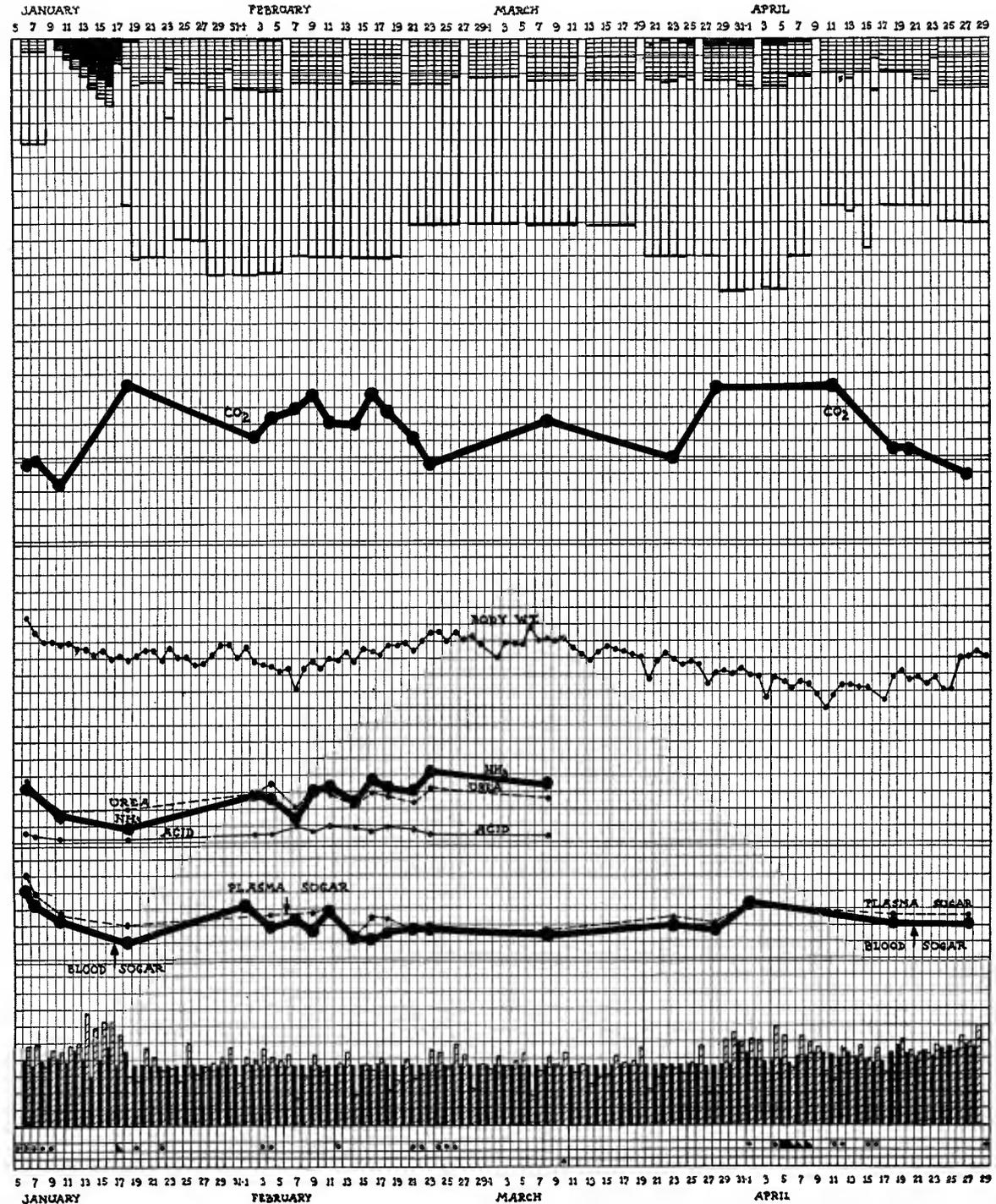
Date.	Glucose excreted in 24 hrs.
1st admission.	
1915	gm.
Oct 27	7.6

CASE NO. 2,48C



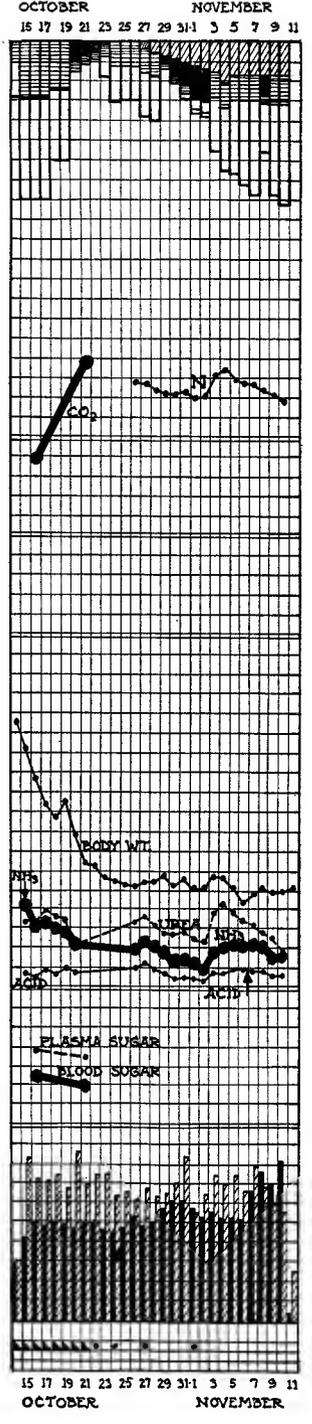
1916

3rd ADMISSION



1916

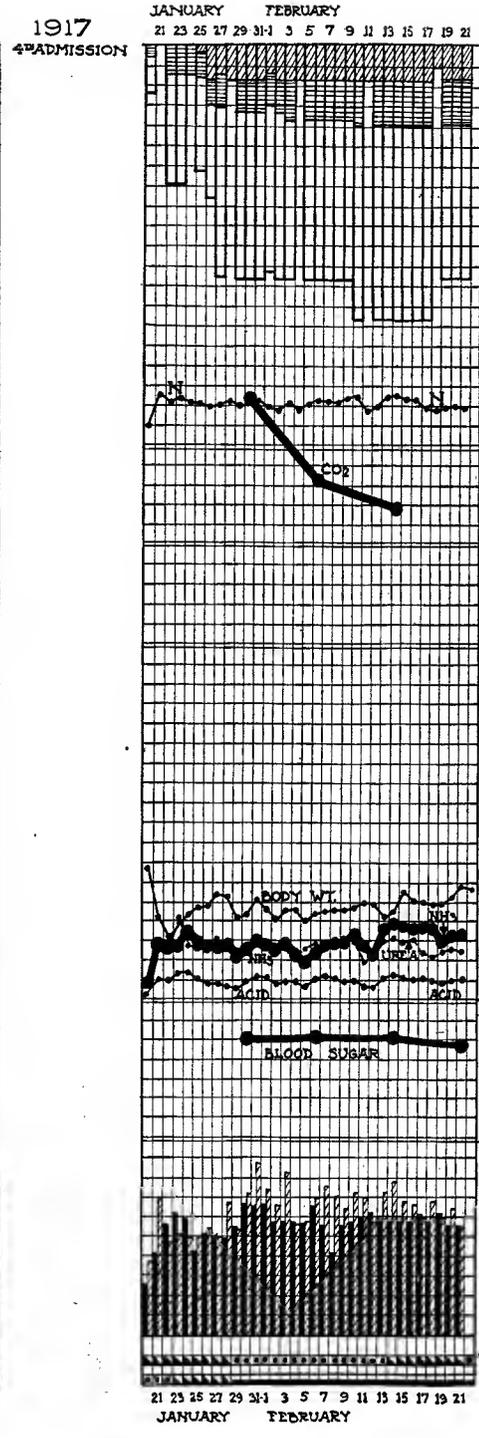
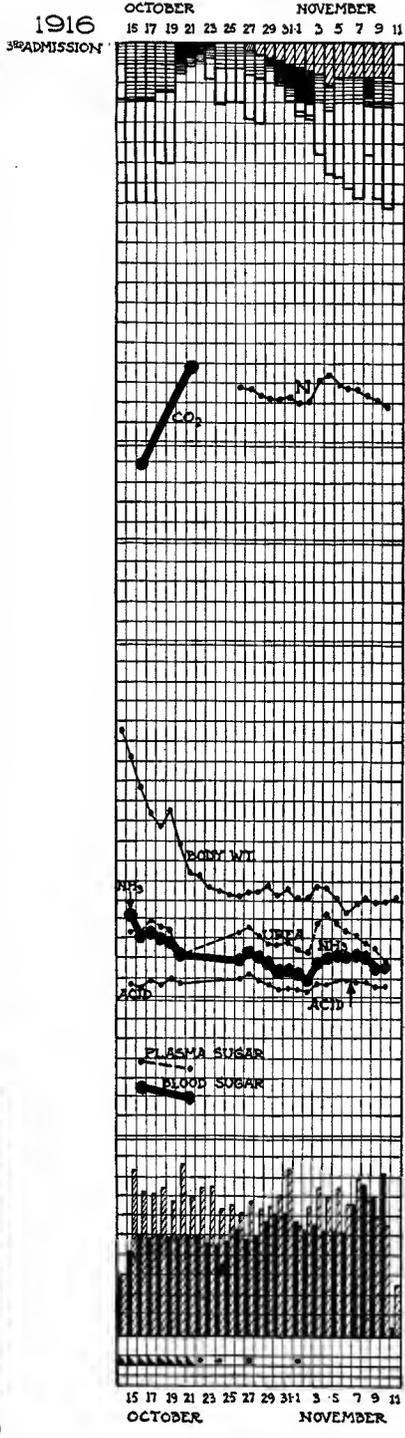
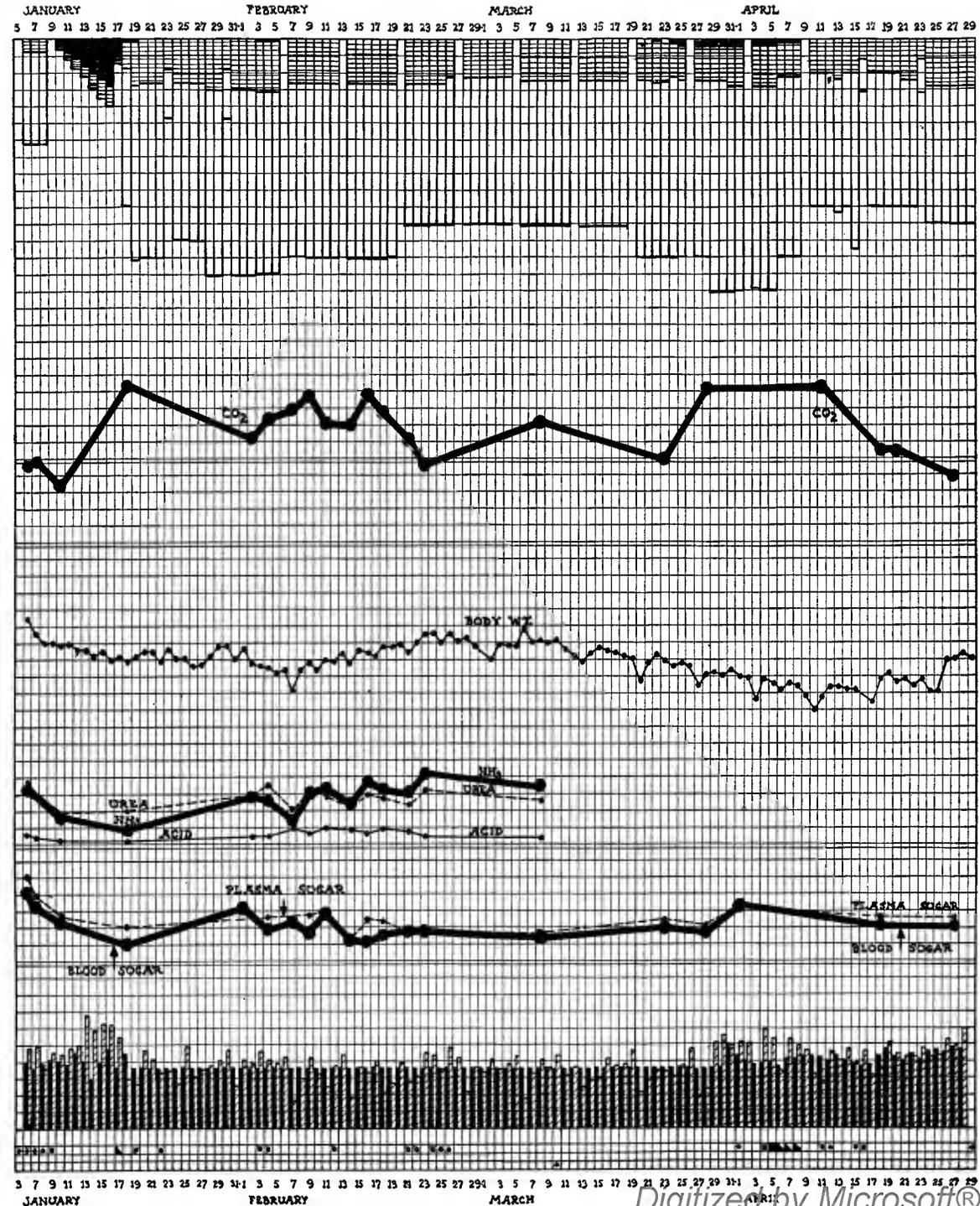
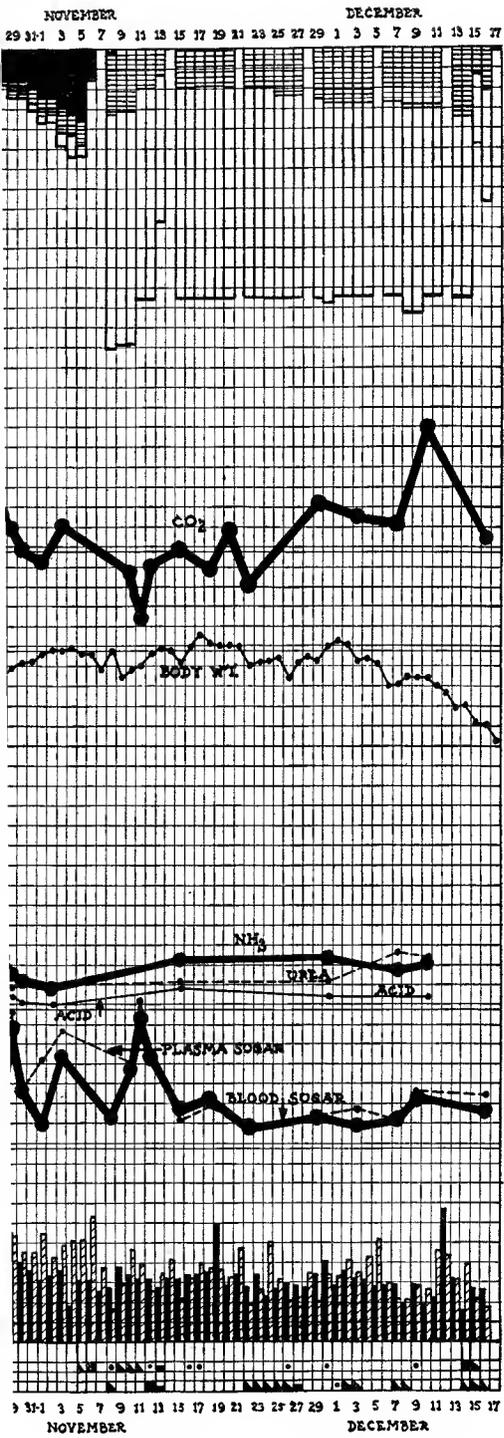
3rd ADMISSION



1917

4th ADMISSION





DIET
100 IN CALORIES
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500 20
1,600 16
1,700 12
1,800 8
1,900 4
2,000 0
3M. TOTAL N PER 24 HRS.

LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂
2,100
2,200
2,300
2,400
-55

BODY WT. ON ADMISSION
48
46
44
42
40

CC. NH₃ ACID
1,600
1,400
1,200
1,000
800
600
400
200
0

CC. NH₃
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0

NORMAL BLOOD SUGAR

CC. FLUID
3,500
3,000
2,500
2,000
1,500
1,000
500
0

INTAKE
OUTPUT

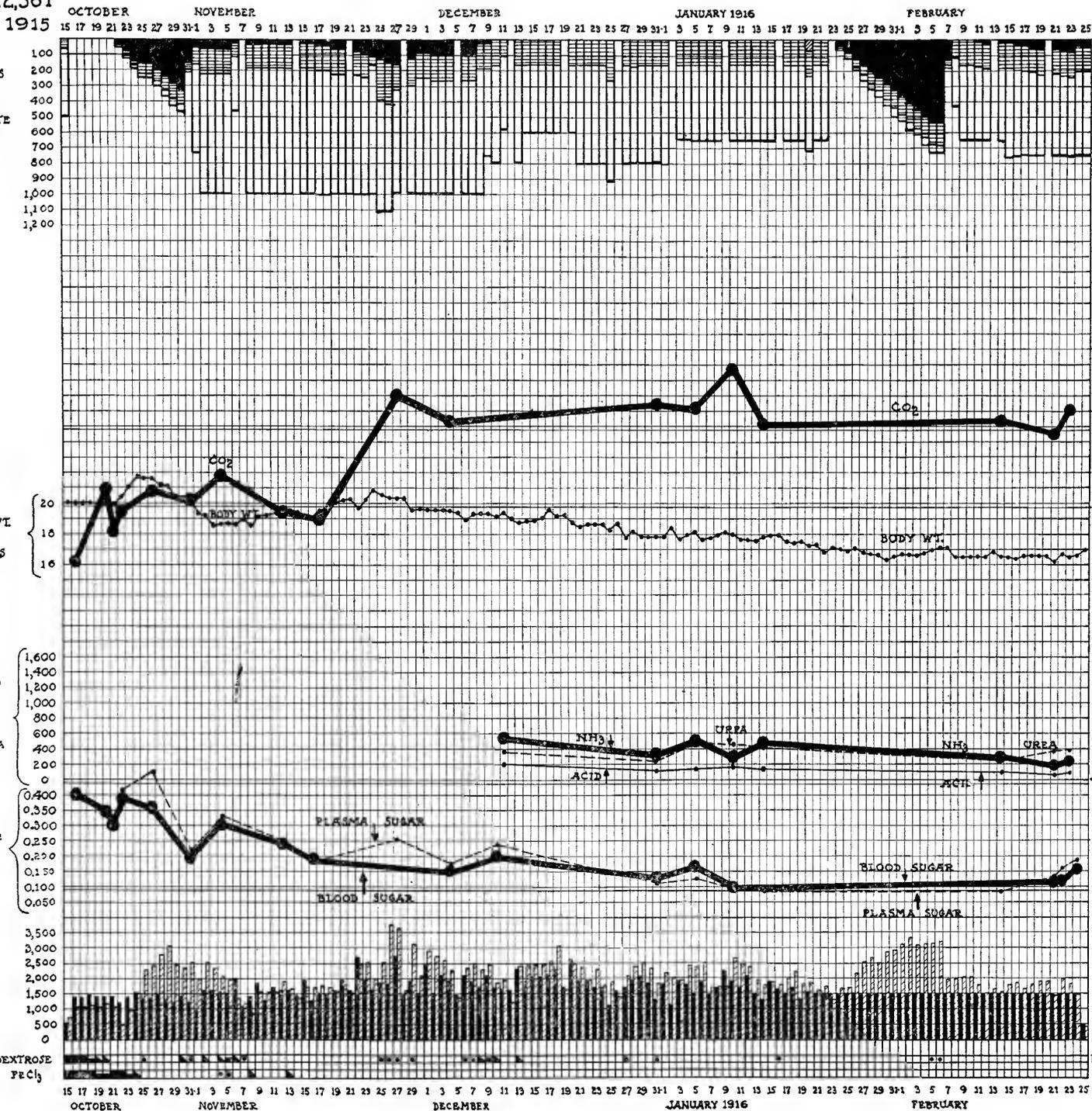
URINE
DEXTROSE
FeCl₃

Date.	Glucose excreted in 24 hrs.
2nd admission.	
1916	gm.
Jan. 5	7.6*
" 6	6.7
" 7	7.9

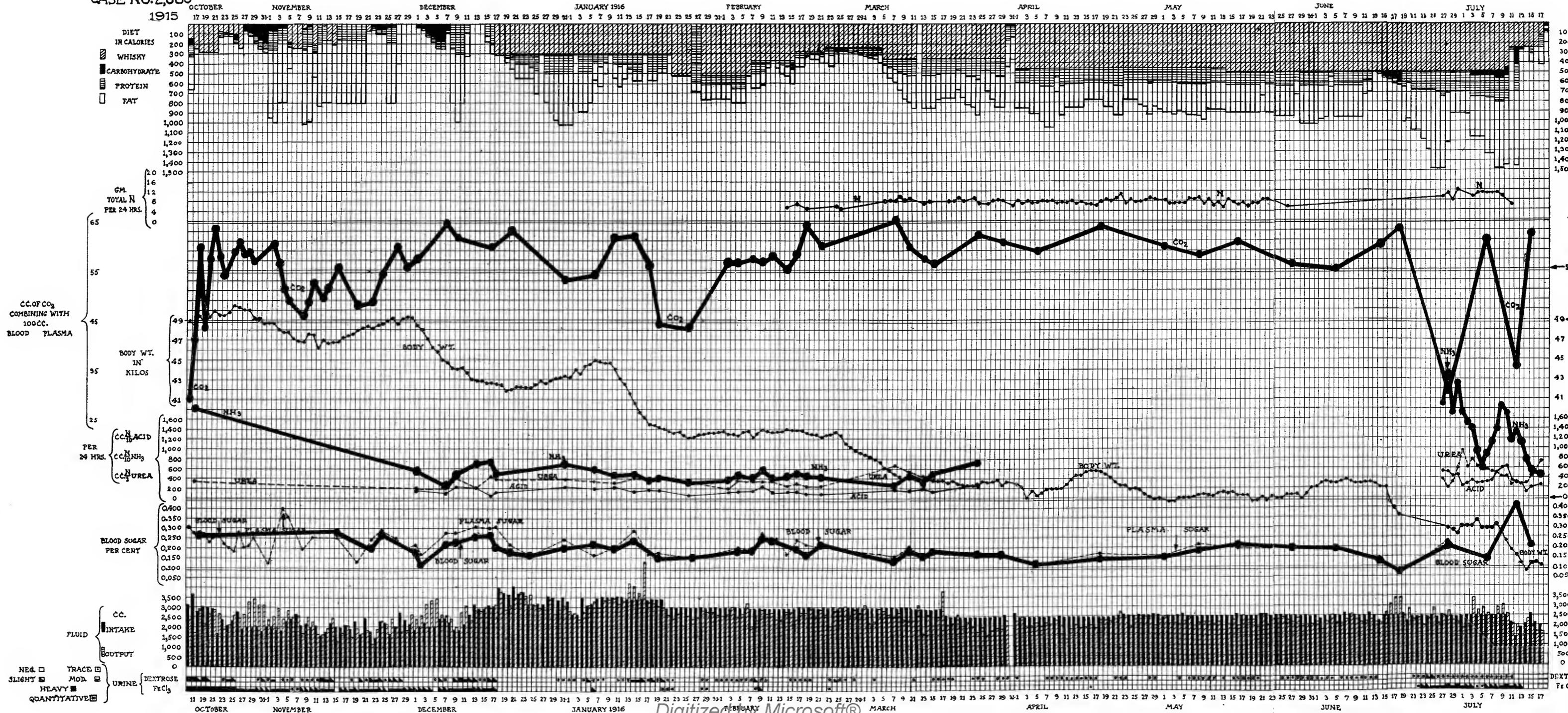
* 8 hr. specimen.

CHART 45. Case No. 52.

CASE NO. 2,561

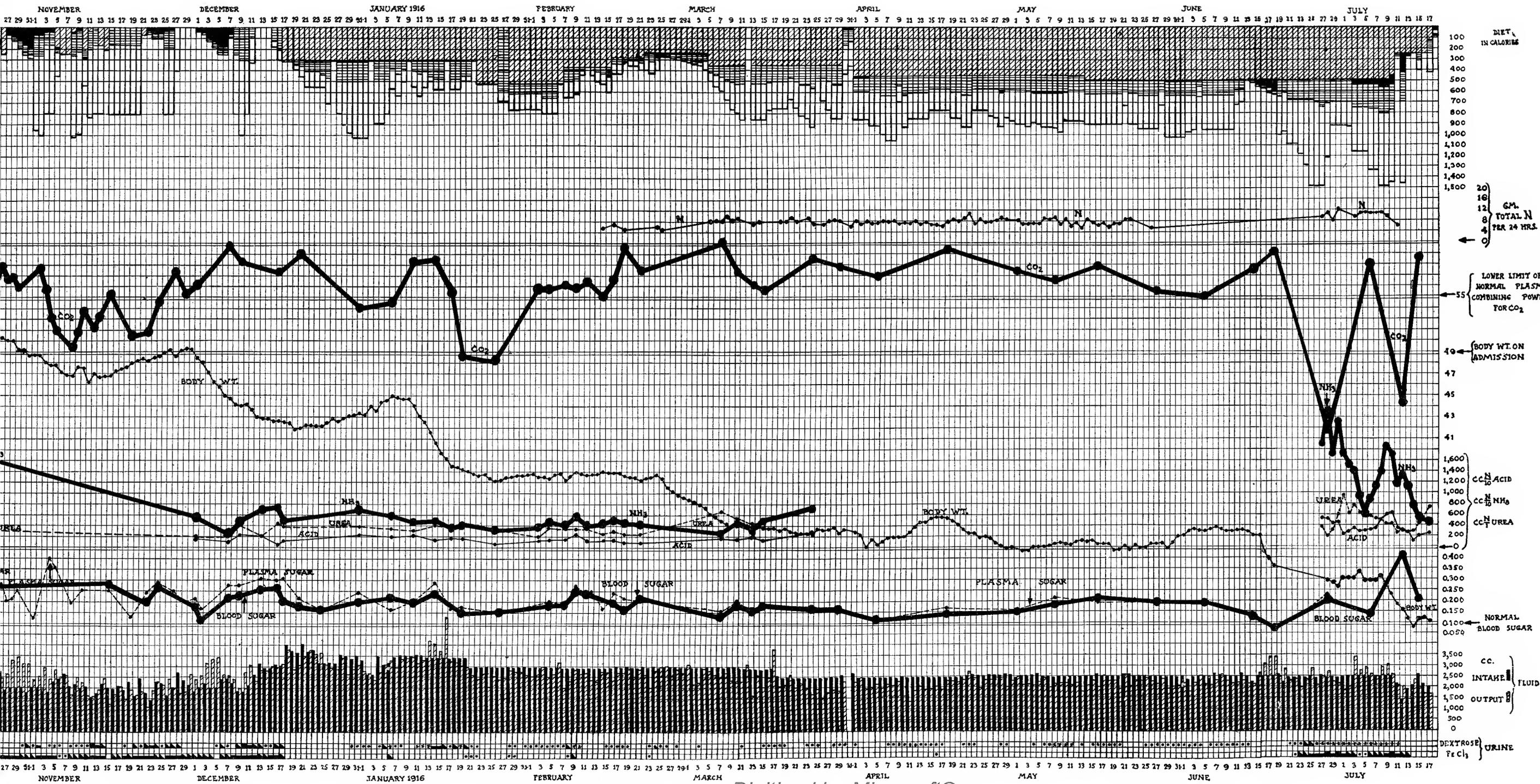


CASE NO. 2,680



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CHART 47. Case No. 54.



100
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500

20
16
12
8
4
0

←

LOWER LIMIT OF
NORMAL PLASMA
COMBINING POWER
FOR CO₂

35

40 ← BODY WT. ON
ADMISSION

47
45
43
41

1,600
1,400
1,200
1,000
800
600
400
200
0

0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050

3,500
3,000
2,500
2,000
1,500
1,000
500
0

DEXTROSE
FeCl₃

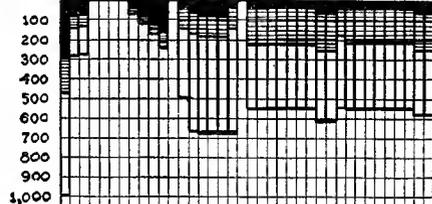
Date.	Glucose excreted in 24 hrs.
1916	gm.
Jan. 6	2.4
" 11	6.7
" 12	7.4
" 13	8.1
" 19	3.2
Feb. 9	5.5
" 10	4.8
May 8	4.5
" 9	6.0
" 10	8.0
" 11	3.9
June 26	17.3
" 27	21.6
" 28	23.9
" 29	15.8
" 30	18.8
July 1	24.7
" 2	29.2
" 3	25.8
" 4	32.8
" 5	18.8
" 6	23.0
" 7	20.3
" 8	34.5
" 9	37.7
" 10	18.7
" 11	1.0

CHART 47. Case No. 54. Digitized by Microsoft®

CASE NO. 2,475

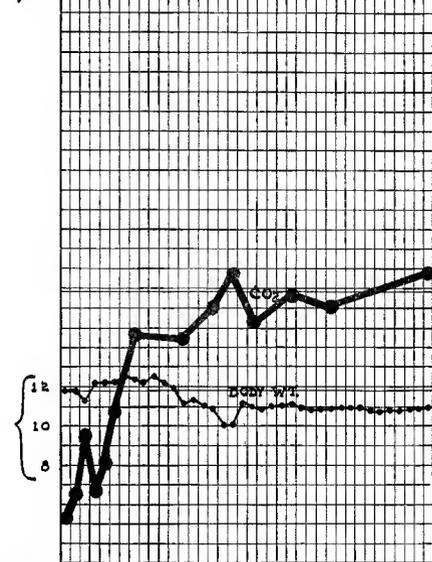
1st ADMISSION 1915 NOVEMBER 3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 DECEMBER

DIET IN CALORIES
 CARBOHYDRATE
 PROTEIN
 FAT



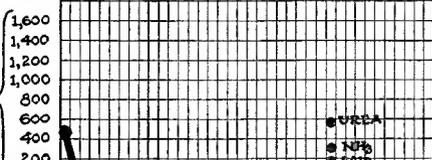
CC. OF CO₂ COMBINING WITH 100 CC. BLOOD PLASMA

BODY WT. IN KILOS

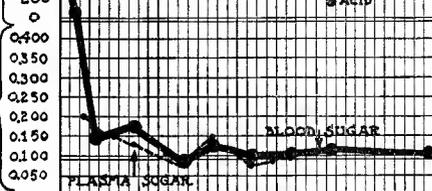


PER 24 HRS.
 CC. N₂ ACID
 CC. N₂ NH₃
 CC. N₂ UREA

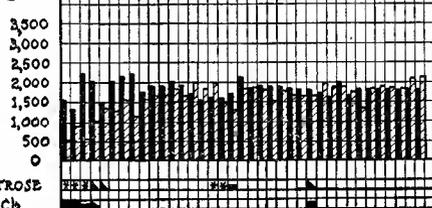
CC. N₂ ACID
 CC. N₂ NH₃
 CC. N₂ UREA



BLOOD SUGAR PER CENT

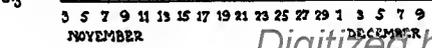


FLUID INTAKE OUTPUT

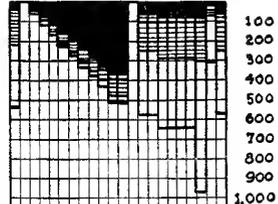


NEG. □ TRACE □ SLIGHT □ MOD. □ HEAVY □ QUANTITATIVE □

URINE DEXTROSE FeCl₃



1916 2nd ADMISSION APRIL 15 17 19 21 23 25 27 29 1 3 5 MAY



DIET IN CALORIES
 CARBOHYDRATE
 PROTEIN
 FAT

LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂

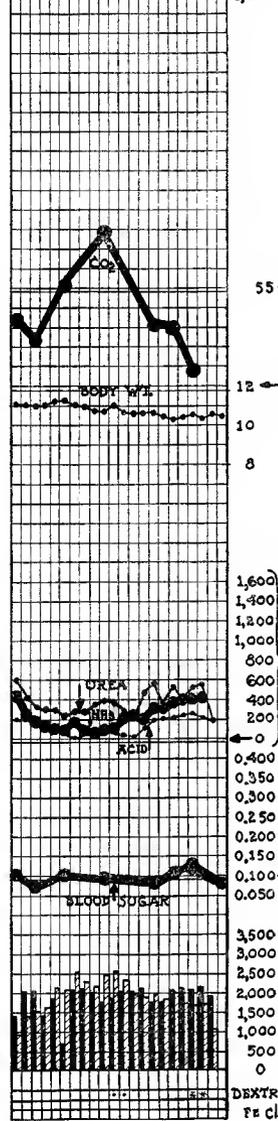
BODY WT. ON ADMISSION

CC. N₂ ACID
 CC. N₂ NH₃
 CC. N₂ UREA

BLOOD SUGAR PER CENT

FLUID INTAKE OUTPUT

URINE DEXTROSE FeCl₃



Date.	Glucose excreted in 24 hrs.
-------	-----------------------------

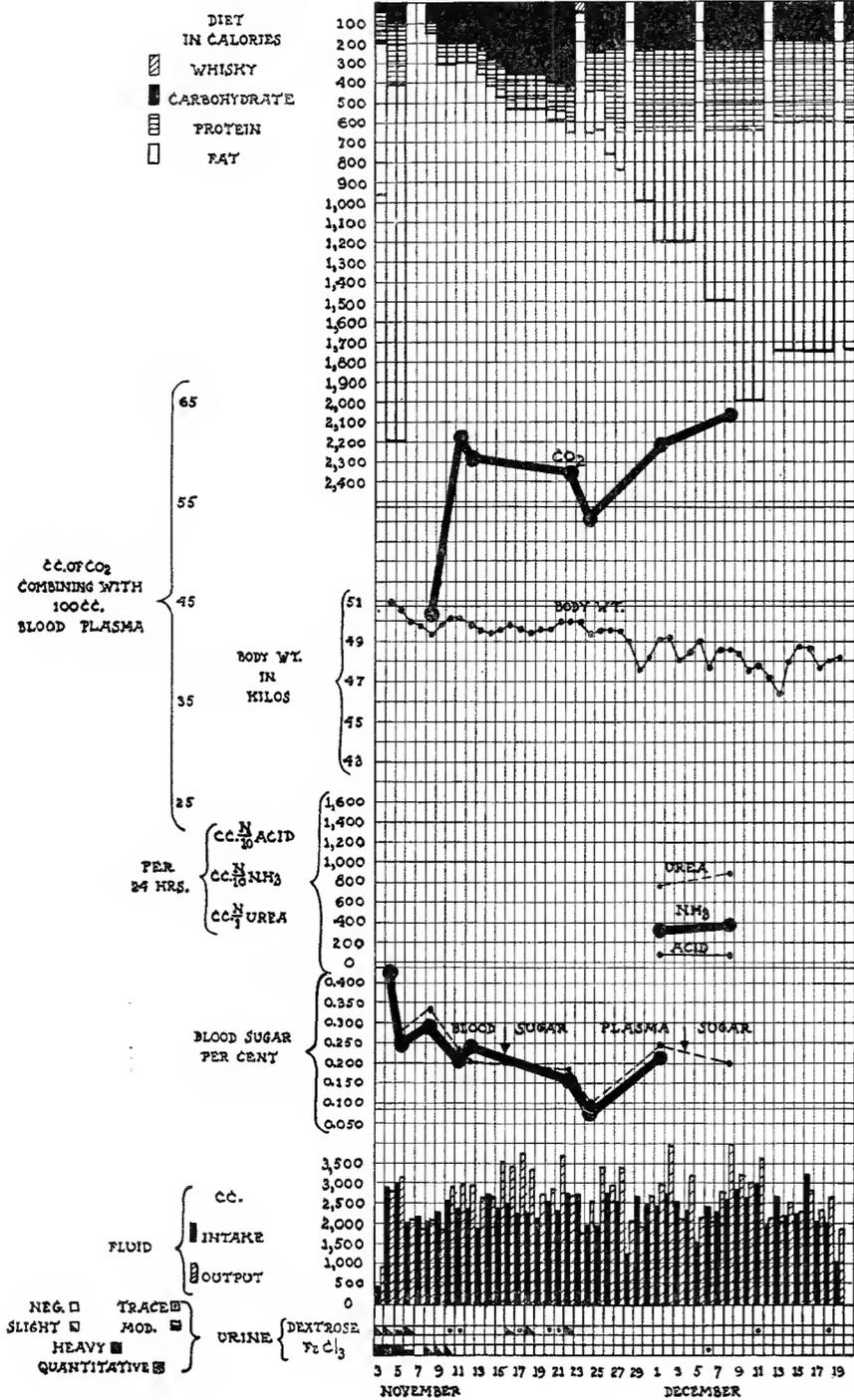
1st admission.	
1915	gm.
Nov. 3	17.05*
" 4	41.6
" 5	9.57
" 18	8.83
" 19	8.53

2nd admission.	
1916	
May 3	3.33
" 4	8.6

* 20 1/2 hr. specimen.

CASE NO. 2487

1st ADMISSION 1915



2nd ADMISSION



3rd ADMISSION

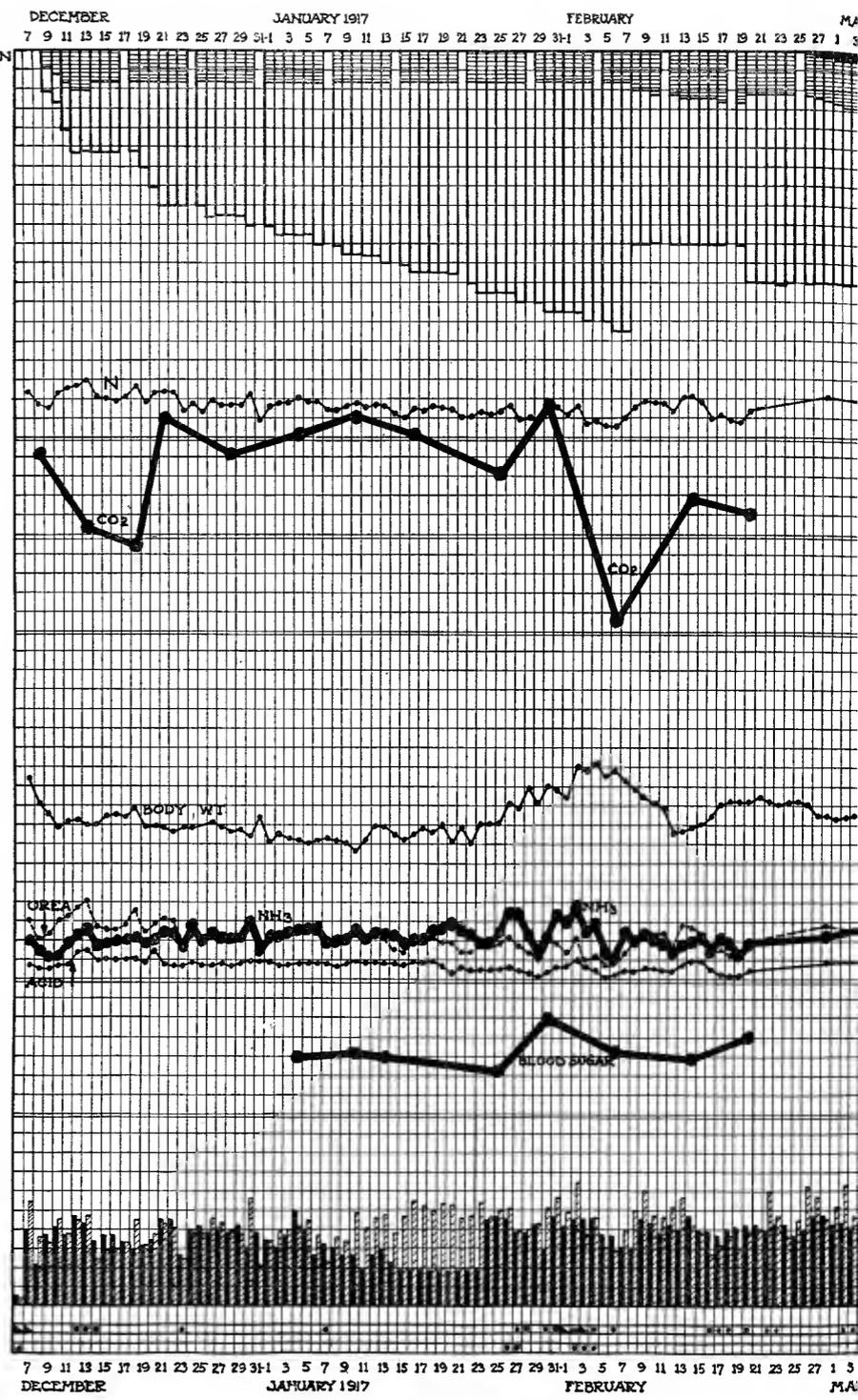
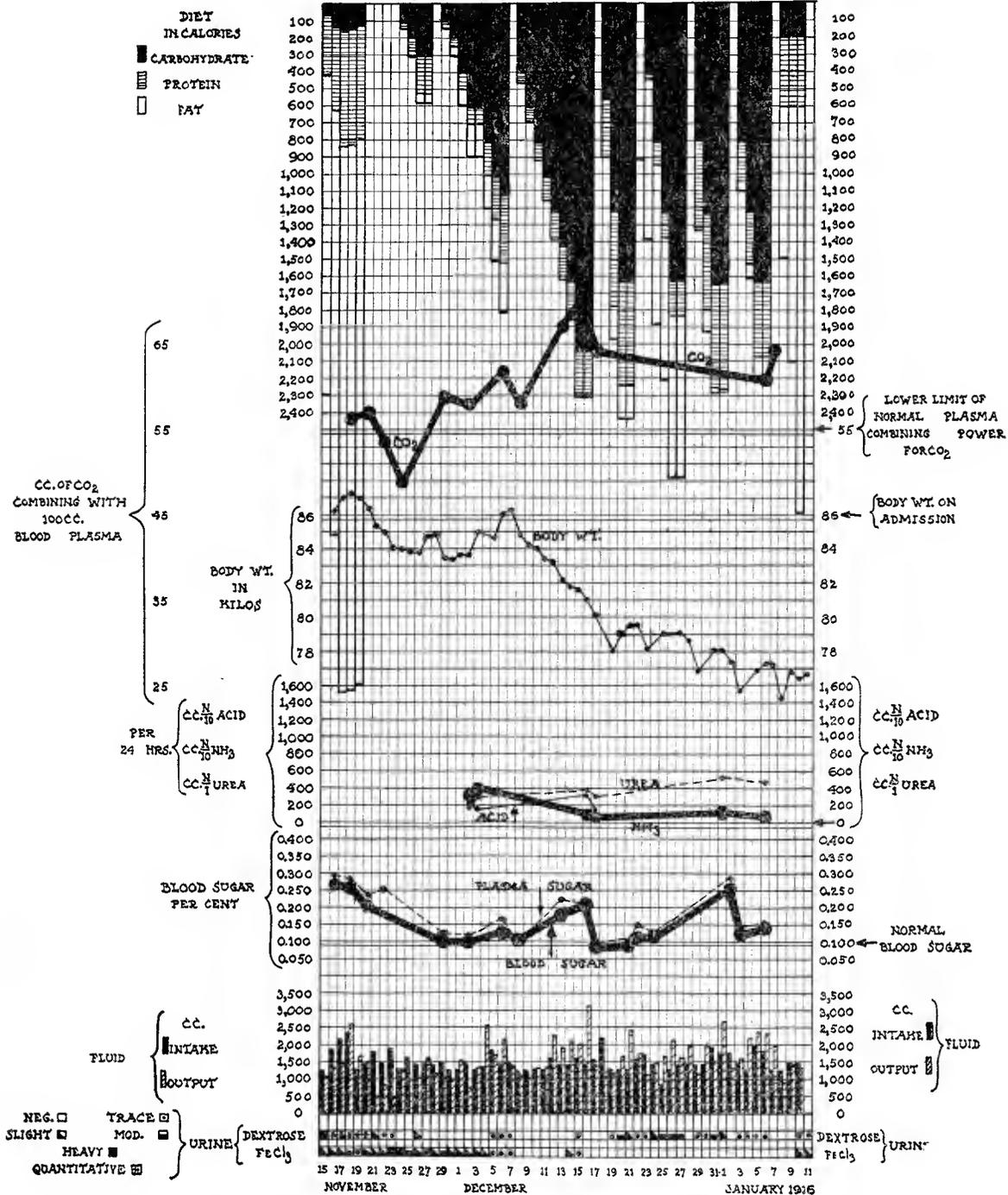


CHART 49. Case No. 56.

CASE NO. 2,516
1915

NOVEMBER DECEMBER JANUARY 1916
15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11



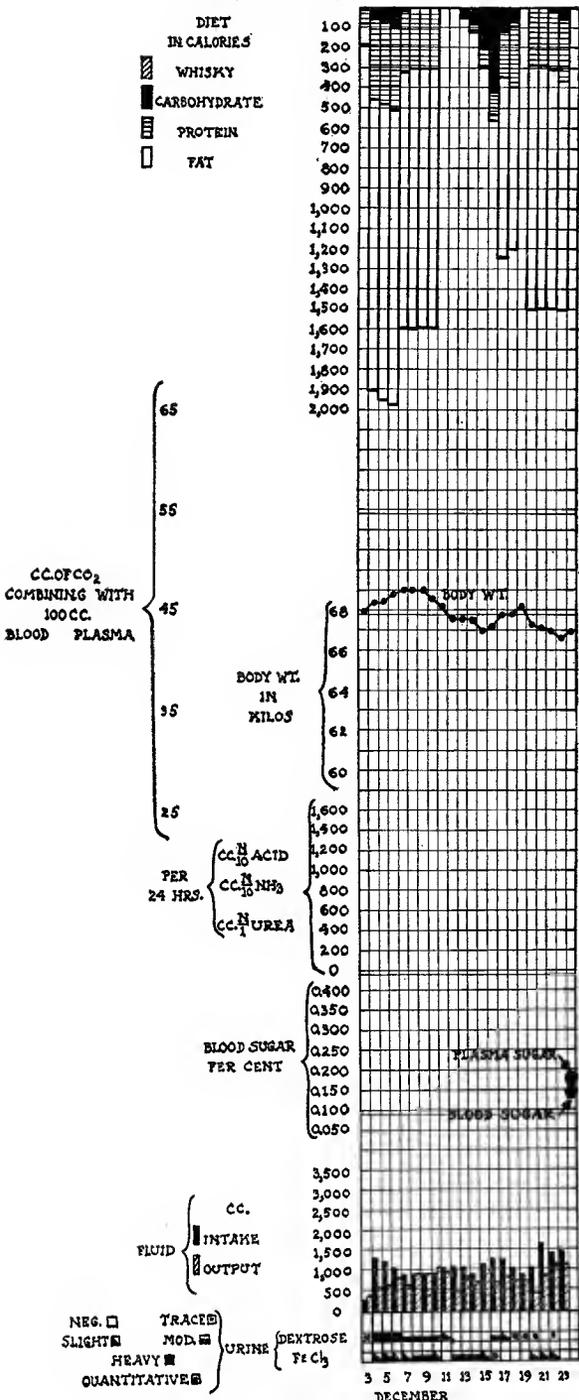
Date.	Glucose excreted in 24 hrs.
1915	
Nov. 16	24.5
" 17	16.7
" 18	31.6
" 19	14.5
" 20	9.3
Dec. 30	3.0

CASE NO. 2,496

1st ADMISSION 1915

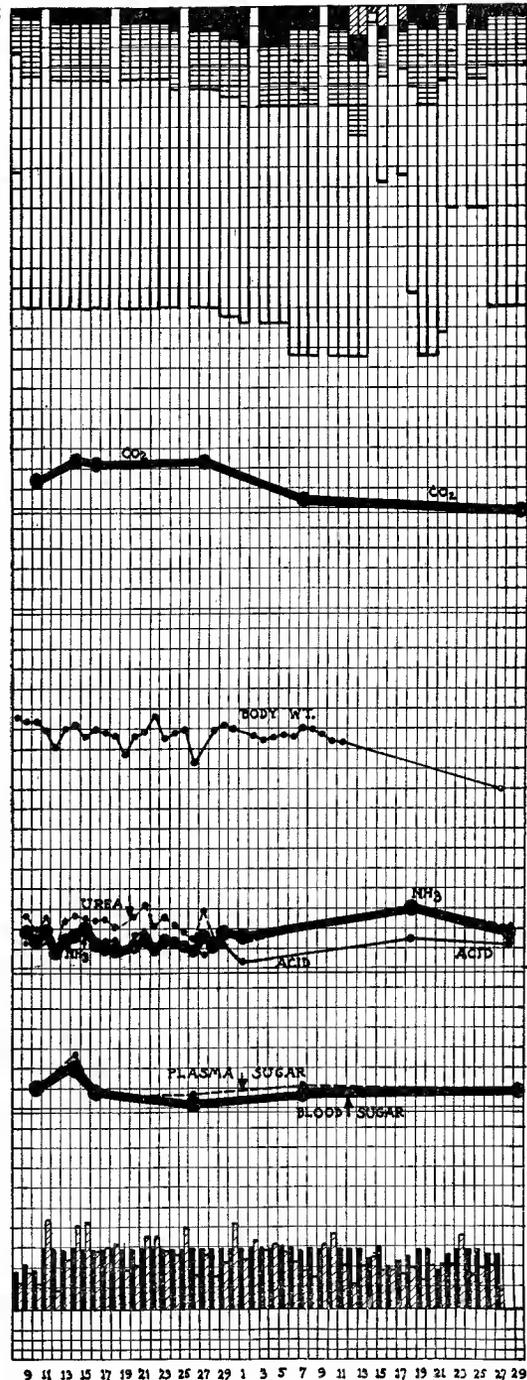
1916

2nd ADMISSION



JUNE 1916

JULY



Date.	Glucose excreted in 24 hrs.
1st admission.	
1915	gm.
Dec. 3	2.0*

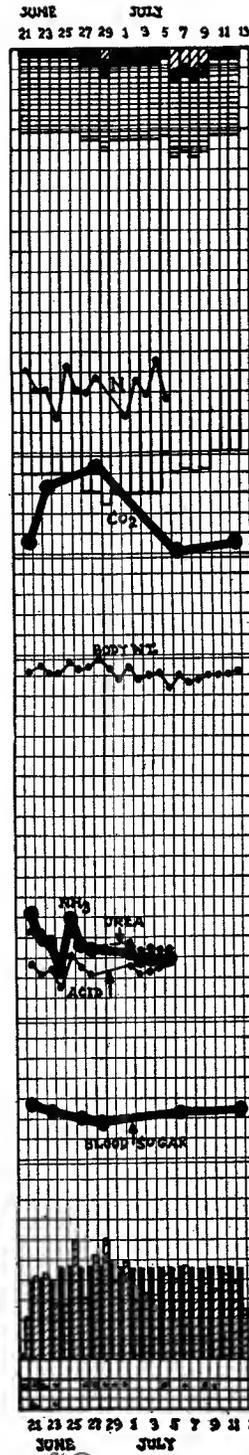
* 18 hr. specimen.

CASE NO. 2,577

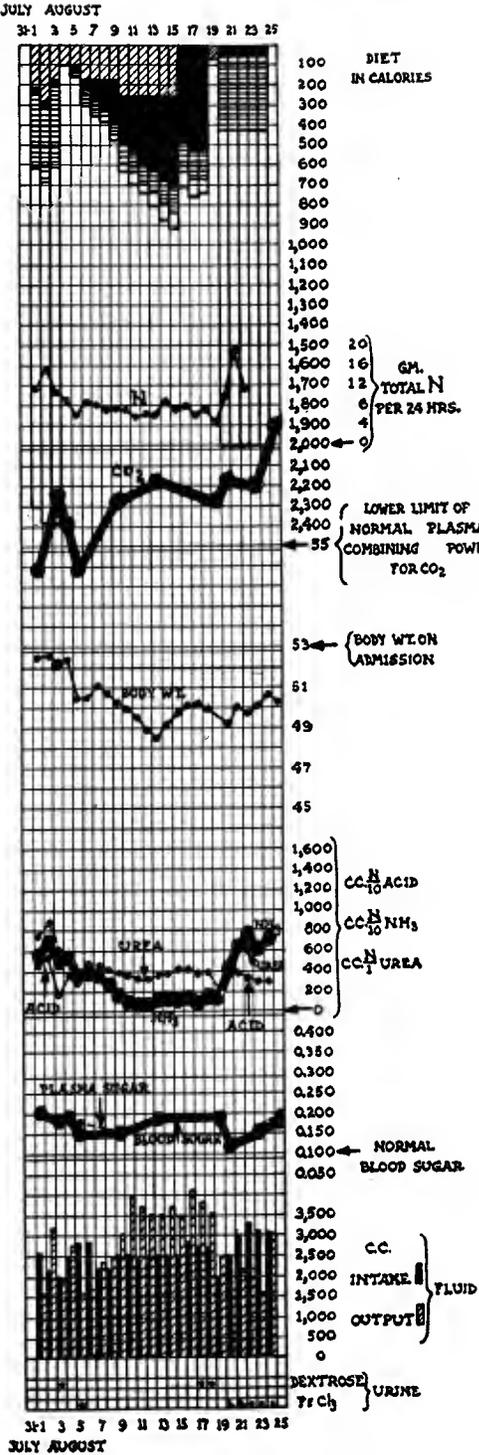
1st ADMISSION 1915



2nd ADMISSION



3rd ADMISSION 1916



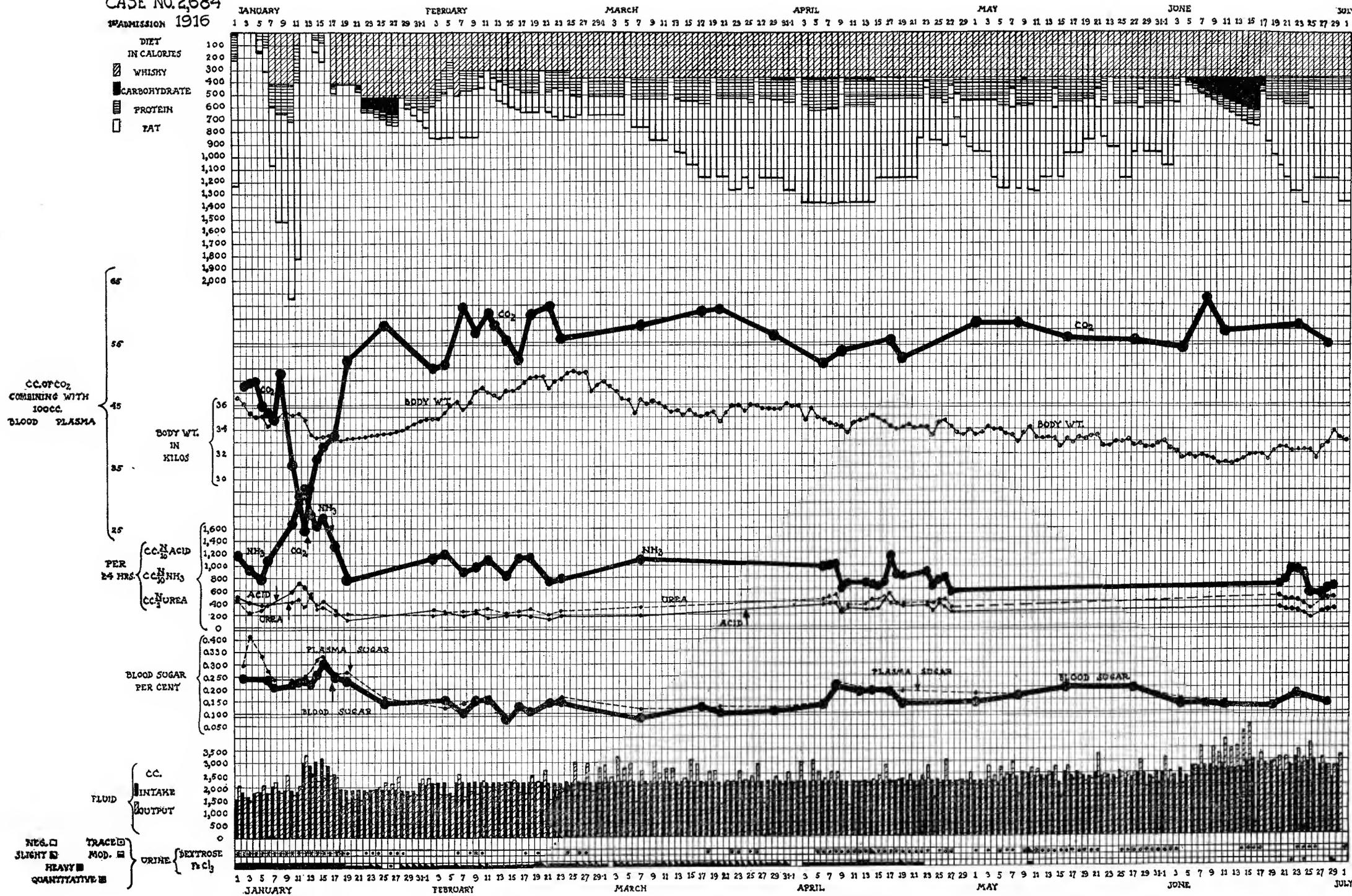
Date.	Glucose excreted in 24 hrs.
1st admission.	
1915	gm.
Dec. 29	8.5*
" 30	17.0

2nd admission.	
1916	gm.
June 21	6.7

* 8 hr. specimen.

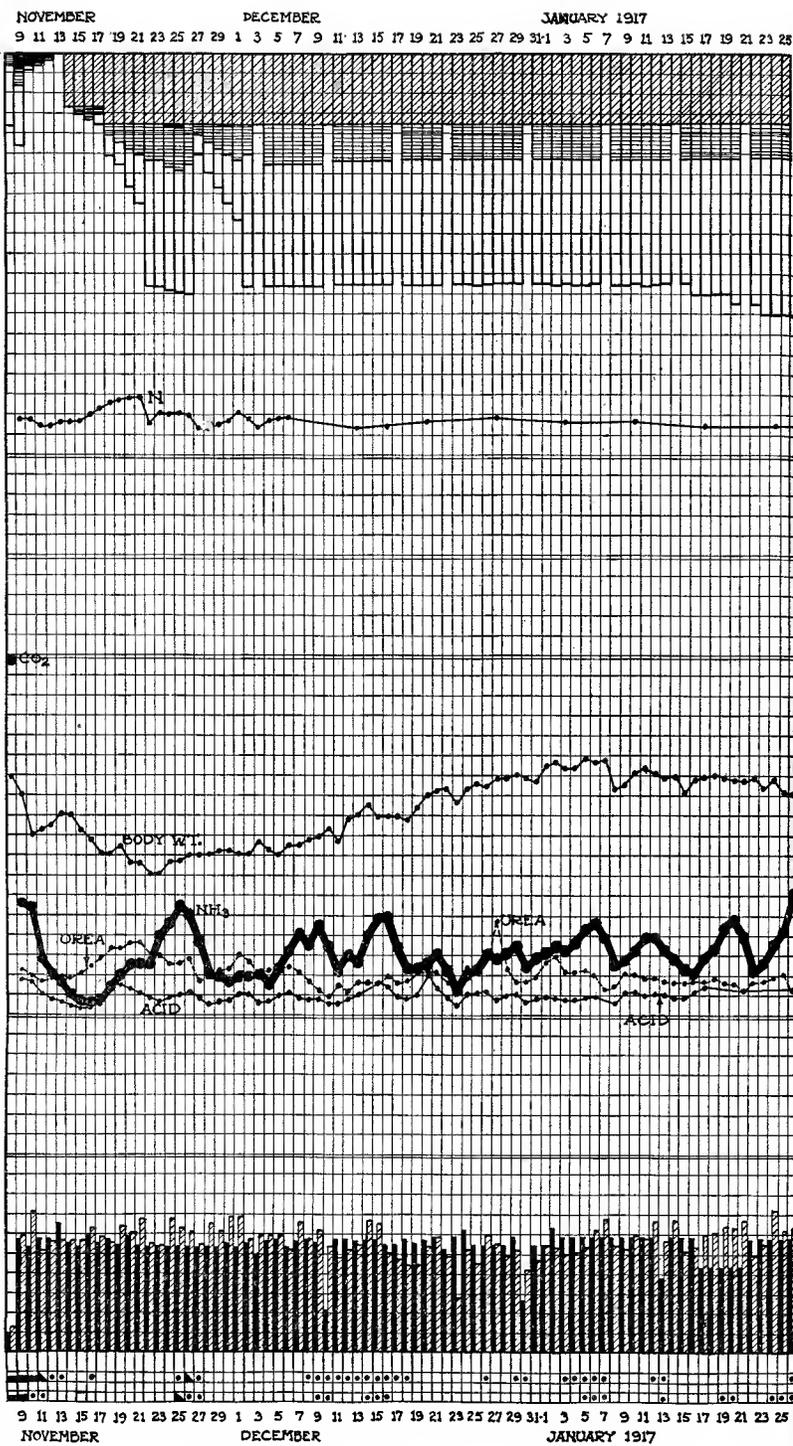
CASE NO. 2684

1st ADMISSION 1916



1916

2nd ADMISSION



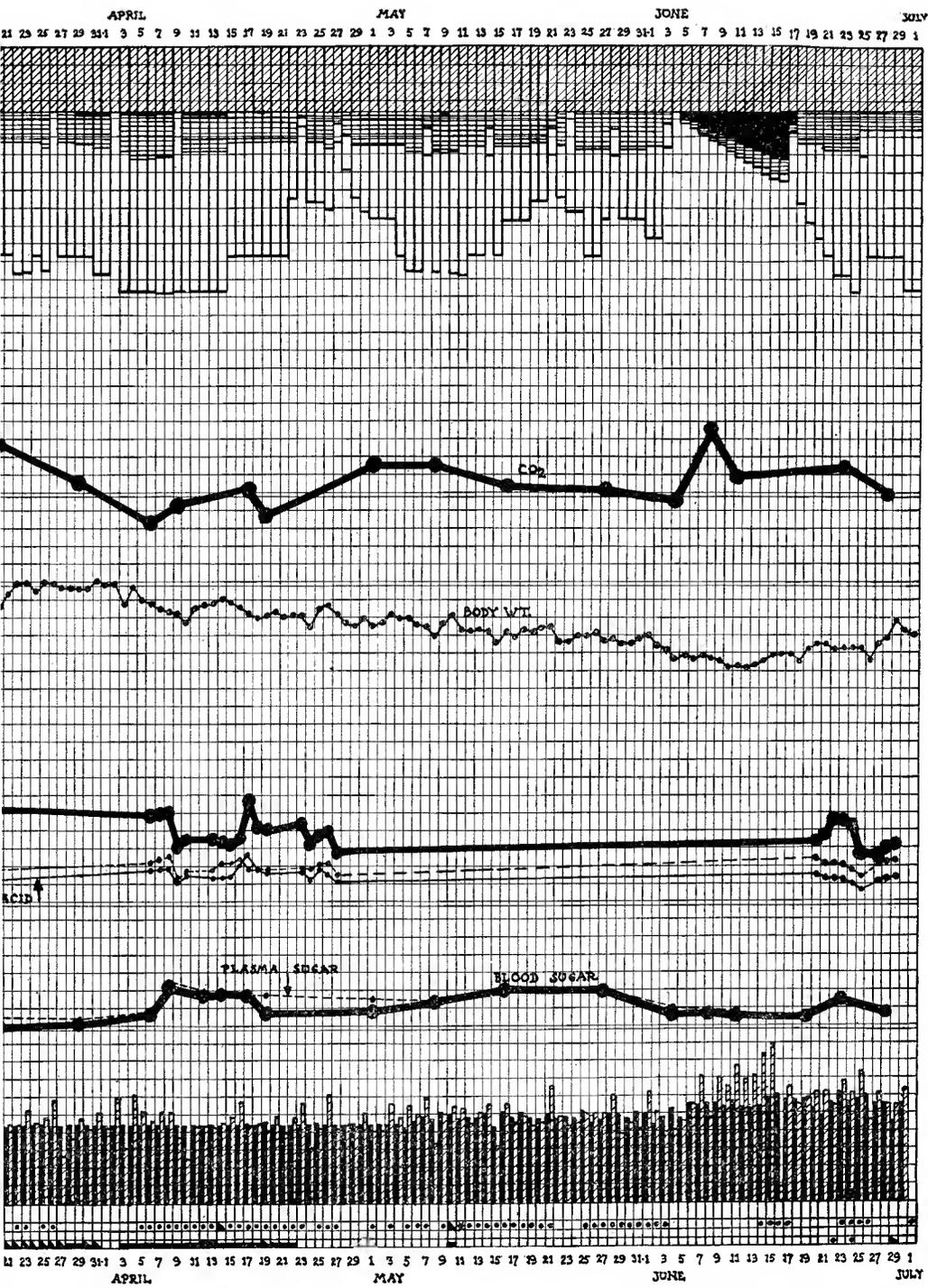
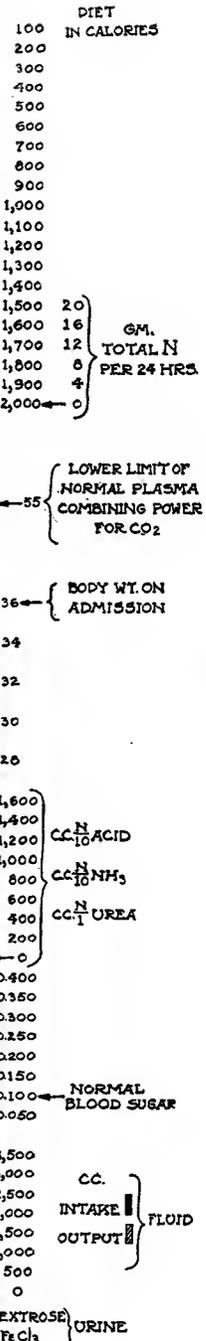
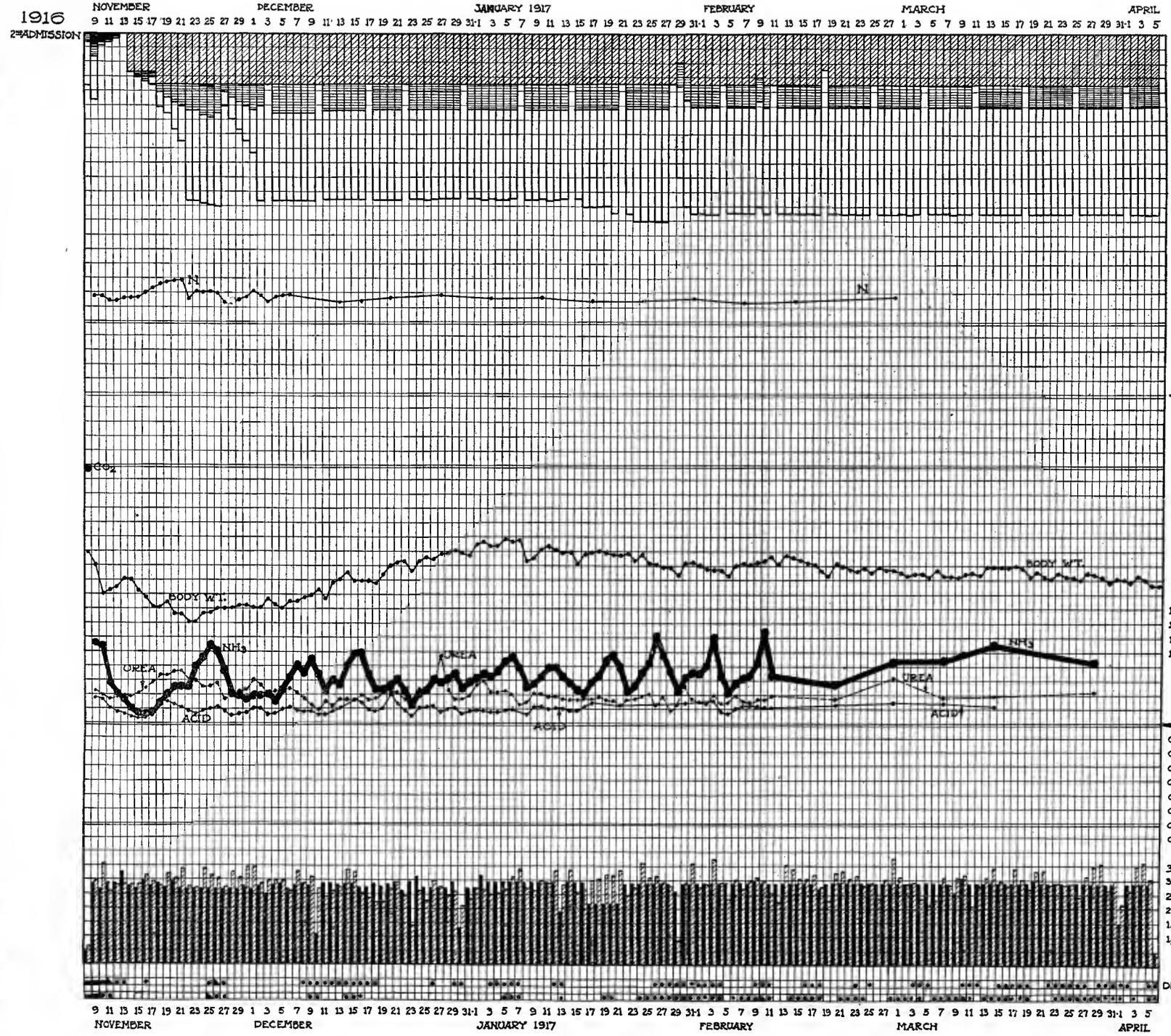


CHART 53. Case No. 60.

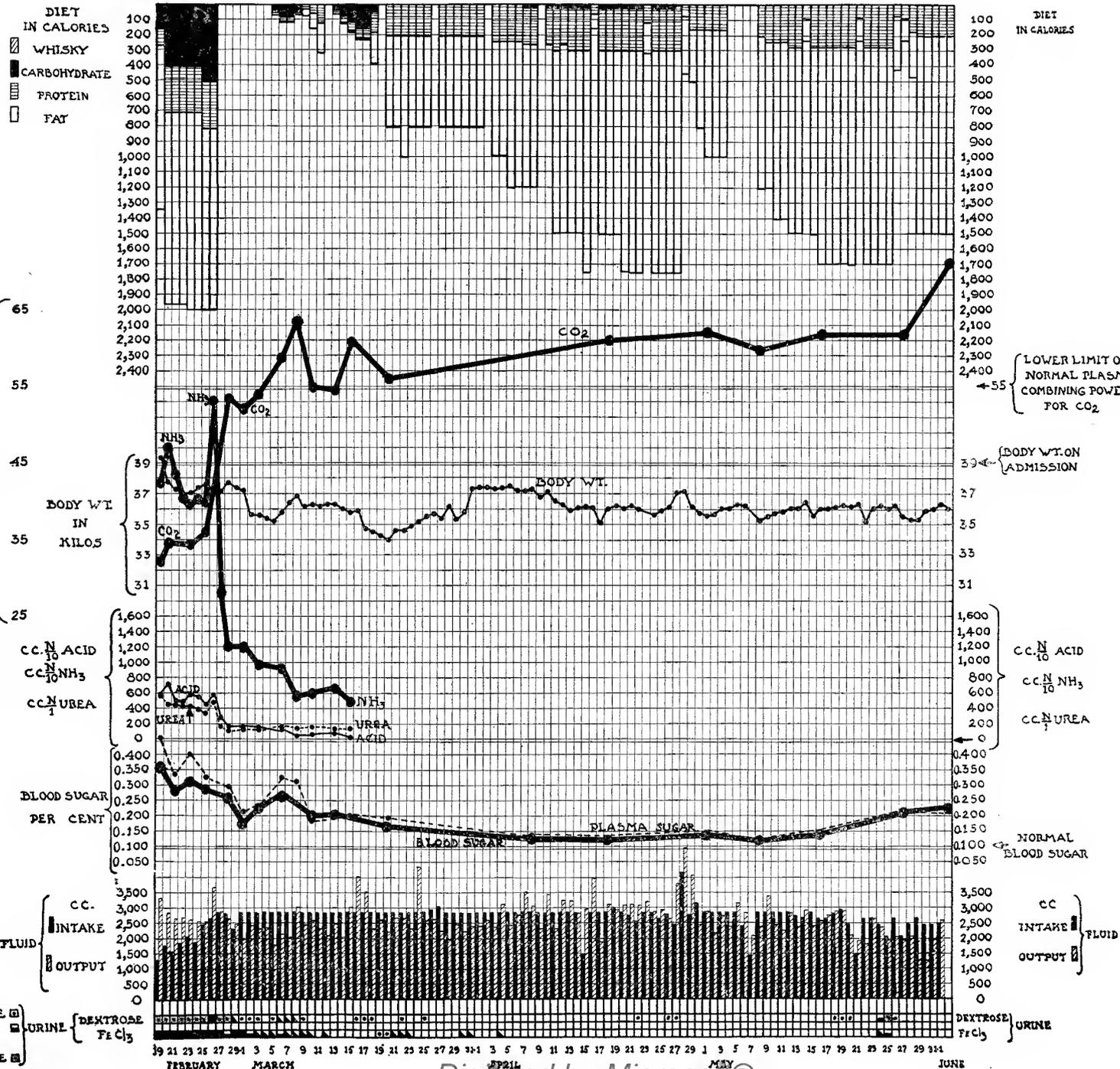


Date.	Glucose excreted in 24 hrs.
1st admission.	
1916	gm.
Jan. 1	28.4*
" 2	11.0
" 3	9.2
" 4	12.1
" 5	15.2
" 6	14.2
" 7	15.3
" 8	10.9
" 9	12.4
" 10	18.3
" 11	24.1
" 12	18.2
" 13	13.8
" 14	19.0
" 15	20.7
" 16	15.1
" 17	11.0
" 18	2.3
Feb. 9	1.6
May 11	5.2

* 12 hr. specimen.

CASE NO. 2646

1916 FEBRUARY MARCH APRIL MAY JUNE
19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31



Date.	Glucose excreted in 24 hrs.
1916	gm.
Feb. 19	145.0
" 20	113.0
" 21	126.0
" 22	116.0
" 23	113.0
" 24	132.0
" 25	131.0
" 27	17.0
" 28	6.0
May 25	14.0

LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂
← 55

BODY WT. ON ADMISSION

CC. N ACID
CC. N NH₃
CC. N UREA

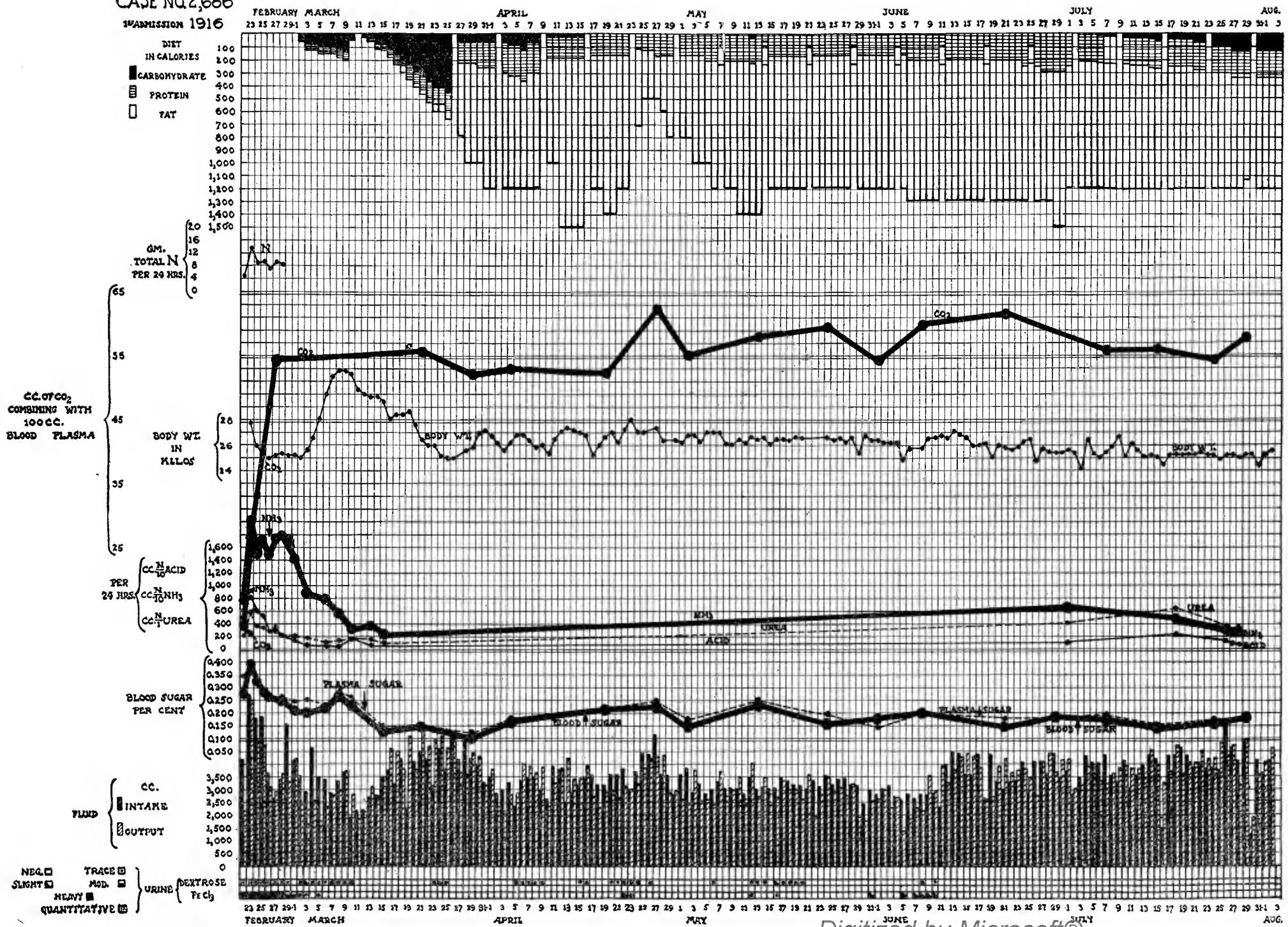
NORMAL BLOOD SUGAR

CC. INTAKE
CC. OUTPUT

URINE

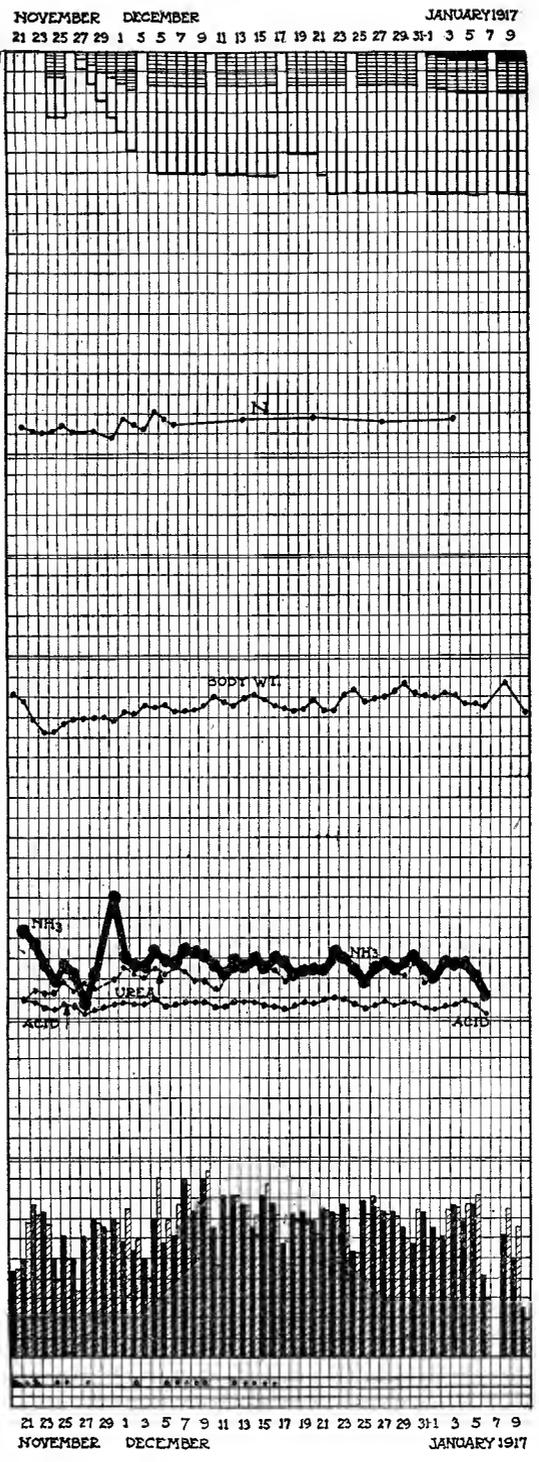
CASE NO. 2,686

1st ADMISSION 1916



1916

2nd ADMISSION



1917

3rd ADMISSION

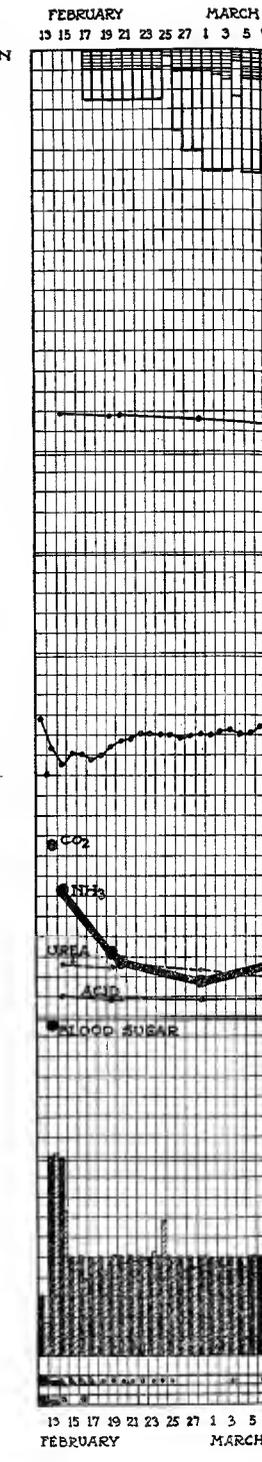
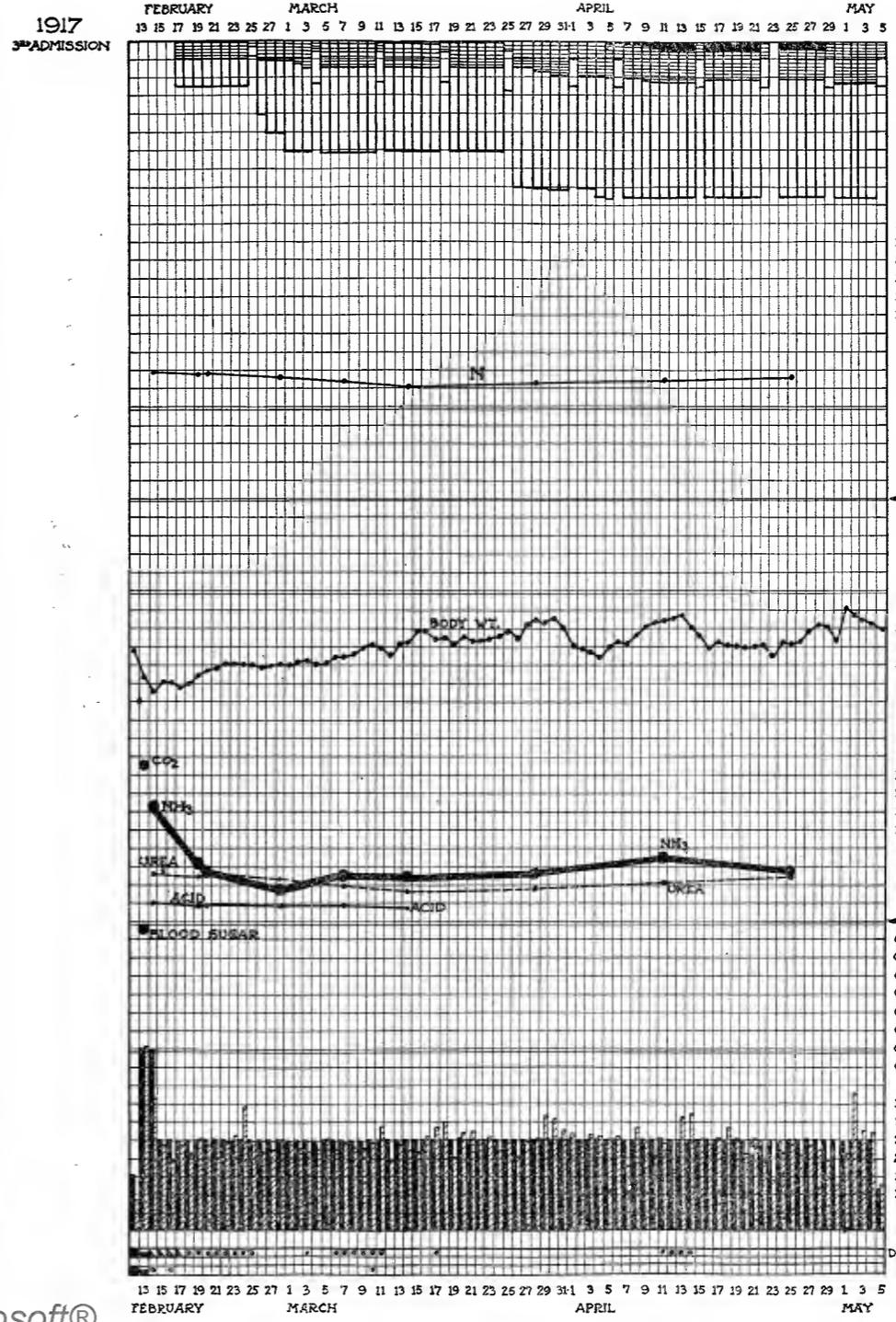
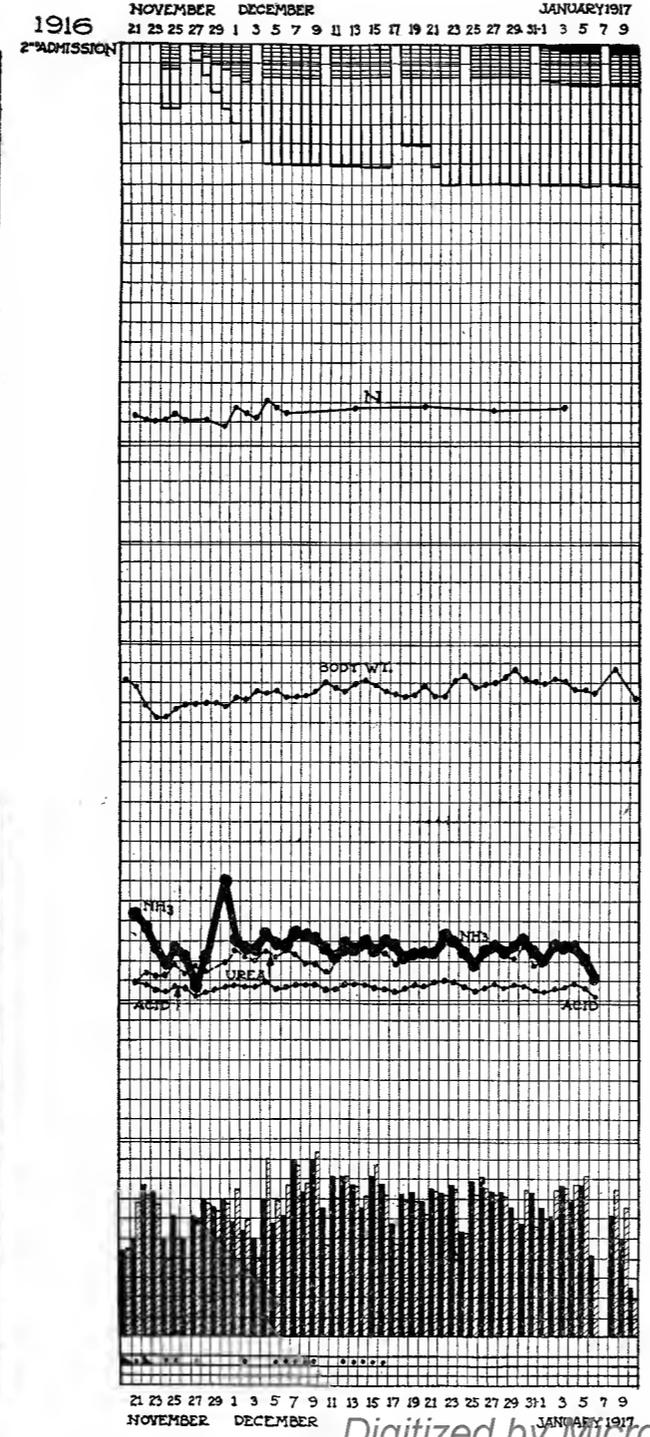
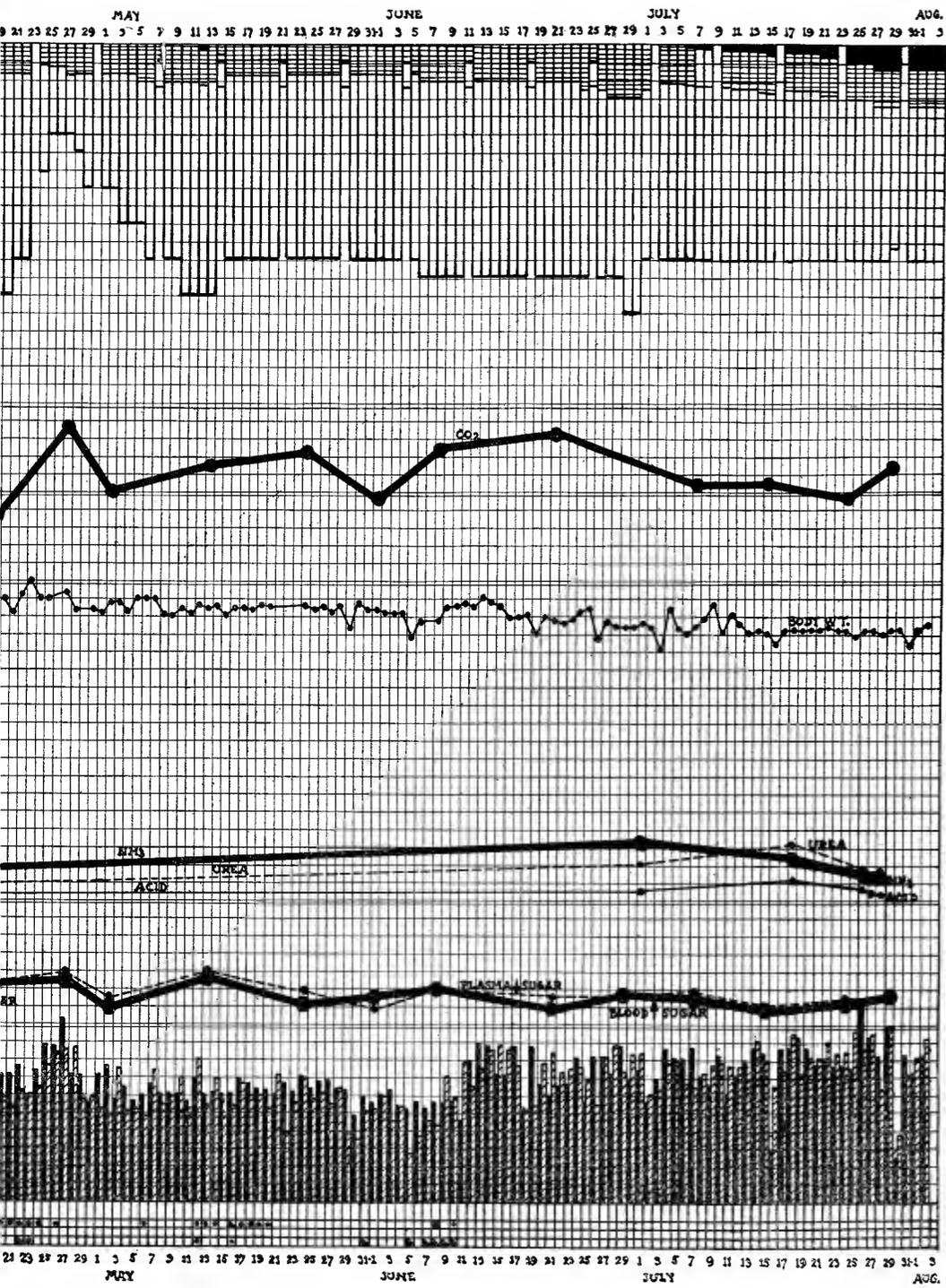


CHART 55. Case No. 63.



100
200
300
400
500
600
700
800
900
1,000
1,100
1,200
1,300
1,400
1,500

20
16
12
8
4
0

GM. TOTAL N PER 24 HRS.

← 55

← 28

← 26

← 24

← 1,600

← 1,400

← 1,200

← 1,000

← 800

← 600

← 400

← 200

← 0

← 0.400

← 0.350

← 0.300

← 0.250

← 0.200

← 0.150

← 0.100

← 0.050

← 3,500

← 3,000

← 2,500

← 2,000

← 1,500

← 1,000

← 500

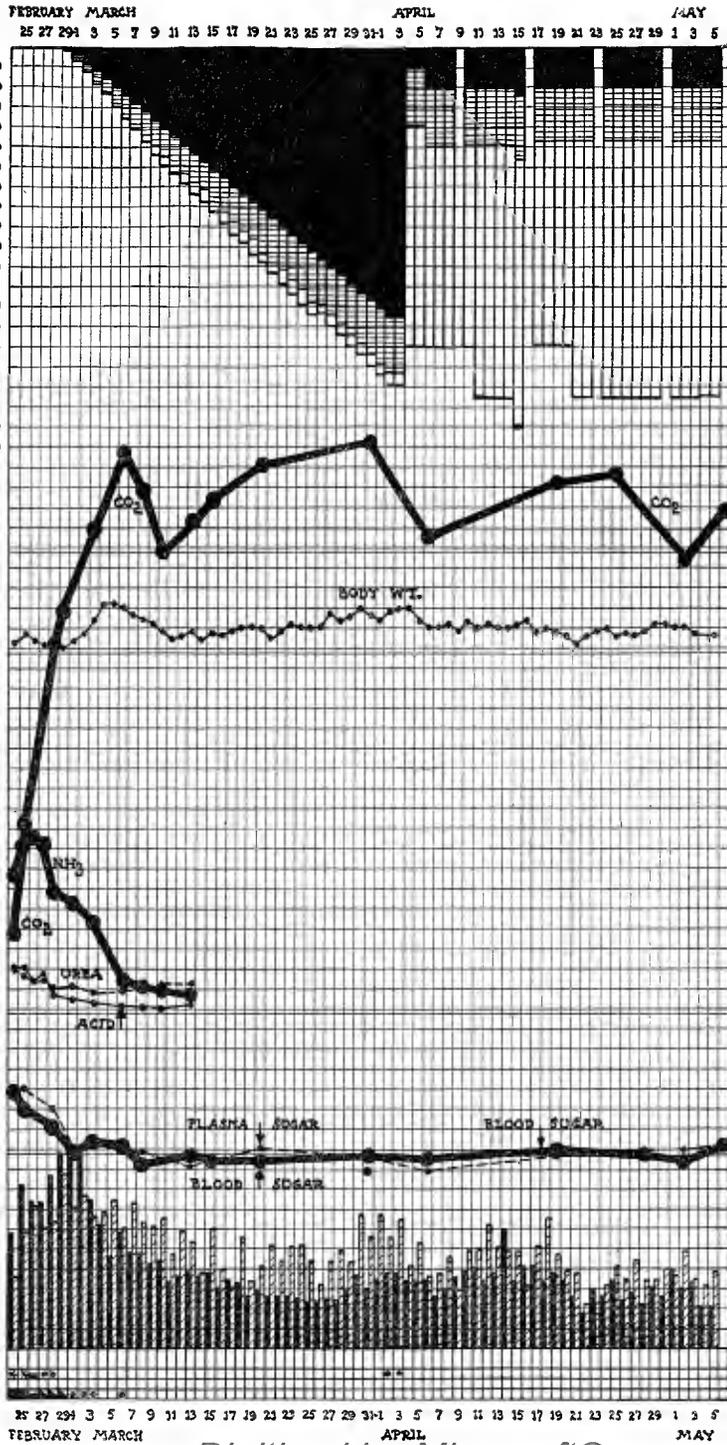
← 0

Date.	Glucose excreted in 24 hrs.
1st admission.	
1916	gm.
Feb. 22	22.9
" 23	41.0
" 24	24.1
" 25	20.9
" 26	12.1
" 27	12.3
" 28	5.9

* 12 hr. specimen.

CHART 55. Case No. 63.

CASE NO. 2,620
1916



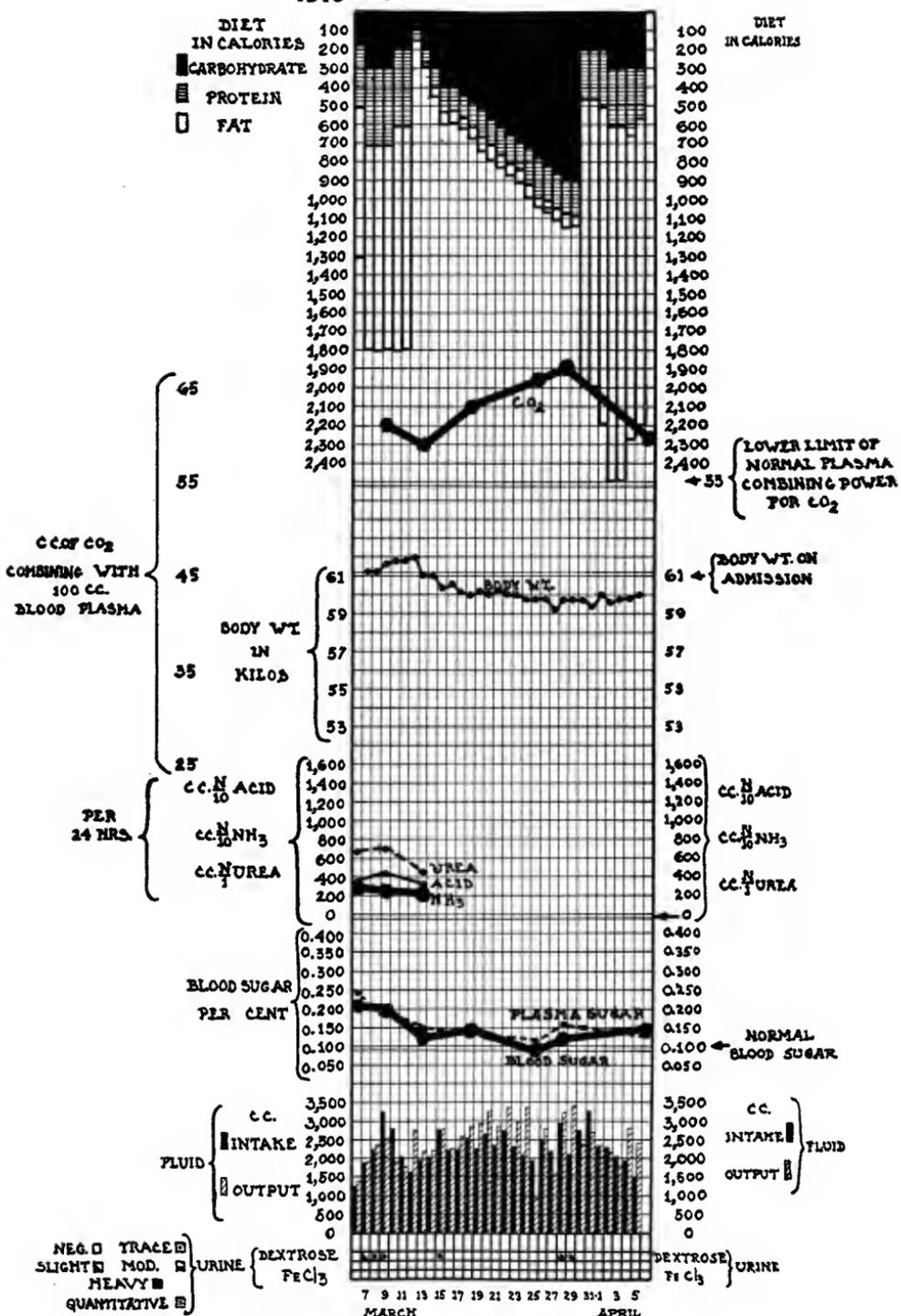
DIET
IN CALORIES

Date.	Glucose excreted in 24 hrs.
1916	gm.
Feb. 24	23.4*
" 25	11.6

* 18½ hr. specimen.

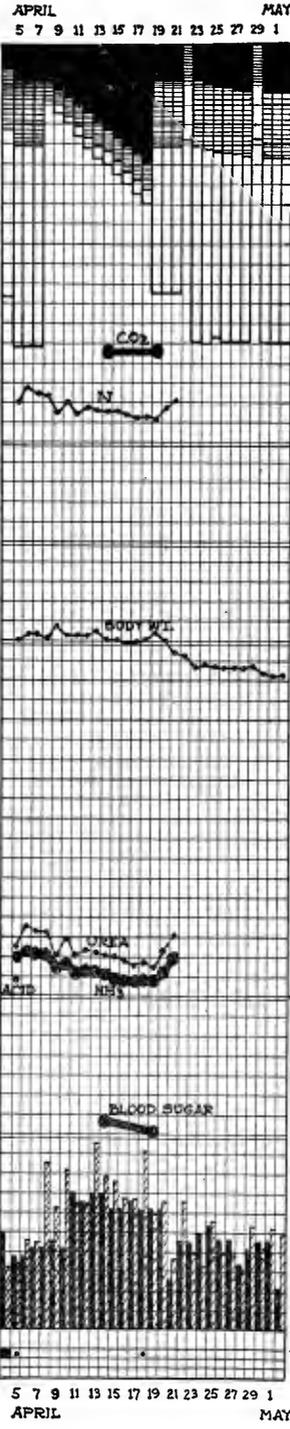
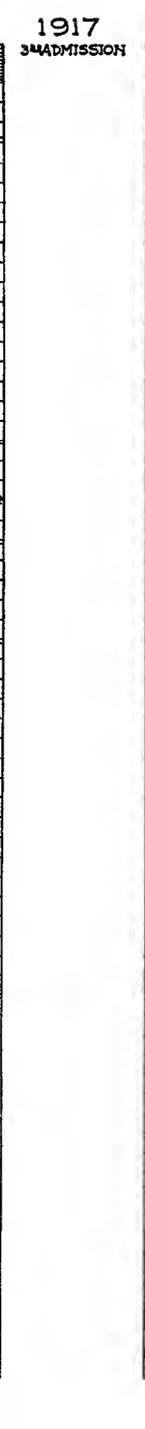
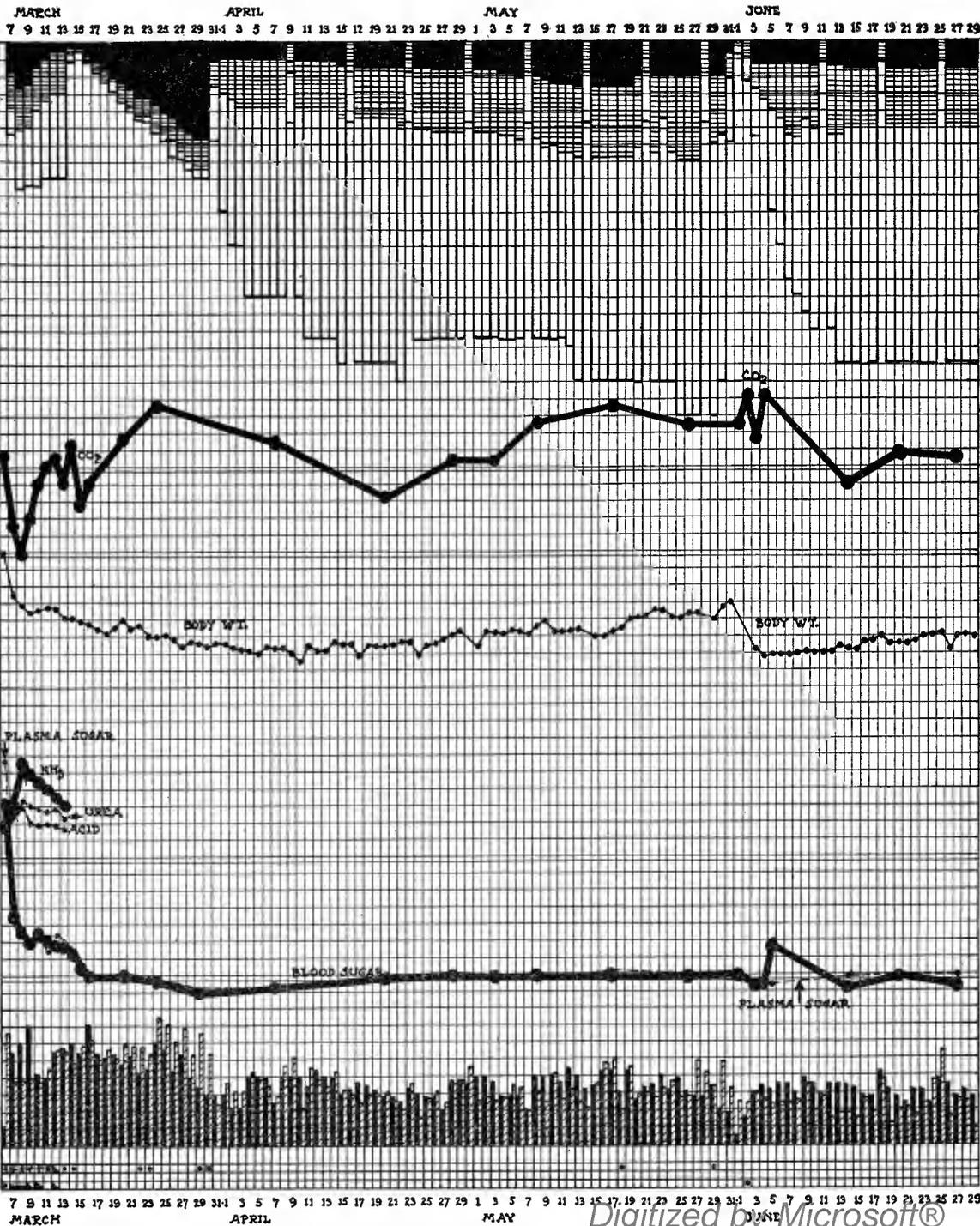
CASE NO. 2,591
1916

MARCH 7 9 11 13 15 17 19 21 23 25 27 29 31-1 3 5
APRIL



CASE NO. 2678

1st ADMISSION 1916



DIET IN CALORIES
 100 CARBOHYDRATE
 200 PROTEIN
 300 FAT
 400
 500
 600
 700
 800
 900
 1,000
 1,100
 1,200
 1,300
 1,400
 1,500
 1,600
 1,700
 1,800
 1,900
 2,000
 2,100
 2,200
 2,300
 2,400

CC OF CO₂ COMBINING WITH 100CC. BLOOD PLASMA
 65
 55
 45
 35
 25

BODY WT. IN KILOGS
 50
 48
 46
 44
 42

PER 24 HRS.
 CC OF CO₂ ACID
 CC OF NH₃
 CC OF UREA
 1,600
 1,400
 1,200
 1,000
 800
 600
 400
 200
 0

BLOOD SUGAR PER CENT
 0.400
 0.350
 0.300
 0.250
 0.200
 0.150
 0.100
 0.050

FLUID INTAKE OUTPUT
 CC.
 3,500
 3,000
 2,500
 2,000
 1,500
 1,000
 500
 0

URINE DEXTROSE FeCl₃

GM. TOTAL N PER 24 HRS.
 20
 18
 16
 14
 12
 10
 8
 6
 4

LOWER LIMIT OF NORMAL PLASMA COMBINING POWER FOR CO₂
 55

BODY WT. ON ADMISSION
 50
 48
 46
 44
 42

CC OF CO₂ ACID
 CC OF NH₃
 CC OF UREA
 1,600
 1,400
 1,200
 1,000
 800
 600
 400
 200
 0

BLOOD SUGAR
 0.400
 0.350
 0.300
 0.250
 0.200
 0.150
 0.100
 0.050

NORMAL BLOOD SUGAR
 0.100

FLUID INTAKE OUTPUT
 CC.
 3,500
 3,000
 2,500
 2,000
 1,500
 1,000
 500
 0

URINE DEXTROSE FeCl₃

Date.	Glucose excreted in 24 hrs.
1st admission.	
1916	gm.
Mar. 6	32.0*
" 7	70.6
" 8	98.0
" 9	37.0
" 10	19.3

* 12 hr. specimen.

CHART 58. Case No. 66.

CASE NO. 2,666

1916 APRIL MAY JUNE
21 23 25 27 29 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15

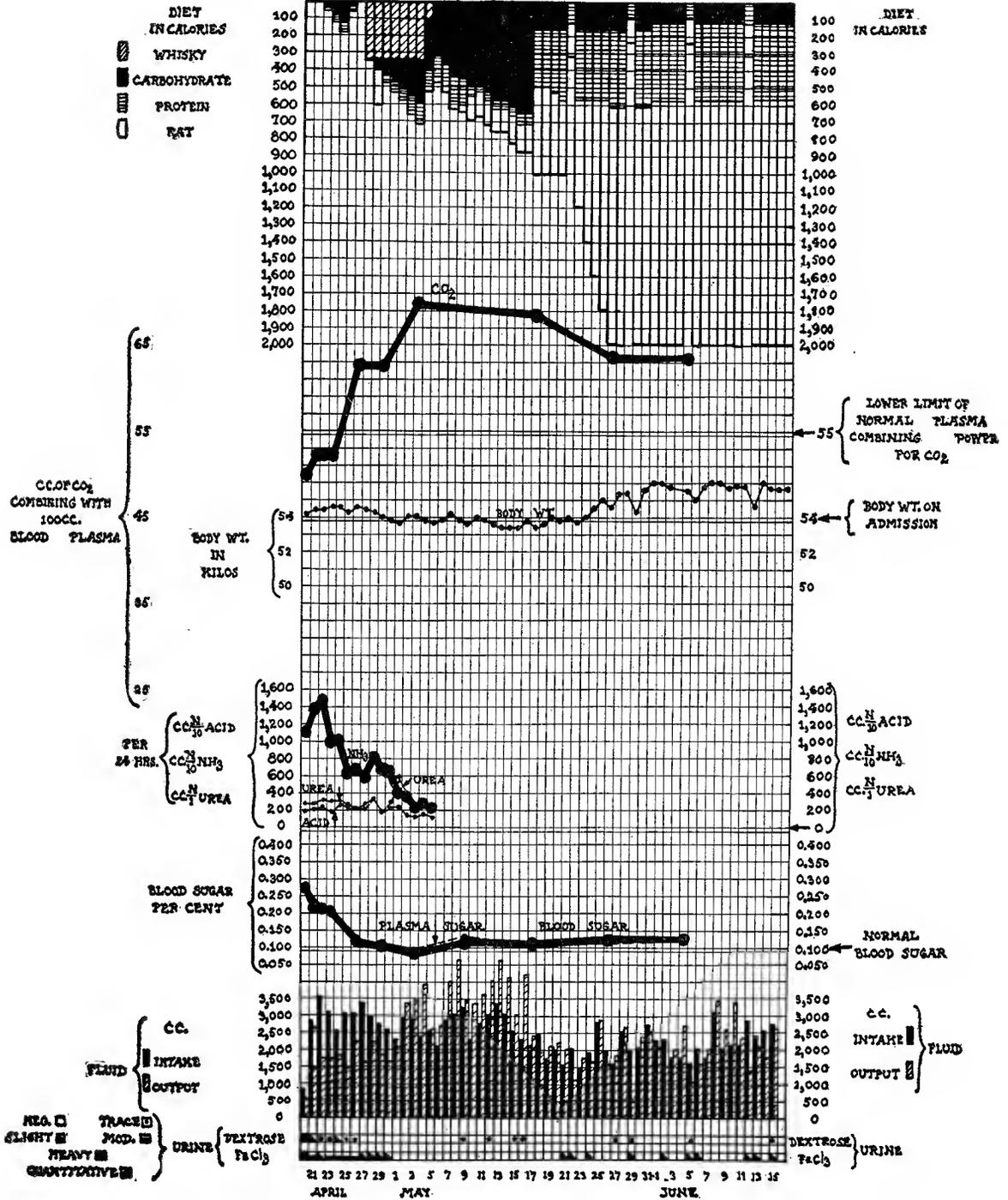
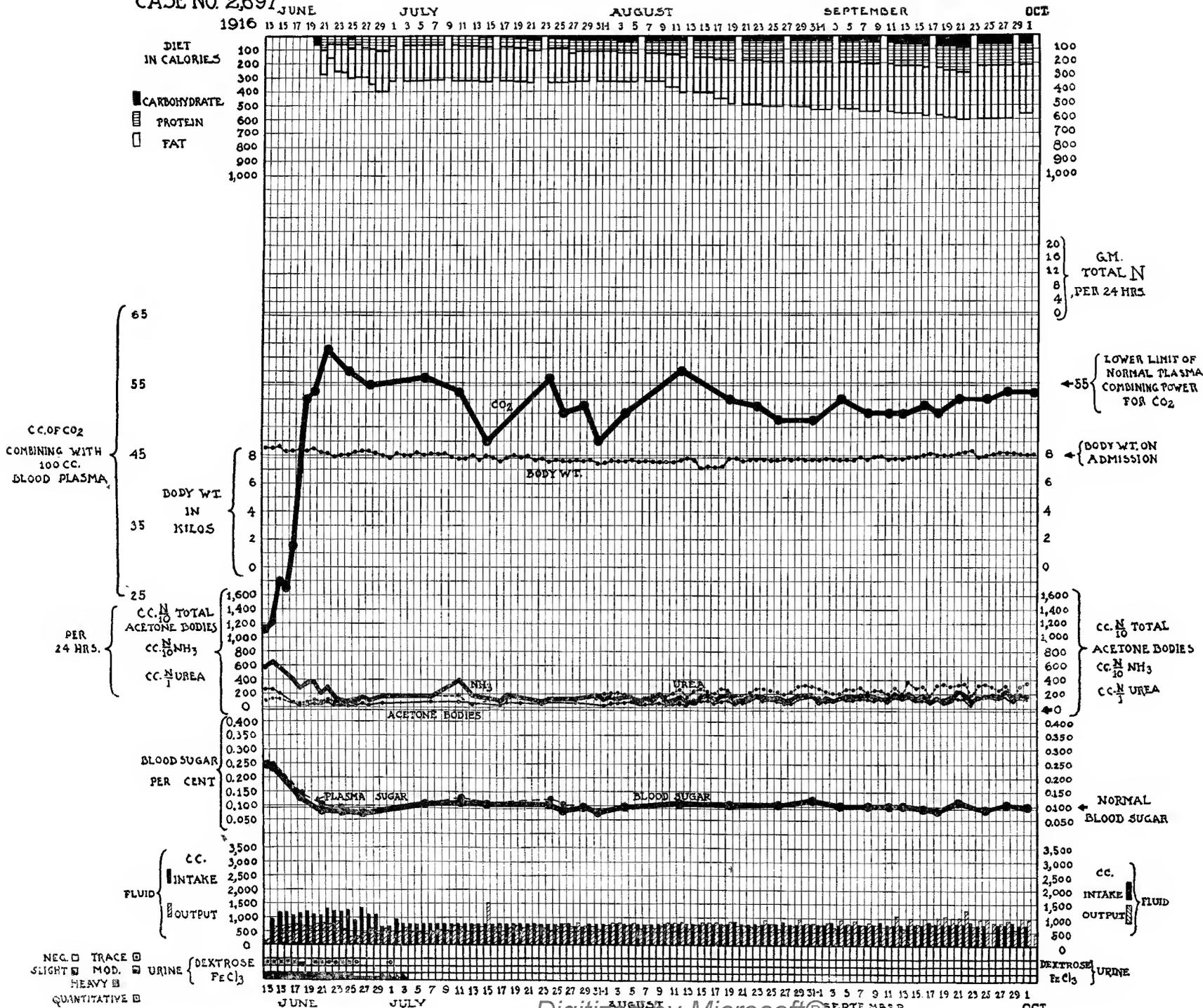


CHART 59. Case No. 67.

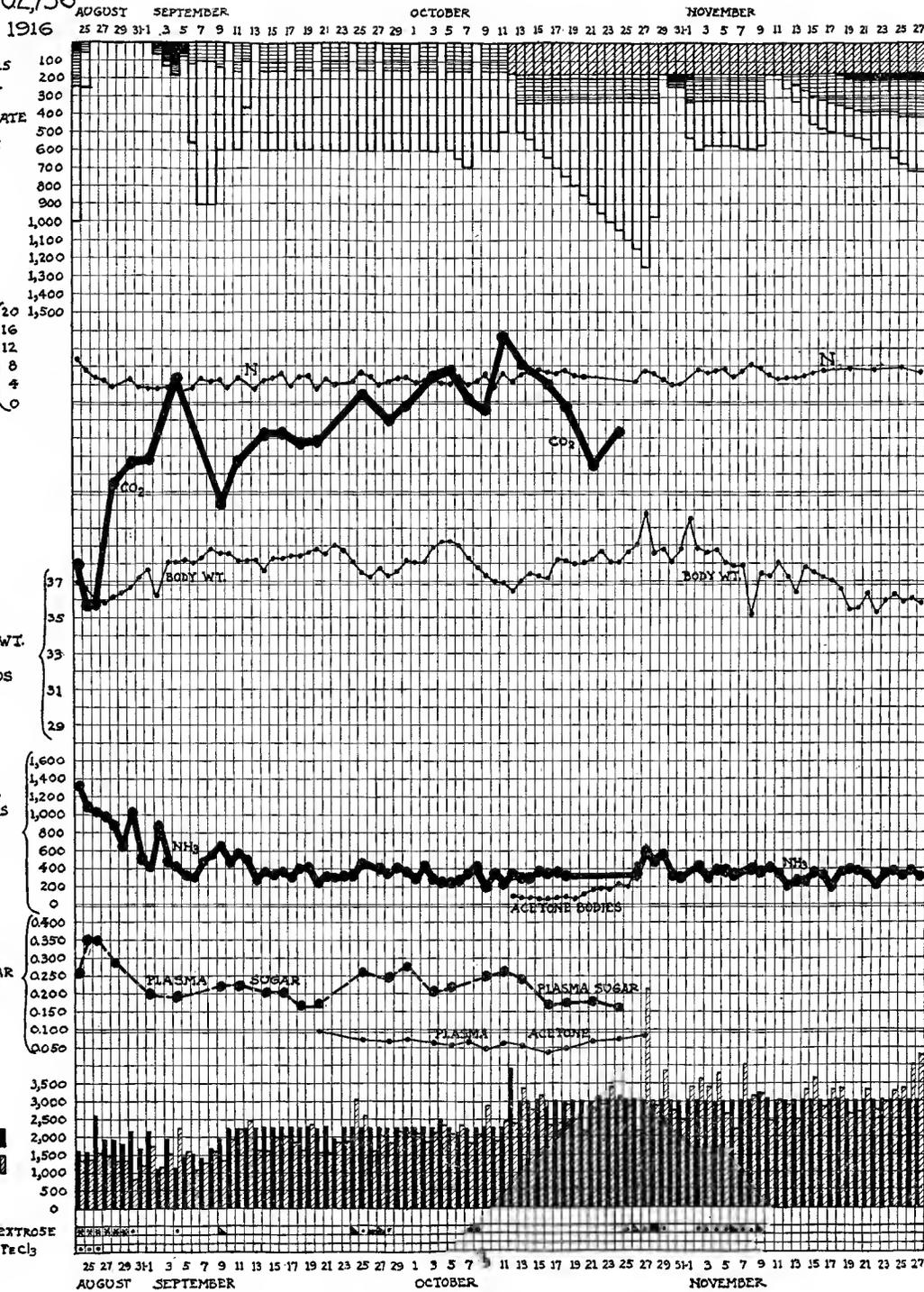
CASE NO. 2,697



Date.	Glucose excreted in 24 hrs.
1916	gm.
June 13	*
" 14	17.2
" 15	17.0
" 16	9.9
" 17	3.4
" 20	3.3
" 21	5.5
" 24	2.3
" 25	7.6

* Single specimen.

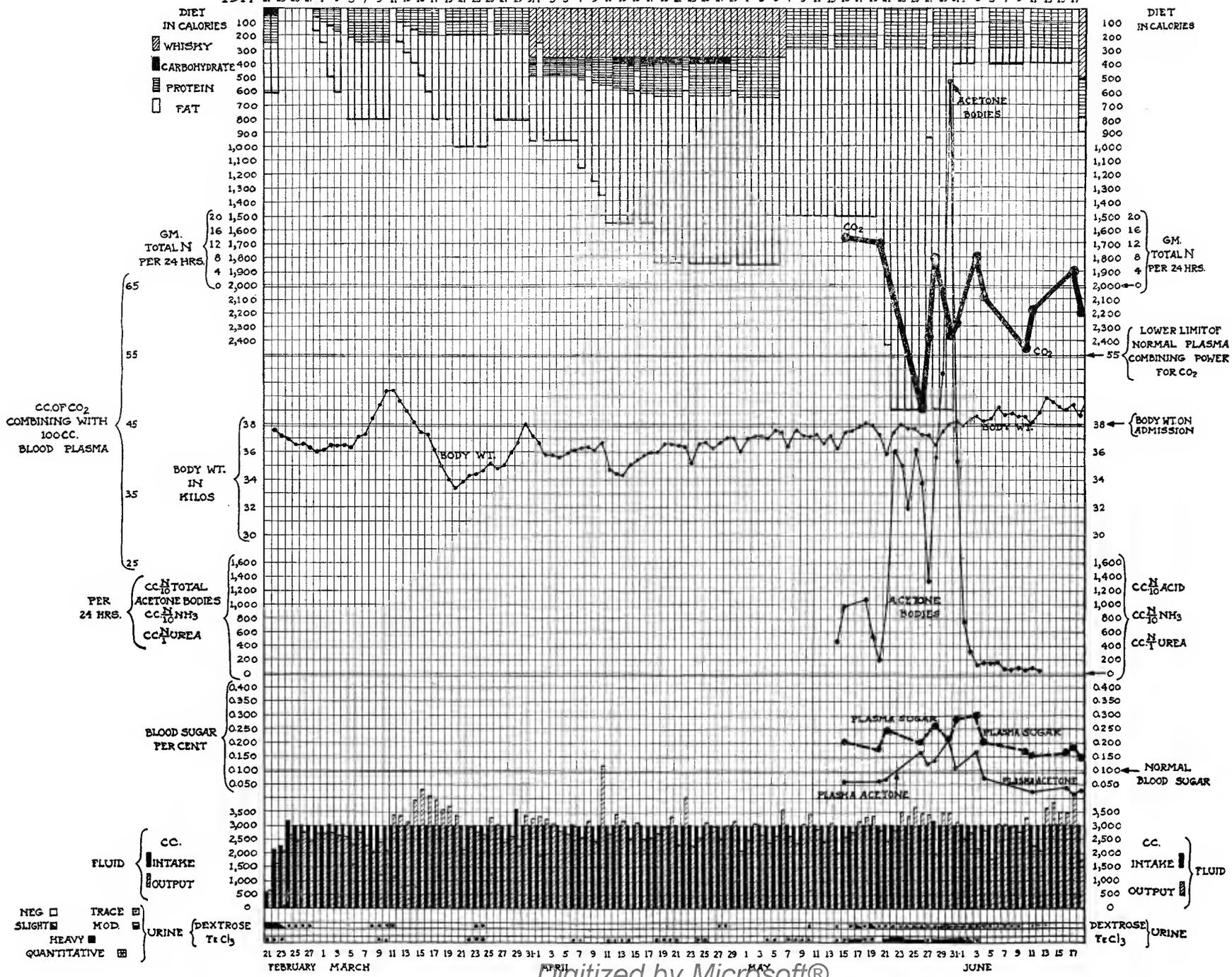
CASE NO. 2736



Date.	Glucose excreted in 24 hrs.
1916	gm.
Aug. 24	35.5
" 25	13.0
" 26	10.5
" 27	9.8
" 28	3.4
" 29	1.1
Oct. 27	9.8

CASE NO. 2,953

1917 FEBRUARY MARCH APRIL MAY JUNE
21 23 25 27 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 1 3 5 7 9 11 13 15 17



Date.	Glucose excreted in 24 hrs.
1917	gm.
May 22	5.9
" 23	10.3
" 24	13.9
" 25	16.3
" 26	18.9
" 27	18.5
" 28	7.4
" 29	26.1
" 30	22.9
" 31	21.6
June 1	22.3
" 2	18.8
" 3	8.4

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