THE PRINCIPLES AND PRACTICE OF MEDICINE

DESIGNED FOR THE USE OF PRACTITIONERS AND STUDENTS OF MEDICINE

BY

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connected with this subject of mineral waters. This deep-rooted belief in the profession was shaken by Sir William Roberts, who claimed to have shown that alkalescence as such has no influence whatever on the sodium biurate. The sodium salts are believed by this author to be particularly harmful, but, in spite of all the theoretical denunciation of the use of the sodium salts, the gouty from all parts of the world flock to those very Continental springs in which these salts are most predominant. Of the mineral springs best suited for the gouty may be mentioned, in the United States, those of Saratoga, Bedford, and the White Sulphur; Buxton and Bath, in England; in France, Aix-les-Bains and Contrexeville; and in Germany, Carlsbad, Wildbad, Homburg, and Marienbad. Excellent results are claimed for mineral waters with special radio-active properties. The efficacy in reality is in the water, in the way it is taken, on an empty stomach, and in large quantities; and the important accessories in the modified diet, proper hours, regular exercises, with baths, douches, etc., play a very important rôle in the "cure."

MEDICAL TREATMENT.—In an acute attack the limb should be elevated and the affected joint wrapped in cotton-wool. Warm fomentations, or Fuller's lotion, may be used. The local hot-air or passive hyperæmia treatment may be tried. A brisk mercurial purge is always advantageous at the outset. The wine or tincture of colchicum, in doses of 20 to 30 minims (1.2 to 2 c. c.) may be given every four hours in combination with the citrate of potash. The action of the colchicum should be carefully watched; its effect is most marked when free purgation follows. It has in a majority of the cases a powerful influence over the symptoms—relieving the pain, and reducing, sometimes with great rapidity, the swelling and redness. It should be stopped as soon as it has relieved the pain. Cinchophen (atophan) is often useful in doses of 15 grains, 1 gm., three or four times a day. It may also be helpful in the subacute and chronic forms. In cases in which the pain and sleeplessness are distressing and do not yield to treatment, morphia is necessary. The patient should be placed on a diet chiefly of milk and barley-water. During convalescence the diet should be increased slowly and gradually the patient may resume the diet previously laid down.

In some of the subacute intercurrent attacks sodium salicylate or acetyl-salicylic acid may be useful. The chronic and irregular forms are best treated by the dietetic and hygienic measures already noted. Potassium iodide is sometimes useful. Albu speaks favorably of lemon-juice as a remedy. The vegetable acids are converted in the system into alkaline carbonates, thus enabling the blood to keep the uric acid compounds in solution, and facilitating their elimination.

Where the arthritic attacks are confined to one joint, such as the great-toe joint, surgical interference may be considered. Riedel reports two successful cases in which he removed the entire joint capsule of the big-toe joint, with permanent relief.

II. DIABETES MELLITUS

Definition.—A disease of metabolism in general with especial disturbance of carbohydrate metabolism in which the normal utilization of carbohydrate is impaired with an increase in the sugar content of the blood and consequent

glycosuria. There is a tendency to subsequent disturbance of the fat metabolism with resulting acidosis (Ketosis).

History.—The disease was known to Celsus. Aretæus first used the term diabetes, calling it a wonderful affection "melting down the flesh and limbs into urine." He suggested that the disease got its name from the Greek word signifying a syphon. Willis in the seventeenth century gave a good description and recognized the sweetness of the urine "as if there has been sugar and honey in it." Dobson in 1776 demonstrated the presence of sugar, and Rollo in 1797 wrote an admirable account and recommended the use of a meat diet. The modern study of the disease dates from Claude Bernard's demonstration of the glycogenic function of the liver in 1857.

Etiology.—The enzymes of the intestinal mucosa convert the starches and sugars of the food into monosaccharides—dextrose, galactose and levulose—which pass into the portal circulation, but the major portion remains in the liver, where it is converted into glycogen. The percentage of sugar in the systemic blood remains constant—0.06 to 0.11 per cent. Part of the sugar passes to the muscles, where it is stored as glycogen. The total storage capacity of the liver is estimated at about one-tenth of its weight, *i. e.*, about 150 gms. for an ordinary organ weighing 1,500 gms. Not all of the glycogen comes from the carbohydrates; a small part in health is derived from the proteins and fats. This treble process of transformation, storage and retransformation of the sugars is effected by special enzymes, which are furnished by internal secretions, chiefly of the pancreas and hypophysis, and are directly influenced by the nervous system. According to Claude Bernard the sugar is simply warehoused on demand in the liver, and given out to the muscles which need it in their work. In any case, the sugar, one of the chief fuels of the body, is burned up, supplying energy to the muscles, and is eliminated as CO_2 and water. The nature of the intermediate stages of the transformation is still under discussion.

The following are the conditions which influence the appearance of sugar in the urine:

(*a*) Excess of Carbohydrate Intake.—In a normal state the sugar in the blood is about 0.1 per cent. In diabetes the percentage is usually from 0.2 to 0.4 per cent. The hyperglycæmia is immediately manifested by the appearance of sugar in the urine. The healthy person has a definite limit of carbohydrate assimilation; the total storage capacity for glycogen is estimated at about 300 gms. Following the ingestion of enormous amounts of carbohydrates the liver and the muscles may not be equal to the task of storing it; the blood content of sugar passes beyond the normal limit and the renal cells immediately begin to get rid of the surplus. Like the balance at the Mint, which is sensitive to the correct weight of the gold coins passing over it, they only react at a certain point of saturation. Fortunately excessive quantities of pure sugar itself are not taken. The carbohydrates are chiefly in the form of starch, the digestion and absorption of which take place slowly, so that this so-called alimentary glycosuria very rarely occurs, though enormous quantities may be taken. The assimilation limit of a normal fasting individual for sugar itself is about 250 gms. of grape sugar, and considerably less of cane and milk sugar. Clinically one meets with many cases in which glycosuria is present as a result of excessive ingestion of carbohydrates, par-

ticularly in stout persons and heavy feeders—so-called lipogenic diabetes—a form very readily controlled.

(*b*) Disturbances in the Nervous System.—Bernard shows that there was a centre in the medulla—the diabetic centre—puncture of which is followed by hyperglycæmia due to an increased outflow of sugar from the liver warehouse. He demonstrated that the efferent path of this influence was through the splanchnic nerves and the afferent through the vagi. The exact location of this centre has never been determined, and its precise rôle in the carbohydrate metabolism is obscure. Clinically, however, it has long been known that many lesions of the nervous system cause glycosuria—tumors, particularly those in the neighborhood of the medulla, injuries both to the brain and to the upper part of the spinal cord, meningitis, and hæmorrhage. Some of these may disturb Bernard's centre in the medulla, but many of them disturb the internal secretion of the hypophysis. Clinically, glycosuria arising from disturbances in the nervous system is not an important variety.

(*c*) Disturbances of the Internal Secretions.—The part played in the carbohydrate metabolism by the ductless glands is of the first importance. Though not yet fully understood, the following are the chief points, so far as they bear on clinical work:

(1) *Pancreatic Secretion.*—Extirpation of the pancreas in a dog is followed by hyperglycæmia and prolonged glycosuria, which is not relieved by feeding pancreas to the animal, but which is checked if experimentally a portion of healthy organ from another dog is inserted into the portal circulation. The pancreas contains structures known as "the islands of Langerhans," which, from the work of Opie and others, are believed to furnish an internal secretion necessary to normal carbohydrate metabolism. A portion of the organ separated from the rest, and its duct ligated, atrophies, but a tissue remains composed of enlarged islands of Langerhans. If the remainder of the pancreas be removed, this atrophied portion is able to ward off glycosuria; but if this is removed glycosuria appears immediately (W. G. MacCallum). In some way the secretion furnished by this organ is essential to the proper preparation of the sugars. Cohnheim suggests a correlation of this internal secretion with a muscle enzyme, to which it acts as an amboceptor, and that it is by the combined action of these two glycolytic bodies that the sugars are normally burned up in the muscles. Many diseases of the pancreas are associated with glycosuria, some with permanent diabetes. Hæmorrhagic pancreatitis, cancer, calculus, chronic interstitial pancreatitis, catarrh of the ducts may all be associated with a profound disturbance in the metabolism of the sugars. In fact, there is no one organ the disease of which is more constantly associated with glycosuria, and the studies of Opie warrant the belief that the essential factor is a disturbance of the function of the internal secretion provided by the islands of Langerhans.

(2) *Hypophysis.*—It was long known that glycosuria occurred in tumors of the region of the hypophysis, particularly in acromegaly, and it follows fractures of the base of the skull. Experimentally, Cushing and his students have shown that the posterior lobe of the pituitary gland has an important influence in carbohydrate metabolism. The secretion of this portion of the gland is discharged into the third ventricle, and any operative disturbance of it, or of the infundibulum, is at once followed by glycosuria, and by a re-

QUANTITY OF FOOD Required by a Severe Diabetic Patient Weighing 60 kilograms. (Joslin.)

Food	Quantity Grams	Calories per Gram	Total Calories
Carbohydrate	10	4	40
Protein	75	4	300
Fat	150	9	1,350
Alcohol	15	7	105
			1,795

STRICT DIET. (Foods without sugar.) Meats, Poultry, Game, Fish, Clear Soups, Gelatine, Eggs, Butter, Olive Oil, Coffee, Tea and Cracked Cocoa.

FOODS ARRANGED APPROXIMATELY ACCORDING TO CONTENT OF CARBOHYDRATES

	5% ±	10% ±	15% ±	20% ±
VEGETABLES	Lettuce, Spinach, Sauerkraut, String Beans, Celery, Asparagus, Cucumbers, Brussels Sprouts, Sorrel, Endive, Dandelion Greens, Swiss Chard, Vegetable Marrow, Cauliflower, Tomatoes, Rhubarb, Egg Plant, Leeks, Beet Greens, Water Cress, Cabbage, Radishes, Pumpkin, Kohl-Rabi, Sea Kale	Onions, Squash, Turnip, Carrots, Okra, Mushrooms, Beets	Green Peas, Artichokes, Parsnips, Canned Lima Beans	Potatoes, Shell Beans, Baked Beans, Green Corn, Boiled Rice, Boiled Macaroni
FRUITS	Ripe Olives (20 per cent. fat), Grape Fruit	Lemons, Oranges, Cranberries, Strawberries, Blackberries, Gooseberries, Peaches, Pineapples, Watermelon	Apples, Pears, Apricots, Blueberries, Cherries, Currants, Raspberries, Huckleberries	Plums, Bananas
NUTS	Butternuts, Pignolias	Brazil Nuts, Black Walnuts, Hickory, Pecans, Filberts	Almonds, Walnuts (Eng.), Beechnuts, Pistachios, Pine Nuts	Peanuts (40%), Chestnuts
Miscellaneous	Unsweetened and Unspiced Pickle, Clams, Scallops, Fish Roe, Oysters, Liver			

30 grams (1 oz.) contain approximately	Protein	Fat	Carbohydrates	Calories
			grams	
Oatmeal	5	2	20	110
Meat (uncooked)	6	2	0	40
" (cooked)	8	3	0	60
Potato	1	0	6	25
Bacon	5	15	0	155
Cream, 40%	1	12	1	120
" 20%	1	6	1	60
Milk	1	1	2	20
Bread	3	0	18	90
Rice	3	0	24	110
Butter	0	25	0	240
Egg (one)	6	5	0	75
Brazil Nuts	5	20	2	210
Orange (one)	0	0	10	40
Grape Fruit (one)	0	0	10	40
Vegetables from 5–6% groups	0.5	0	1	6

1 gram protein contains 4 calories.
1 " carbohydrate contains 4 calories.
1 " fat contains 9 calories.
1 " alcohol contains 7 calories.

1 kilogram—2.2 pounds.
6.25 grams protein contain 1 gram nitrogen.
A patient "at rest" requires 30 calories per kilogram body weight.

CHART XIV.—DIABETIC FOOD TABLES. (JOSLIN.)

and diacetic acid determined, as they usually indicate a serious disturbance in the fat metabolism. It is well to remember that the acetone bodies may be only temporarily present, and it is not necessary to sign the patient's death warrant so soon as they appear. A patient may live for many years with traces, and they may disappear after having been present for months.

Treatment.—In families with a marked predisposition to the disease the use of starchy and saccharine articles of diet should be restricted. The personal hygiene of a diabetic patient is of the first importance. Sources of worry should be avoided, and he should lead an even, quiet life, if possible in an equable climate. The heat waste should be prevented by wearing warm clothes and avoiding cold. A warm, or, if tolerably robust, a cold, bath should be taken every day. An occasional Turkish bath is useful. Systematic, moderate exercise should be taken. When this is not feasible, massage should be given.

DIET.—Each patient presents his own problem and must be studied individually. The endeavor should be made to keep the urine sugar free and acid free. In this the proper use of fasting, as advocated by Allen, is of great aid but it should not be employed carelessly. The object of treatment is to increase the carbohydrate tolerance; it is important not to overtax the patient's powers of using carbohydrates by giving more than he can utilize. In mild cases the carbohydrate intake may be gradually reduced, sugar as such being cut off first and the carbohydrate intake reduced by a certain proportion each day until the urine is sugar free. In the medium and severe cases fasting is useful. The purpose of it should be explained to the patient and his co-operation secured. The time of fasting required to render the urine sugar free varies from one to five days. The patient should be put to bed; water may be taken freely and tea or coffee allowed (without sugar or cream) if desired. If sugar persists after the second day of fasting 300 c. c. of meat broth or bouillon may be given. When the urine is sugar free it is necessary to determine the carbohydrate tolerance.

The profession, and much more the diabetic patient, owes much to E. P. Joslin of Boston for his studies on diabetes. We quote some of his directions:

"In severe, long-standing, complicated, obese and elderly cases, as well as in all cases with acidosis, or in any case if desired, without otherwise changing habits or diet, omit fat, after two days omit protein and then halve the carbohydrates daily until the patient is taking only 10 grams; then fast. In other cases begin fasting at once. Fast four days, unless earlier sugar-free. Allow water freely, tea, coffee and thin, clear meat broths as desired."

"If glycosuria persists at the end of four days, give 1 gram protein or 0.5 gram carbohydrate per kilogram body weight for two days and then fast again for three days unless earlier sugar-free. If glycosuria remains, repeat and then fast for one or two days as necessary. If there is still sugar, give protein as before for four days, then fast one, and then gradually increase the periods of feeding, one day each time, until fasting one day each week. I have seen no uncomplicated case fail to get sugar-free by this method."

"When the twenty-four-hour urine is free from sugar, give 5 to 10 grams carbohydrate (150 to 300 grams of 5 per cent. vegetables) and continue to add 5 to 10 grams carbohydrate daily up to 50 grams or more until sugar appears."

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markable lowering of the assimilation limit for sugars. On the other hand, a deficiency of this secretion, or the removal of this portion of the gland alone, is followed by a remarkable increased tolerance for carbohydrates.

Clinically, this sequence is not infrequently seen. A tumor which at first irritates the gland, as in the early stages of acromegaly, may cause glycosuria, but later, as the posterior lobe of the gland is destroyed, there is an extraordinarily high assimilation limit for sugars, and associated with it a great increase in the deposition of fat in the body, a syndrome to be referred to later. Intravenous or subcutaneous injection of the extract of the posterior lobe promptly lowers this high assimilation limit for carbohydrates.

(3) *Adrenals and Thyroids.*—We have less positive information about the relation of carbohydrate metabolism to the internal secretions of these glands. Glycosuria does not necessarily follow lesions of the adrenals, but epinephrin has a powerful influence on the carbohydrate metabolism, and glycosuria may be readily produced in animals by subcutaneous injection, and by the local application of epinephrin to the pancreas. Clinically, we know practically nothing of an adrenal glycosuria. It does not occur in Addison's disease. It has occasionally been noticed in the prolonged therapeutic use of epinephrin. In disturbances of the thyroid gland glycosuria is not uncommon. There is a lowered tolerance for sugar in Graves' disease which is sometimes associated with a true diabetes, and in the remarkable instances of acute myxœdema the amount of sugar in the urine may be large. The use of thyroid extract is occasionally followed by glycosuria. On the other hand, patients may take the extract continuously for many years without glycosuria.

Possibly the glycosuria associated with pregnancy is due to a disturbance in the internal secretions. It is a transient condition, usually disappearing with parturition, and rarely leads to diabetes. It may recur in successive pregnancies.

(*d*) Disturbances in the Function of the Liver.—One of the most remarkable features in carbohydrate metabolism is that the great warehouse of the sugars may be damaged to any degree without causing hyperglycæmia or glycosuria. Whether or not there is a type of disease to which the name of "liver diabetes" may be given is doubtful. There are cases of cirrhosis of the liver and of gallstones—particularly those associated with enlargement of the organ—in which glycosuria is present, but they are probably all associated with coincident affections of the pancreas. In the "bronze diabetes," which is accompanied by great hypertrophy of the liver, the glycosuria is probably pancreatic.

(*e*) Disturbances in the Kidney Functions.—Disease of the kidneys is rarely associated with glycosuria. Occasionally one finds it in chronic nephritis, but the existence of a true diabetes depending upon renal changes has not been proved. There is a remarkable experimental diabetes of great interest in connection with carbohydrate metabolism. If phloridzin, a glucoside prepared from the bark of the apple-tree, is given by mouth or subcutaneously to man or animals glycosuria results, and even continues on a nitrogenous diet, and in man when fasting. The amount of sugar excreted may be large, yet there is no hyperglycæmia. It seems that the sugar is directly manufactured by the kidney epithelium, and largely from the proteins.

(*f*) Miscellaneous Disturbances.—The carbohydrate metabolism may

be upset in acute fevers, in many of which a transient glycosuria is present. It is not uncommon after the administration of ether, less so after chloroform. Metabolic disturbances in gout are not infrequently associated with glycosuria, and cachexias and profound anæmias may be accompanied by transient glycosuria. A mental shock, a severe nervous strain and worry precede many cases. Patients suffocated by smoke, or poisoned by coal gas, may have sugar in the urine.

INCIDENCE.—According to statistics diabetes appears to be about as frequent in the United States as in European countries. In England and Wales the deaths increased from 2,767 in 1902 to 4,542 in 1916. The disease is on the increase in the United States. The statistics for 1870 gave 2.1; for 1890, 3.8; for 1900, 9.3; and for 1915, 17.5 deaths to the 100,000 population. This may be due to the great increase in the consumption of sugar. Among 27,618 patients admitted to the medical wards of the Johns Hopkins Hospital in twenty-two years there were 276 cases of diabetes, or one per cent.

HEREDITARY INFLUENCES play an important rôle and cases are on record of its occurrence in many members of the same family. Morton, who calls the disease *hydrops ad matulam* (Phthisiologia, 1689), records a remarkable family in which four children were affected, one of which recovered on a milk diet and diascordium. An analysis of the cases in our series gave only 6 cases with a history of diabetes in relatives (Pleasants). Naunyn obtained a family history of diabetes in 35 out of 201 private cases, but in only 7 of 157 hospital cases. There are instances of the coexistence of the disease in man and wife. Among 516 married pairs collected by Senator, in which either husband or wife was diabetic, in 18 cases the second partner had become diabetic. Similarity in habits probably accounts for this.

SEX.—Men are more frequently affected than women, the ratio being about three to two. Of the 276 cases of diabetes referred to, 179 were in males and 97 in females (Futcher). It is a disease of adult life; a majority of the cases occur from the third to the sixth decade. Of the 276 cases, the largest number—70—occurred between fifty and sixty years of age.

DIABETES IN CHILDREN.—This usually occurs among the better classes. Hereditary influences are marked. The course of the disease is, as a rule, much more rapid than in adults. While the disease is usually severe there are not infrequent cases of a mild type. One case is mentioned of a child apparently born with glycosuria, who recovered in eight months.

Persons of a neurotic *temperament* are often affected. It is a disease of the higher classes. Van Noorden states that the statistics for London and Berlin show that the number of cases in the upper ten thousand exceeds that in the lower hundred thousand inhabitants.

RACE.—Hebrews seem especially prone to it; one-fourth of Frerichs' patients were of the Semitic race. Diabetes is comparatively rare in the colored race, but not so uncommon as was formerly supposed. Of the series of 276 cases, 29, or 10.6 per cent., were in negroes.

Metabolism in Diabetes.—Glycosuria, neurotic, dietetic or toxic, may be a matter of simple overflow, but the essence of true diabetes is a waste of the carbohydrates, which hurry through the body, in great part never warehoused as glycogen. Why this should be, whether the liver and muscles are at fault in refusing to transform the carbohydrate, or whether the defect is the en-

zymes of the ductless glands, are problems awaiting solution. Naunyn held that hyperglycæmia is due to a failure of the liver and muscles to store up glycogen as in health. On the other hand, Lépine, Opie, and others support the view that the glycolytic ferments are lacking—the former may depend on the latter. In either case the result is a failure of the normal oxidation of the carbohydrates. Hyperglycæmia is responsible for the thirst and the polyuria, and there is a very considerable daily loss of energy in warming the liquids taken to the temperature of the body, according to Benedict and Joslin nearly 6 per cent. of the total heat of the day; and it is this excess of sugar in the system that renders the body so favorable a culture medium for pus organisms. There is loss of energy with the steady waste of sugar fuel; practically every gram of sugar excreted in the urine results in a loss of 4.1 calories, consequently a diabetic patient excreting 100 grams of sugar and 20 grams of β-oxybutyric acid loses 500 calories in this way, so that the patients are apt to be underfed, unless this loss is made up by a full amount of other food (Benedict and Joslin). Studies upon the respiratory quotient—which is the ratio between the CO_2 given out and the O taken in by a healthy individual on a mixed diet (expressed by the fraction 0.9)—favor the view that there is failure in the proper combustion of the carbohydrates. Benedict and Joslin conclude that a respiratory quotient above 0.74 indicates a fairly liberal supply of glycogen stored in the body; while a respiratory quotient of 0.70, or below that, indicates that the patient has no available carbohydrates, and has lost in a measure the power of storing them. And here comes the special danger; as the carbohydrates pass through the body unburned, the energy must be provided from the proteins and fats. The metabolism of the former does not appear to be seriously disturbed, and the carbohydrate portion of the protein molecule is well tolerated and in part supplies the place of the lost sugars. The danger is in the metabolism of the fats. The carbohydrates are not used as fuel; the proteins are easily utilized, but apparently it takes so much draught to burn them that not enough is left to consume the fats completely; and the products of incomplete combustion accumulate in the system and suffocate the patient as effectually as does the CO of a charcoal stove. The chief product of this incomplete combustion of the fats is the β-oxybutyric acid, which itself is the source of the diacetic acid and acetone, and the special danger of the disease is now recognized to be the production of an acidosis in consequence of this imperfect fat metabolism. One of the most valuable advances in our knowledge of the metabolism of the disease has been the work of Beddard, Pembrey and Spriggs and more recently of Poulton, who have shown that the amount of CO_2 in the alveolar air may be taken as a measure of the acidosis. The acetone bodies in the urine indicate a large production in the body but this may have been completely compensated. The blood examination is more important to determine the degree of accumulation and with even slight degrees there are changes in the alveolar air.

The CO_2 tension of the alveolar air is reduced. In slight acidosis this is between 32 and 38 mm. Hg, in moderate acidosis 28 to 32 mm. Hg, and in severe acidosis less than 28 mm. Hg (normal 38-45 mm. Hg). The lowest figure noted by Joslin was 9 mm. Hg.

Renal Diabetes.—This term is applied to a condition in which there is glycosuria without increase of the sugar in the blood. In it the glycosuria

is independent of the carbohydrate intake and the blood sugar is normal or decreased in amount. The kidney cells allow sugar to escape. As a rule it is discovered accidentally as there are rarely any symptoms. The condition is rare and the patients should be followed for a long time to exclude Diabetes Mellitus.

Morbid Anatomy.—The *nervous system* shows no constant lesions. In a few instances there have been tumors or sclerosis in the medulla, or a cysticercus has pressed on the floor. A secondary multiple neuritis is not rare, and to it the so-called diabetic tabes is probably due, and changes occur in the posterior columns of the cord similar to those which have been found in pernicious anæmia. In the sympathetic system the ganglia have been enlarged and in some instances sclerosed. The *heart* is hypertrophied in some cases. Endocarditis is very rare. Arterio-sclerosis is common. The *lungs* show important changes. Acute broncho-pneumonia or lobar pneumonia (either of which may terminate in gangrene) and tuberculosis are common. The so-called diabetic phthisis is always tuberculous and results from a caseating broncho-pneumonia. In rare cases there is a chronic interstitial pneumonia, non-tuberculous. Fat embolism of the pulmonary vessels may occur in connection with diabetic coma.

The *liver* is usually enlarged; fatty degeneration is common. In the so-called diabetic cirrhosis—the *cirrhosis pigmentaire*—the liver is enlarged and sclerotic, and cachexia develops with melanoderma. Dilatation of the stomach with enlargement of the duodenum and colonic stasis are common.

Pancreas.—Of 15 autopsies in 27 fatal cases, in 9 the pancreas was found atrophic. In one of these fat necroses were present, in another calculi. Hyaline degeneration of the islands of Langerhans is a special feature in certain cases. Chronic interstitial pancreatitis is common.

The *kidneys* show a diffuse nephritis with fatty degeneration. Hyaline change is often found in the tubal epithelium, particularly of the descending limb of the loop of Henle, and in the Malpighian tufts.

Symptoms.—*Acute* and *chronic* forms are recognized, but there is no essential difference between them, except that in the former the patients are younger, the course is more rapid, and the emaciation more marked.

The *onset* is gradual, and either frequent micturition or inordinate thirst first attracts attention. Very rarely it sets in rapidly, after a sudden emotion, an injury, or after a severe chill. When fully established the disease is characterized by great thirst, the passage of large quantities of saccharine urine, a voracious appetite, and, as a rule, progressive emaciation.

Among the GENERAL SYMPTOMS *thirst* is one of the most distressing. Large quantities of water are required to keep the sugar in solution and for its excretion in the urine. The amount of fluid consumed will be found to bear a definite ratio to the quantity excreted. Instances, however, are not uncommon of pronounced diabetes in which the thirst is not excessive; but in such cases the amount of urine passed is never large. The thirst is most intense an hour or two after meals. As a rule, the digestion is good and the appetite inordinate. The condition is sometimes termed *bulimia* or *polyphagia*. Lumbar pain is common.

The tongue is usually dry, red, and glazed, and the saliva scanty. The

gums may become swollen, and in the later stages aphthous stomatitis is common. Constipation is the rule.

In spite of the enormous amount of food consumed a patient may become rapidly emaciated. This loss of flesh bears some ratio to the polyuria, and when, under suitable diet, the sugar is reduced, the patient may gain in flesh. The skin is dry and harsh, and sweating rarely occurs, except when tuberculosis coexists. Drenching sweats have been known to alternate with excessive polyuria. General pruritus or pruritus pudendi may be very distressing, and occasionally is one of the earliest symptoms. The temperature is often subnormal; the pulse is usually frequent, and the tension increased. Many diabetics do not show marked emaciation. Patients past the middle period of life may have the disease for years without much disturbance of the health, and may remain well nourished. These are the cases of the *diabète gras* in contradistinction to *diabète maigre.*

The Urine.—The amount varies from 3 to 4 litres in mild cases to 15 to 20 litres in very severe cases. In rare instances the quantity of urine is not much increased. Under strict diet the amount is much lessened, and in intercurrent febrile affections it may be reduced to normal. The specific gravity is high, ranging from 1.025 to 1.045; but in exceptional cases it may be low, 1.013 to 1.020. The highest specific gravity recorded is by Trousseau—1.074. Very high specific gravities—1.070 +—suggest fraud. The urine is pale in color, almost like water, and has a sweetish odor and a distinctly sweetish taste. The reaction is acid. Sugar is present in varying amounts. In mild cases it does not exceed 1½ or 2 per cent., but it may reach from 5 to 10 per cent. The total amount excreted in the twenty-four hours may range from 10 to 20 ounces (320 to 640 grams) and in exceptional cases from 1 to 2 pounds.

Ketonuria.—The ketone bodies, acetone, diacetic acid and β-oxybutyric acid are present, sometimes in small amounts in mild cases but increasing with the severity of the disease; and are indications of acidosis. In coma the excretion of β-oxybutyric acid may be as much as 100 gm. or more a day.

Glycogen has also been found in the urine, and in rare instances sugars other than glucose occur, lactose, levulose, and pentose, and to these conditions the term *melituria* is sometimes applied. *Albumin* is not infrequent.

Pneumaturia, gas in the urine, due to fermentation in the bladder, is occasionally met with. Cammidge's reaction may be present. Fat may be passed in the urine in the form of a fine emulsion (lipuria).

Blood in Diabetes.—The water content is lower than normal. Polycythæmia may be present to 6 or 8 millions of red cells per cmm. Towards the end and with complications there may be a leucocytosis and the leucocytes may contain glycogen. Hyperglycæmia is rarely above 0.4 per cent. The increase in the blood sugar may persist after glycosuria has disappeared.

The alkalinity is lessened and the specific gravity reduced. Lipæmia is present in many cases and may be readily recognized by the presence of dancing particles among the red cells in a slide of fresh blood. The blood lipoids are increased from the normal figure of about 0.6 per cent. to 0.83 per cent. in mild cases, to 0.9 in moderately severe and 1.4 per cent. in severe cases (Joslin). Lipæmia may be present without acidosis and is sometimes due to

surcharging of the blood stream with the products of fatty digestion as in the normal lipæmia of sucklings.

Complications.—(*a*) Coma (*Acidosis*)—There are three groups of cases: (1) Typical dyspnœic coma, the air-hunger of Kussmaul, in which with loud and deep in- and expirations, the pulse grows weak, and the patient gradually fails and dies, sometimes within twenty-four hours. The breath very often has the fruity odor of acetone. It may come on without any premonition and the patient may waken out of sleep in dyspnœa. An acyanotic dyspnœa is one of the best indications of acidosis. (2) Cases in which, without any previous dyspnœa or distress, the patient is attacked with headache, a feeling of intoxication, thick speech and a staggering gait, and gradually falls into deep coma. (3) Cases in which, particularly after exertion, the patient is attacked suddenly with weakness, giddiness and fainting; the hands and feet are cold and livid, the pulse small, respiration rapid; the patient becomes drowsy, and death occurs within a few hours. Dyspepsia, constipation, abdominal pain, marked irritability and restlessness may precede the onset of coma and should suggest its possibility.

(*b*) Cutaneous.—Boils and carbuncles are extremely common. Painful onychia may occur. Eczema is also met with, and at times an intolerable itching. In women the irritation of the urine may cause the most intense pruritus pudendi, and in men a balanitis. Rarer affections are xanthoma and purpura. Gangrene is not uncommon, and is associated usually with arterio-sclerosis. Perforating ulcer of the foot occurred in 7 of 276 cases. Bronzing of the skin (*diabète bronzé*) occurs in certain cases in which the diabetes arises as a late event in the disease known as hæmochromatosis, which is further characterized by pigmentary cirrhosis of the liver and pancreas. With the onset of severe complications the tolerance of the carbohydrates is much increased. Profuse sweats may occur.

(*c*) Pulmonary.—The patients are not infrequently carried off by *acute pneumonia,* which may be lobar or lobular. *Gangrene* is very apt to supervene, but the breath does not necessarily have the foul odor of ordinary gangrene. Abscess following lobar pneumonia occurred in one of our cases. *Tuberculous broncho-pneumonia* is common and may run a rapid course.

(*d*) Renal.—*Albuminuria* is a tolerably frequent complication. The amount varies greatly, and, when slight, does not seem to be of much moment. Œdema of the feet and ankles is not an infrequent symptom. General anasarca is rare, however, owing to the marked polyuria. It is sometimes associated with arterio-sclerosis. It occasionally precedes the occurrence of the diabetic coma. Occasionally cystitis is a troublesome symptom.

(*e*) Nervous System.—*Peripheral Neuritis.*—Neuralgia, numbness and tingling, uncommon symptoms in diabetes, are probably minor neuritic manifestations. The involvement may be general of the upper and lower extremities. Sometimes it is unilateral, or the neuritis may be in a single nerve—the sciatic or the third nerve. Herpes zoster may occur.

Diabetic Tabes (so-called).—This is a peripheral neuritis, characterized by lightning pains in the legs, loss of knee-jerk—which may occur without the other symptoms—and a loss of power in the extensors of the feet. The gait is the characteristic *steppage,* as in alcoholic, and other forms of neuritic paralysis. Changes in the posterior columns of the cord have been found.

Diabetic Paraplegia.—This is also in all probability due to neuritis. There are cases in which power has been lost in both arms and legs.

Mental Symptoms.—The patients are often morose, and there is a strong tendency to become hypochondriacal. Some patients display an extraordinary degree of restlessness and anxiety.

(*f*) Special Senses.—Cataract is liable to occur, and with rapidity in young persons. Diabetic retinitis closely resembles the albuminuric form. Hæmorrhages are common. Sudden amaurosis, similar to that which occurs in uræmia, may occur. Paralysis of the muscles of accommodation may be present; and, lastly, atrophy of the optic nerves. Aural symptoms may come on with great rapidity, either an otitis media, or in some instances inflammation of the mastoid cells. Ocular tension may be lowered in coma.

(*g*) Sexual Function.—Impotence is common, and may be an early symptom. Conception is rare; if it occurs, abortion is apt to follow. A diabetic mother may bear a healthy child; there is no known instance of a diabetic mother bearing a diabetic child. The course of the disease is usually aggravated after delivery.

Diagnosis.—There is no difficulty in determining the presence of sugar in the urine if the proper tests are applied. Alcapton may prove very deceptive, and in one reported case of ochronosis (Osler) a diagnosis of diabetes was made by four or five of the leading physicians in Europe, one of whom was an authority on diabetes. Deception may be practised. One patient had urine with a specific gravity of 1.065, but the reactions were for cane sugar; and there is a case in the literature in which, when the cane sugar fraud was detected, the woman bought grape sugar and put it into her bladder.

To determine whether the case is one of simple glycosuria or diabetes is not always easy, as the one readily merges into the other. The younger the individual the greater the probability that the case is true diabetes. It is well to test the assimilation limit; 100 grams of glucose given in solution two hours after a breakfast of a roll and butter with coffee should not give glycosuria. To do so indicates a deficiency in the capacity to store carbohydrates and a possibility that diabetes may follow. Transient glycosuria occurs in a great many conditions already mentioned. For practical purposes the common form is that met with in persons above 50 years of age, who eat and drink too much and tend to grow stout. The detection of a little sugar in the urine may have the great advantage of frightening the patient into a more rational mode of life. The forms following anæsthesia, accidents, business worries, fright and that which occurs in pregnancy are, as a rule, readily controlled.

Prognosis.—The younger the patient the less likely is recovery. In children the disease may run a very rapid course, and death may occur within a few weeks, or a child may die in coma before the condition has been recognized. On the other hand, in persons over fifty sugar may be present in the urine for years without any impairment of strength or health. The outlook is good in the fat, bad in the lean. It is particularly good in the stout, active, business man, whose glycosuria has come on as a result of worry, work, and excess in food and drink. An early diagnosis, obesity and a gain in tolerance are hopeful features.

The following steps should be taken to estimate the gravity of a case. The carbohydrate tolerance should be estimated and the presence of acetone

"When the urine has been sugar-free for three days, add about 20 grams protein and thereafter 15 grams protein daily in the form of egg-white, fish or lean meat (chicken) until the patient is receiving 1 gram protein per kilogram body weight or less if the carbohydrate tolerance is zero."

"Add no fat until the protein reaches 1 gram per kilogram body weight (unless the protein tolerance is below this figure) and the carbohydrate tolerance has been determined, but then add 5 to 25 grams daily, according to previous acidosis, until the patient ceases to lose weight or receives in the total diet about 30 calories per kilogram body weight."

"The return of sugar demands fasting for twenty-four hours or until sugar-free. Resume the former diet gradually, adding fat last in order to maintain as high a carbohydrate tolerance as possible, sacrificing body weight for this purpose. This rule should be inflexibly followed, especially with children."

"Whether sugar reappears in the urine or not it is desirable upon one day each week to rest that function of the body which controls the assimilation of sugar by either a complete fast day or a diet of low caloric value. My plan is patterned on the following rule: Whenever the tolerance is less than 20 grams carbohydrate, fasting should be practised one day in seven; when the tolerance is over 20 grams carbohydrate, cut the diet in half on one day each week (half-day)."

Days of Reduced Diet.—In every case it is wise to restrict the diet on one day a week. In mild cases the quantity of carbohydrate should be reduced to one-half or one-third of the usual amount. In moderate or severe cases a complete fast of one day is advisable. A day when only eggs and the 5 per cent. vegetables are taken is also an advantage. The exact amount allowed in any case must depend on the carbohydrate tolerance; the lower this is the greater importance of a fast day.

Saccharine may be used in place of sugar. It is an advantage in using vegetables which are boiled in cooking, to do the boiling in three different waters. All the water should be removed after each boiling. This reduces the amount of carbohydrate. It is well to do this with patients who demand bulk in the diet.

The patient should keep an accurate record of his diet and the amounts taken. It is well for him to have scales to determine the exact weights so that the intake is known accurately. Tables of food values are of assistance in determining the amount of protein, carbohydrate and fat in the diet. He should be taught to examine the urine for sugar, daily in severe cases, once or twice a week in milder cases. It is not necessary for the patient to gain weight or even to equal his former normal weight.

Medical Treatment.—This is not satisfactory and there is no drug which appears to have a direct curative influence. Opium and its derivatives are sometimes useful for irritable patients but are rarely required. Potassium bromide may be given for the same purpose. The use of arsenic has been recommended and is indicated, either alone or with iron in case of anæmia. The bowels should be kept freely open and for this such drugs as mineral oil, cascara, senna and phenolphthalein are most useful. Purging should be avoided.

Coma.—The urine should be watched carefully for acetone and diacetic acid. Their presence is a sign for reduction in the diet, especially the fats.

If sugar is present fasting is usually indicated. If signs of coma appear the patient should be put to bed and kept as quiet as possible. The stomach should be washed out and the bowels moved by enema. Fluid should be given freely to an amount of 1,000 c. c. every six hours, as thin broth, tea, coffee or water by mouth. If necessary some may be given by rectum. If this is not possible the fluid should be given subcutaneously or intravenously. If the patient has been on full diet, cut out the fat, but continue the same amount of protein and carbohydrate, the latter being given in simple form, such as thin oatmeal gruel, orange juice, milk or bread. At least a gram of carbohydrate per kilo of body weight may be given. If the circulation is failing, digitalis should be given. Joslin advises against the use of alkalies and while the general practice has been to give sodium bicarbonate his opinion carries great weight. If alkali has been given he advises a reduction in the dose of 30 grams a day.

Of the complications, the *pruritus* and *eczema* are best treated by cooling lotions of boric acid or hyposulphite of soda (1 ounce; water, 1 quart), or the use of ichthyol and lanolin ointment. With co-existing pulmonary tuberculosis the usual diabetic treatment can be employed.

The decision as to the performance of an operation should be carefully made. The patient should be given a thorough study and put in the best possible condition so that he is sugar and acid free.

III. DIABETES INSIPIDUS

Definition.—A chronic affection characterized by the passage of large quantities of normal urine of low specific gravity.

The condition is to be distinguished from diuresis or polyuria, which is a frequent symptom in hysteria and some forms of nephritis. There may be excessive polyuria with abdominal tumors and aneurism, tuberculous peritonitis and carcinoma. Willis in 1674 first recognized the distinction between a saccharine and non-saccharine form of diabetes.

Etiology.—The disease is most common in young persons. Of the 85 cases collected by Strauss, 9 were under five years; 12 between five and ten years; 36 between ten and twenty-five years. Males are more frequently attacked than females. The affection may be congenital. A hereditary tendency has been noted in many instances, the most extraordinary of which has been reported by Weil. Of 91 members in four generations, 23 had persistent polyuria without any deterioration in health.

It may follow injury to the base of the skull. It is sometimes associated with adiposity and defective genital development (pituitary disease). Recent observations have shown a striking relationship between pituitary disease and diabetes insipidus. In some cases it is due to insufficiency of the pars intermedia of the pituitary body. In a case reported by Cushing there was polyuria for three months after a sellar decompression operation, regarded as due to an irritative lesion of the pituitary. Tumors, lesions of the medulla and pituitary, malignant metastases in the pituitary, injury and syphilis, usually basal and meningitic, are possible factors. Hemianopsia is present in a number of the cases. Disturbance of the function of the pituitary gland, more particularly the pars intermedia, may be regarded as the essential factor, cer-