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TOTAL DIETARY REGULATION IN THE TREATMENT OF DIABETES.

BY

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(*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 publication[1] 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 frictione, maximeque in sole, vel ad ignem; balneum rarum esse debet, neque longa in eo mora, cibus 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 (διαβαίνειν, to run through, διαβήτης, a siphon). In a passage translated by Schnée[4],

vehementior esse debet et exercitatio et frictio; longior in balneo mora, cibis 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 transflux 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 forepart 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 Bouchardat 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 exmanitur, cum siti, ardore viscerum, lumborum coxarumque intumescentia, et salivae spumosae 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 Cawley[12] (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 scirrhous."

"*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 gummous 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 Bardsley (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, $1\frac{1}{2}$ pints of milk and $\frac{1}{2}$ 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 foxglove." 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.

[16] Watt, 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, have 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.

Lavoisier[19] (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 overproduction 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.[26] 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 Pavy[27] (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 first[29] 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, lx, 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). Glycerol[32] 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, Friedreich, 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 Kulz, 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 Külz 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 Kulz 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. Külz 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 "Beitrage " "Mein Bestreben ging vor Allem dahin, moglichst exacte Beobachtungen zu liefern In wieweit mir dies gelungen ist, in wie weit diese Untersuchungen geeignet sind, unsere Kenntnisse von diesem in vieler Beziehung noch so rathselhaften 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 Külz 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. Külz 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. Rumpf[36] claims as the greatest merit of the Külz 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 Külz, and the majority of diabetics still receive treatment by means of printed lists of "allowed" and "forbidden" foods. Külz 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 Kulz did not know of any previous use of exercise till after completion of his experiments.

[36] Preface to Kulz (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 Kulz, 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 observaton 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 tatsachlich 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 undernutrition may be employed ((5), pp 392, 409); but prolonged undernutrition 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 contraindication (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 Karell 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 Kulz, 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 literatureup 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 pecuhar 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, Röth, 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 Kulz 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 Kulz 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."

Cammidge ((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 2½ 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 "distoxication 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 Arnold[41] 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 phloridzinized 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 melhtus 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 Muller has published nothing in regard to the principles attributed to him. On the contrary, Staubli 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-

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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

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[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 Ernahrung bei Diabetes ist vor einigen Jahren in der deutschen Literatur durch Schlesinger erortert worden, und er hat gezeigt, dass Diabetiker haufig bei einer an kalorien auffallend armen Nahrung sich erhalten. Ein Nutzen fur die Kranken wird aus dieser Arbeit nicht erkenntlich. Dann hat Weintraud vor Jahren in seinen aus der Naunynschen Klinik kommenden in der Bibliotheka medica erschienenen Arbeit auf die Bedeutung einer zeitweiligen Unterernahrung hingewiesen, und Sie finden diese Gesichtspunkte in dem Buch von Naunyn uber Diabetes ausfuhrlich dargelegt. Wir verwenden in Deutschland zeitweilige Unterernahrung, sogenannte Hungertage, ganz gewohnlich zur Reduktion des Zuckers, und scheuen uns nicht das Korpergewicht 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 fuhrt 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 haufig schwer geschadigt ist, tritt die Hungeracidosis gewohnlich noch starker hervor, und erschwert die Behandlung durch Unterernahrung Eine generelle Verordnung der Unterernahrung bei Diabetes durfte schon aus dem Grunde nicht ganz ohne Bedenken sein, weil die Diabetiker unter einander so ungeheuere Verschiedenheiten zeigen, dass man sich huten muss alle Falle 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 quotient[48] 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 writers[49] 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 "oatmeal 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,[8] 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

[8] 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 decaffeinized 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 Henderson[4] 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 preeminent. 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 method[5] of determining the CO_2-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 air[6] 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 CO_2 capacity Quantitative analyses for acetone bodies[8] 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 undernutrition 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 persistance 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 Woodyatt[9] 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 Noorden[10] 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 Fitz[11] 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 Woodyatt 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 CO_2 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 CO_2 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
	vol per cent	
—	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 CO_2 curve, and that feeding cleared up the symptoms even though the CO_2 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 CO_2 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 Cammidge, *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 Fitz[13] 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
	vol per cent	*mg*		*gm*	*per cent*	*mg.*
—	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 CO_2 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 veins[15] or, in case of leakage, necrosis about them. Stronger alkalies 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's[16] 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 alkalies 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 CO_2 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-Levy[17] 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; CO_2 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's[22] 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 Haggard[30] 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, lxv, 135–141

[29] Morriss, W H., *J. Am Med. Assn.*, 1917, lxviii, 1391–1394.

[30] Henderson, Y., and Haggard, H. W , *J Biol Chem* , 1918, xxxii, 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,[31] 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

[31] 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's[34] 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 Cæsarean 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, vitamines, 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 Taylor[36] 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

Lusk[38] 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. Williams[89] 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-

[89] 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 treament 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 Hiller[40] 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 Benedict[41] instrument Epstein's[42] 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 particulatly 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.

[44] Legal (*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, lxvii, 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 established[45] are that the blood fat may be several times the normal without noticeable turbidity; that the lipoid 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 Gray[45] 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 cachetic 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 dietetian 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 vitamines 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. lxix, 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 Otis[48] 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 Bartlett[49] 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_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_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_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_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 Guareschi[52] states that bran milled to an impalpable powder is 91 to 92 per cent digestible, and emphasizes its value for food and for vitamines. 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. Absir*, 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 Waukesha Health Products Company, Waukesha, 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 Janney[53] 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

[53] 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., *Vrtljschr 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 mankmd 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 suffi*ciently* 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	
	gm	gm.	gm	gm	
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.	
	gm	gm.	gm	
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	gm.	cc	Carbohydrate gm	Protein gm	Fat 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.			Protein	Fat	Carbohydrate	
	gm	cc.	gm.	gm.	gm.	
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	gm	cc	Protein gm.	Fat gm.	Carbohydrate 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	gm	cc	Protein gm	Fat gm	Carbohydrate gm	
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	gm	cc	Protein gm	Fat 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	gm	cc.	Protein gm.	Fat. gm	Carbohydrate 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				
Supper						
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.

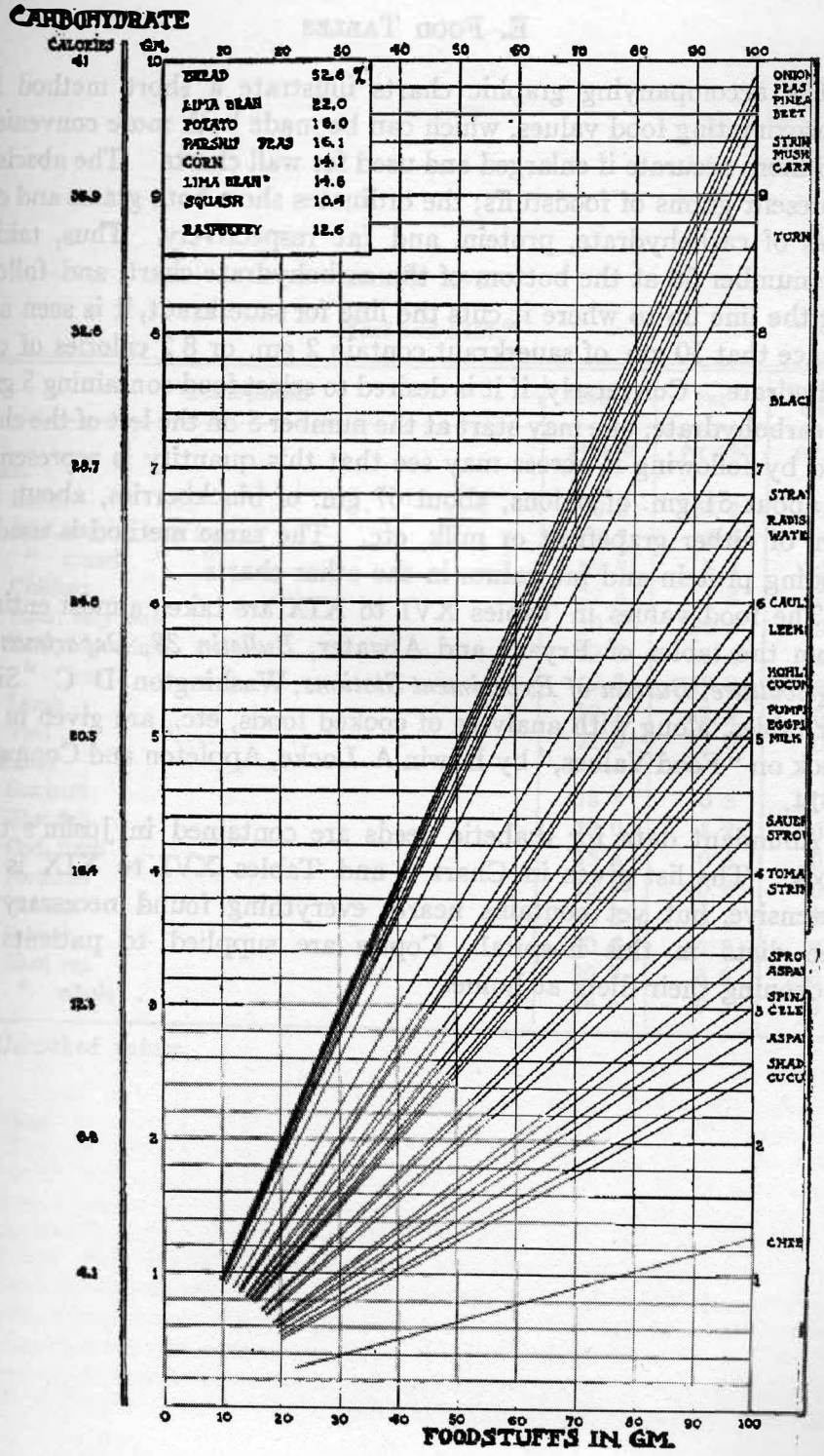
Food	gm	cc.	Protein gm.	Fat. gm	Carbohydrate gm.	
7 30 a m.						
Egg..	50		7 4	5 3		
Milk.	25		0 8	1.0	1.3	
Butter.	7			5 8		
Asparagus T C....	75					
Clear soup.		100				
Bran biscuit (1)						
11 00 a.m.						
Egg..	50		7.4	5.3		
Milk...	25		0 8	1.0	1.3	
Canned asparagus.	107		1 6	0 1	3 0	
Butter.	6			4 9		
Clear soup.		100				
1 00 p m						
Milk.	50		1.6	2.0	2.5	
Butter.	6			4.9		
Raw tomato.	60		0 5	0 2	2 3	
Clear soup.		100				
Bran biscuit (1).						
3 00 p m						
Milk.	25		0 8	1 0	1.3	
Clear soup.		100				
5 30 p m.						
Egg.	50		7.4	5 3		
Milk.	25		0.8	1 0	1 3	
Butter.	7			5.8		
Celery.	75		1 0		2 2	
Bran biscuit (1).						
Clear soup.		100				
Gm			30 1	43 6	15 2	
Calories			125 0	405 0	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.	gm	cc	Protein gm	Fat. gm	Carbohydrate gm		Substitutes
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. / Flounder 160 gm. / Veal 79 gm. / Roast Lamb 113 gm less butter 15 gm } (in place of roast beef).
Butter	20			16 5			
Lettuce	25		0 4	0 1	0 8		Radishes 25 gm. (in place of lettuce)
Raw tomato	150		1 2	0 6	5 9		Beets 61 gm (in place of tomato).
Canned Brussels sprouts	295		4 4	0 3	10 0		Carrots 109 gm. (in place of Brussels sprouts). Celery 200 gm. (in place of cauliflower).
Cauliflower	100		1 6	0 8	6 0		
Cream cheese	19		4 9	6 0			
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
GM.
BREAD 52.6 %
LIMA BEAN 22.0
POTATO 18.0
PARSNIP PEAS 16.1
CORN 14.1
LIMA BEAN* 14.6
SQUASH 10.4
RASPBERRY 12.6
41
36.9
32.8
28.7
24.6
20.5
16.4
12.3
8.2
4.1
0
10
20
30
40
50
60
70
80
90
100
ONION
PEAS
PINEA
BEET
STRIN
MUSH
CARR
TURN
BLACI
STRA
RADIS
WATE
CAUL
LEEK
KOHL
COCON
PUMP
EGGPL
MILK
SAUER
SPRO
TOMA
STRI
SPRO
ASPA
SPINA
CELE
ASPA
SHAD
CUCU
CHIE
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	Carbohydrate
	per cent	*per cent*	*per cent*
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
	per cent	*per cent*	*per cent*
*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, lxix, 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
	per cent	*per cent*	*per cent*
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
	per cent	*per cent*	*per cent*
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