should be avoided. When from any cause a stimulant is indicated, claret, dry sherry, or good whisky is preferable. Champagne is particularly pernicious. Persons with a marked tendency to lithæmia should be urged to restrict the appetite and to take only a moderate amount of food. Over-eating is not far behind excessive drinking in its injurious effects. Indeed, a majority of people over forty years of age take more food than is required to maintain the equilibrium of health. Gout, in many cases, is evidence of an overfed, overworked, and consequently clogged machine.

The skin should be kept active: if the patient is robust, by the morning cold bath with friction after it; but if weak or debilitated, the evening warm bath should be substituted. An occasional Turkish bath with active shampooing is advantageous. The secretion of urine should be fully maintained, and the specific gravity reduced by diluents to at least 1·015. The bowels should be kept open and an occasional saline purgative may be administered. The patient should dress warmly, avoid rapid alterations in temperature, and be careful not to have the skin suddenly chilled. Gouty persons derive much benefit from taking certain waters, such as Saratoga, the Bedford, the White Sulphur of Virginia, in this country; the Bath and Harrogate, in England; and those of Carlsbad, Kissingen, Homburg, Vichy, and Contrexéville, on the continent.

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. Steaming the joint is sometimes beneficial. A brisk mercurial purge is always advantageous at the outset. The wine or tincture of colchicum, in doses of twenty to thirty minims, may be given every four hours in combination with the citrate of potash or the citrate of lithium. The colchicum should be carefully watched. 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 promptly stopped as soon as it has relieved the pain. In cases in which the pain and sleeplessness are more distressing and do not yield to colchicum, morphia may be necessary. The patient should be placed on a low diet, chiefly of milk and barley-water, but if there is any debility, strong broths may be given, or eggs. It is occasionally necessary to give small quantities of stimulants. Potash water, Apollinaris, or Seltzer water should be taken freely. Waters with the sodium salts should be avoided. During convalescence meats and fish and game may be taken, and gradually the patient may resume the diet previously laid down.

In the chronic and irregular forms of gout the treatment by hygiene and diet is most suitable. Colchicum is not often required, though in small doses it is sometimes beneficial. Lithium salts do good, since a combination of uric acid with lithium is more soluble than the sodium salt. There is no good native lithia water. The medicine is best given

in potash water, in a glassful of which five grains of the citrate of lithium may be taken three times a day, or the *liquor lithiæ effervescens* of the British Pharmacopœia may be used. The mineral waters above mentioned are particularly beneficial, partly in themselves, and partly owing to the strict regulations to which the patient is subjected when taking the "cure." Ammoniacum, guaiacum, and preparations of quinine and iron are sometimes serviceable in the chronic gout. Iodide of potassium and the benzoates are also recommended. The local treatment of joints affected with chronic gout is not satisfactory. Hydrotherapeutic measures, the Paquelin, and massage may be tried.

VII. DIABETES MELLITUS.

Definition.—A disorder of nutrition, in which sugar accumulates in the blood and is excreted in the urine, the daily amount of which is greatly increased.

Etiology.—Hereditary influences play an important *rôle*, and cases are on record of its occurrence in many members of the same family. There are instances of the coexistence of the disease in husband and wife. Men are more frequently affected than women. It is a disease of adult life; a majority of the cases occur from the third to the sixth decade. It is rare in childhood, but cases are on record in children under one year of age. Persons of a neurotic temperament are often affected. It is a disease of the higher classes. Hebrews seem especially prone to it; one fourth of Frerichs' cases were of the Semitic race. In a considerable proportion of the cases of diabetes the subjects have been excessively fat at the beginning of, or prior to, the onset of the disease. It must be remembered, however, that a slight trace of sugar is not very uncommon in obese persons. This so-called lipogenic glycosuria is not of grave significance, and is only occasionally followed by true diabetes. There are instances on record in which obesity with diabetes has occurred in three generations. It is more common in cities than in country districts. Gout, syphilis, and malaria have been regarded as predisposing causes. Mental shock, severe nervous strain, and worry precede many cases. The combination of intense application to business, over-indulgence in food and drink, with a sedentary life, seem particularly prone to induce the disease. It may set in during pregnancy, and in rare instances may only occur at this period. Injury to or disease of the spinal cord or brain has been followed by diabetes. In the carefully analyzed cases of Frerichs there were thirty instances of organic disease of these parts. The medulla is not always involved. In only four of his cases, which showed organic disease, was there sclerosis or other anomaly of this part. An irritative lesion of Bernard's diabetic centre in the medulla is an occasional cause. I saw with Riess, at the Friedrichshain, Berlin, a woman who had anomalous

cerebral symptoms and diabetes, and in whom there was found post mortem a cysticercus in the fourth ventricle.

Of late years lesions of the pancreas have been held to cause diabetes, and in a certain number of cases this organ is affected. The disease has occasionally followed the infectious fevers. A few cases have followed injury without involvement of the brain or cord.

In comparison with European countries diabetes is a rare disease in America. The last census gave only 2·8 per one hundred thousand of population, against a ratio of from five to nine in the former. In this region the incidence of the disease may be gathered from the fact that among thirty-five thousand patients under treatment at the Johns Hopkins Hospital and Dispensary there were only ten cases.

We are ignorant of the nature of the disease. Normally the carbohydrates taken with the food are stored in the liver as glycogen, and then utilized as needed by the system. Glycogen can also be formed from the proteids of the food, and under certain circumstances sugar may be directly formed from the body proteids. Whenever the sugar in the systemic blood exceeds a definite amount it is discharged by the kidneys, producing glycosuria. Theoretically the condition may be supposed to be induced by:

(*a*) The ingestion of a larger quantity of carbohydrates and peptones than can be warehoused, so to speak, in the liver as glycogen, so that part has to pass over into the hepatic blood. Some of the instances of lipogenic or dietetic glycosuria are of this nature.

(*b*) Disturbances of the liver function: (1) Changes in the circulation under nervous influences. Puncture of the medulla, lesions of the cord, and central irritation of various kinds are followed by glycosuria, which is attributed to a vaso-motor paralysis (more rapid blood-flow) induced by these causes. On this view the disease is a neurosis. (2) Instability of the glycogen, owing either to imperfect formation or to conditions of the cells which render it less stable. Phloridzin and other substances which cause diabetes very probably act in this way.

(*c*) Defective assimilation of the glucose in the system. How and under what normal circumstances the sugar is utilized we do not yet know. Theoretically faulty metabolism would explain the condition.

Interesting observations have of late made it probable that the pancreas may in some cases be the seat of the trouble. Lesions of this organ have frequently been met with in diabetes. Von Mering and Minkowski have shown that extirpation of the gland in dogs is followed by glycosuria, but, if a small portion remains, sugar does not appear in the urine, facts which have been confirmed by Lepine and others. The pancreas, on this view, has, like the liver, a double secretion—an external, which is poured into the intestines, and an internal, which passes into the blood. This latter is supposed to be of the nature of a ferment, in the presence of which alone the normal assimilative processes can take place with the glycogen. Disease of the pancreas causes diabetes by preventing the formation of

the glycolytic ferment. Even when, as in a majority of instances of diabetes, the organ is apparently normal, a functional trouble may disturb the formation of this ferment. The fact that if a small portion of the gland is left, in the experiments upon dogs, diabetes does not occur, is analogous to the remarkable circumstance that a small fragment of the thyroid is sufficient to prevent the development of articifial myxœdema. It has recently been stated by Falkenberg that extirpation of the thyroid gland in dogs is also followed by diabetes.

Morbid Anatomy.—Saundby * has recently analyzed the changes which occur in this disease.

The *nervous system* shows no constant lesions. In a few instances there have been tumors or sclerosis in the medulla, or, as in the case above mentioned, a cysticercus has pressed on the floor. Cysts have been met with in the white matter of the cerebrum and perivascular changes have been described. Glycogen has been found in the spinal cord. In the peripheral nervous system there are instances in which tumors have been found pressing on the vagus. A secondary multiple neuritis is not rare, and to it the so-called diabetic tabes is probably due.

In the sympathetic system the ganglia have been enlarged and in some instances sclerosed, but there is nothing peculiar in these changes. The *blood* may contain as high as 0·4 per cent of sugar instead of 0·15 per cent. The plasma is usually loaded with fat, the molecules of which may be seen as fine particles. When drawn, a white creamy layer coats the coagulum, and there may be lipæmic clots in the small vessels. There are no special changes in the red or white corpuscles. Gabritschewsky has shown that the "polynuclear" leucocytes in diabetes contain glycogen. Glycogen can occur in normal blood, but it is here extra-cellular. It has been also found in the polynuclear leucocytes in leukæmia. The *heart* shows no characteristic changes. Endocarditis is very rare. The *lungs* show important changes. Acute broncho-pneumonia or croupous 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. Fatty embolism of the pulmonary vessels has been described in connection with diabetic coma.

The *liver* is usually enlarged, fatty degeneration is common, and French writers have described a form of cirrhosis. Letulle, who has described remarkable examples of this so-called diabetic cirrhosis—the *cirrhose pigmentaire*—thinks the change is due to abnormal destruction of the blood-cells. It may be associated with bronzing of the skin.

The *pancreas*, as pointed out by Lancereaux, shows important changes. Saundby states that in seven out of fifteen cases it was atrophied, abnor-

* Bradshaw Lecture, Royal College of Physicians of London, 1890; and Lectures on Diabetes, E. B. Treat, New York, 1891.

mally firm and fibroid in four, and normal in only four. A patient of W. T. Bull died of diabetes after extirpation of the pancreas. In some instances there is a pigmentary cirrhosis analogous to that which occurs in the liver, and this induration seems to be an important change. Cancer of the pancreas has been met with, and Longstreth found, in one instance, cystic disease. Fat necrosis of the pancreas has also been found. Neither the *stomach* nor the *intestines* show any characteristic lesions.

The *kidneys* are sometimes fatty, and show a hyaline change in the tubular epithelium, particularly in the descending limb of the loop of Henle. It also occurs in the capillary vessels. Saundby confirms the occurrence of this hyaline change, and its restriction to the epithelium of Henle's tubes.

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 more rapid, and the emaciation more marked.

It is also possible to divide the cases into (1) *lipogenic* or *dietetic*, which includes the transient glycosuria of stout persons; (2) *neurotic*, due to injuries or functional disorders of the nervous system; and (3) *pancreatic*, in which there is a lesion of the pancreas. It is, however, by no means easy to discriminate in all cases between these forms. Of late attempts have been made to separate a clinical variety analogous to experimental pancreatic diabetes. Hirschfeld, from Guttmann's clinic, has described cases running a rapid and severe course usually in young and middle-aged persons. The polyuria is less common or even absent, and there is a striking defect in the assimilation of the albuminoids and fats, as shown by the examination of the fæces and urine. In four of seven cases autopsies were made and the pancreas was found atrophic in two, cancerous in one, and in the fourth exceedingly soft.

The *onset* of the disease 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.

The Urine.—The amount varies from six or eight pints in mild cases to thirty or forty pints 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. 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 one and a half or two per cent, but it may reach from five to ten per cent. The total amount excreted in the twenty-four hours may range from ten to twenty ounces, and in

exceptional cases from one to two pounds. The following are the most satisfactory tests:

Fehling's Test.—The solution consists of sulphate of copper (grs. 90½), neutral tartrate of potash (grs. 364), solution of caustic soda (fl. ozs. 4), and distilled water to make up six ounces. Put a drachm of this in a test-tube and boil (to test the reagent); add an equal quantity of urine and boil again, when, if sugar is present, the yellow suboxide of copper is thrown down. The solution must be freshly prepared, as it is apt to decompose.

Tromner's Test.—To a drachm of urine in a test-tube add a few drops of a dilute sulphate-of-copper solution and then as much *liquor potassæ* as urine. On boiling, the copper is reduced if sugar be present, forming the yellow or orange-red suboxide. There are certain fallacies in the copper tests. Thus, a substance called glycuronic acid is met with in the urine after the use of certain drugs—chloral, phenacetin, morphia, chloroform, etc.—which reduces copper. It has been found in the urine of an apparently healthy man (Ashdown).

Fermentation Test.—This is free from all doubt. Place a small fragment of yeast in a test-tube full of urine, which is then inverted over a glass vessel containing the same fluid. If sugar is present, fermentation goes on with the formation of carbon dioxide, which accumulates in the upper part of the tube and gradually expels the urine.*

Of other ingredients in the urine, the urea is increased, the uric acid does not show special changes, and the phosphates may be greatly in excess. Ralfe has described a great increase in the phosphates, and in some of these cases, with an excessive excretion, the symptoms may be very similar to those of diabetes, though the sugar may not be constantly present. The term phosphatic diabetes has sometimes been applied to them. *Acetone* and acetone-forming substances are not infrequently present. Le Nobel's test for acetone is as follows: "Pour an ounce of urine into a urine glass; add a drachm or two of nitro-prusside of sodium (five grains to one ounce) and a few drops of strong liquid ammonia. After standing a few minutes a rose-violet color is developed, which, if much acetone is present, may require diluting with water in order to bring out the brilliancy of its color" (Saundby).

Glycogen has also been described as present in the urine.

Albumen is not infrequent. It occurred in nearly thirty-seven per cent of the examinations made by Lippman at Carlsbad.

Among the *general symptoms* of the disease, *thirst* is one of the most distressing. A very large amount of water is required to keep the sugar in solution and for its excretion in the urine. The amount of water consumed will be found to bear a definite ratio to the quantity excreted. Instances, however, are not uncommon of pronounced diabetes in which the

* For quantitative and other tests the student is referred to Tyson, On the Urine, or the standard works on urinalysis.