Diabetes, mellitus and insipidus / by Andrew H. Smith.

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MELLITUS AND INSIPIDUS.

BY

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PREFACE.

The object of this little work is not to compress into the fewest possible words all that is known or surmised in regard to Diabetes, but to give the points which will most interest those who have to manage cases of this disease. Consequently, but little space is given to the discussion of undetermined questions of physiological and pathological chemistry, etiology, etc, Those who wish to go deeply into these matters will find in the literature of the subject a mass of facts and theories from which they may form their own opinions.

The writer has endeavored to reflect his own experience in the pages of what in the nature of the case must be largely a compilation. It is hoped that the reader, if he finds nothing new in them, will at least find something practical and helpful.

In their preparation much use has been made of the admirable article by Dr. Tyson, in Pepper's System of Medicine, and also of his compendium of the literature of Diabetes in the Annual of the Universal Medical Sciences for 1888 and 1889. From these sources and the references they give it is possible to trace back to nearly everything that has been written on Diabetes, and Dr. Tyson has laid all who shall write here after on the subject under lasting obligations.

DIABETES (MELLITUS.)

CHAPTER I.

CLINICAL HISTORY AND COMPLICATIONS.

Leaving out of consideration the conditions in which sugar appears transiently in the urine in the course of various affections, or as the result of special articles of diet, the term *Diabetes* will be restricted to the designation of that form of disease of which saccharine urine is the leading and persistent feature. With the unnatural quality, is usually, though not necessarily, associated increased volume of the urine.

The limits of this work will not permit a detailed statement of the many interesting and ingenious researches into the nature of this affection which have occupied so much attention during the past quarter of a century. As the result of these investigations, however, we seem warranted in accepting as proven that the seat of the sugar formation is the liver; that under the influence of disordered nervous action the physiological function of the liver as a sugar produc-

ing organ is enormously increased; while at the same time the consumption of sugar in the economy is diminished; and that in consequence sugar accumulates in the blood, whence it is excreted by the kidneys.

In most cases the attention of the patient is first attracted by observing that the calls to urinate are unduly frequent, and that the quantity of urine is greater than the normal. It may also be noticed that the urine imparts a peculiar stiffness to any fabric upon which it has dried. Sometimes the first intimation of the disease is conveyed by eczema of the prepuce or labia, caused by the irritation of the saccharine urine.

Very early in the case an abnormal thirst is observed. This becomes more and more urgent in proportion as the quantity of urine increases, until the patient is scarcely ever free from its importunity. Throughout the day large and frequent draughts of water are taken, and at night, between calls to evacuate the bladder and attempts to assuage the thirst, the sleep is broken and unrefreshing, thus adding another to the exhausting influences of the disease.

Along with the thirst is developed a dryness of the mouth, amounting in some instances to a burning sensation; at the same time the patient is conscious of a sweetish, fruity taste. The breath has also a sweetish, slightly etherial odor.

In most cases the appetite is increased, and the

amount of food taken is sometimes enormous. Yet, although the digestion may remain for some time unimpaired, there is loss rather than gain in flesh. The emaciation may become extreme. In some instances it is the first symptom which excites attention. That the tissues should waste rapidly and to an extreme degree, is the natural consequence of the excessive drain upon the system, not only in the amount of sugar excreted, but in the excess of urea which usually accompanies it. The sugar being produced at the expense of the principal fat-producing elements of the food, the adipose tissue suffers more in proportion than the muscular fibre. The exclusion of starch and sugar from the diet as a measure of treatment, of course operates in the same direction. But the nitrogenous elements of the body suffer also, contributing ultimately to the production of sugar, while the urine contains an abnormal proportion of azotized principles, as will be more fully considered hereafter.

This loss of flesh causes the skin of the face to become wrinkled. The surface of the body is generally dry and harsh, often furfuraceous. The contact of the urine may occasion eczema of the genitals, especially in women, and this may go on to excoriation, and occasionally to ulceration or gangrene.

In the advanced stages impotence is not uncommon.

The digestive organs very generally show signs

of derangement. Flatulence and eructation indicate that digestion is slow, allowing time for fermentation of the contents of the alimentary canal. Gastric uneasiness is present, and the bowels are often obstinately constipated.

The enormous loss of the materials from which heat is produced, and the general disturbance of the processes of assimilation and disassimilation, together with the large amount of fluid taken into the system at a temperature lower than that of the body, result in a marked reduction of the bodily heat. In uncomplicated cases, this is proportionate to the gravity of the disease. In mild cases the temperature will range from 97° to 98°; in severe cases it may fall as low as 93°, or even lower. In this condition an affection usually accompanied by hyperpyrexia, as for example, pneumonia, may run its course without bringing the temperature up to its normal standard.

Anæmia is a natural result of the drains to which the system is subjected, but it may easily escape observation for a time, being masked by an unusual redness of the lips and a passive dilatation of the capillaries of the face. Consequent upon this thinness of the blood, dropsy is frequently developed, despite the discharge of perhaps five or six times the natural amount of fluid from the body. The œdema is soft and painless, and is usually confined to the lower extremities. It comes and goes in accordance with the changing conditions of the circulation.

Boils and Carbuncles are of frequent occurrence in diabetics, and especially in elderly people. The presence of a carbuncle should always suggest the examination of the urine for sugar, even if no other indication of diabetes is apparent.

Gangrene resembling the senile form in its appearance and progress, is an occasional though rare complication. It most frequently attacks the toes, but may appear upon any part of the body in which the circulation is inactive.

Changes in the Eye.—Mitchell, pointed out many years ago, that injecting a solution of sugar beneath the skin of a frog would produce in the course of twenty-four hours an opacity of the crystalline lens, which would promptly disappear when the animal was restored to the normal medium. These experiments threw much light upon the fact already known that diabetics were especially liable to cataract. This is indeed the change most frequently observed in the eye. It occurs in about three or four per cent. of the cases of diabetes. Richardson subsequently found that artificial cataract could be produced by a variety of saline solutions, as well as by the sugar used in Mitchell's experiments. The only essential condition was that the density of the solution should be greater than that of the blood. The fluids of the lens are withdrawn by osmosis, passing into the denser contiguous humors. A deposition of calcareous matter

takes place in the lens after a time, and the opacity which might otherwise have been transient is rendered permanent.

Diabetic cataract is one of the very late phenomena of the disease, and indicates that the system is profoundly involved. It usually affects both eyes, either at the same time or successively. It is remarkable for the rapidity with which the opacity when once begun goes on to completion. Dickinson states that the whole process is concluded not infrequently within a week.

The variety is usually the soft, but in elderly persons it may be firm, and contain a hard nucleus as in other forms of senile cataract.

These cases are not well adapted for operation, as the wound does not heal readily, as a rule. Moreover, the general health is apt to be so greatly impaired by the time diabetic cataract makes its appearance, that the remnant of life left to the patient seems scarcely to warrant an operation with such doubtful issue. Changes in the fundus are occasionally observed, which bear a strong resemblance to those occurring in Bright's disease. Hæmorrhages, some of considerable size, are present in most cases. These sometimes lead to secondary retinitis. When associated with opacity of the vitreous, these changes are specially significant of diabetes, and have sufficed for a diagnosis prior to examination of the urine.

Under the influence of diet these appearances may improve or disappear, but they are apt to recur (Gowers).

Albuminuria occurs as one of the later complications in a considerable proportion of cases. It is probably due in part to irritation of the kidneys by the sugar passing through them, but the frequency with which a gouty diathesis coincides with diabetes, should not be lost sight of as a causative factor.

A very large proportion of diabetics ultimately develop pulmonary phthisis, which does not vary materially from the ordinary course except that its progress is usually more rapid. It closes the career of most of those who do not become victims of diabetic coma: As the fatal termination approaches, it is common to find the quantity of sugar in the urine greatly diminished, and at last, in many cases, no trace of it can be discovered. Dickinson suggests that this is due to increased consumption during the pyrexia.

Diabetic Coma.—This condition occurs as one of the later manifestations of the disease, and, indeed, often ushers in the fatal termination. It usually is gradual in its approach, being preceded by various nervous phenomena, such as pains in the head, dizzinesss, somnolency, muscular pains, vomiting, dyspnœa somewhat similar to that observed in uremia, irregular cardiac action, etc. With these symptoms there is an odor in the breath resembling acetone,

and the urine gives the reaction of acetone with ferric perchloride, viz., a deep wine color. From these circumstances the coma, as well as the symptoms above mentioned, has been supposed to depend upon the presence of acetone in the blood, and the condition has been styled acetonæmia. But it is amply demonstrated that the nervous symptoms, including coma, may be present without any evidence of acetone in the blood, and that, on the other hand, acetone may be present and no disturbance of the brain or nervous system take place. Moreover, acetone in large doses may be administered to animals without producing anything more than a slight intoxication resembling that from alcohol. It seems, therefore, that the toxic symptoms culminating in coma cannot justly be attributed to acetonæmia.

The importance and gravity of diabetic coma may be inferred from the experience of Frerichs, that of 250 deaths from diabetes, 153 were due to this cause.

According to Jaccoud there are three forms of attack. In the first, or typical form, the symptoms in the early stage are chiefly abdominal and resemble those of acute indigestion. There are nausea, vomiting, constipation, abdominal pain, meteorism, etc. Indeed the picture may resemble that of peritonitis, but with this striking difference, that the temperature instead of being elevated is subnormal. Dyspnœa is usually present. With the disappearance of these

symptoms, which last about three days, come on apathy, drowsiness, and finally coma, which constitutes the second stage. This lasts from 24 to 48 hours, when the patient dies, with a temperature from three to six, or more degrees below the normal. In some cases the coma comes on more promptly, and the entire duration of the two stages may not be more than 36 or even 24 hours. During the second stage the odor of acetone is usually present in the breath.

In the second form, the abdominal symptoms and dyspnœa are absent, and in their stead are headache and dizziness, which, after lasting a few hours, or perhaps half a day, are succeeded by somnolence, coma and death.

In the third form, which is very rare, the first symptom is extreme weakness, amounting to almost total want of power, with increasing feebleness of the pulse, and more or less of a cyanotic hue of the face and extremities, the condition terminating in somnolence and coma.

The phenomena of diabetic coma are well illustrated in a case in which the writer was consulted while this chapter was in preparation.

F. T., aged 16, was found 18 months before to be passing saccharine urine. He had also mitral insufficiency, but was little affected by it. He had been under a variety of treatment by different physicians, and during the previous three months had

emaciated excessively. Still he was fairly comfortable, and was with the family at the seashore, there being nothing in his condition to excite immediate apprehension. The daily excretion of sugar of late had been almost seven ounces. Diet was not being rigidly observed. Patient was as well as usual at breakfast, which he took with the family. Shortly afterward he complained of nausea and gastric distress, and there were soon efforts at vomiting. He felt extremely weak and went to bed. His extremities became cold and the ankles were puffed. Face flushed and hot. At 3 P. M. was seen by the writer. The most striking symptom was rapid and exaggerated respiration, resembling that of an animal in a partial vacuum. The respirations numbered 48 per minute and the amplitude was remarkably great. There were no pulmonary rales, and no approach to cyanosis. Face flushed, lips bright red. Odor of breath slightly fruity. Temperature 103½, a notable departure from the usual condition. Pulse 120, feeble and irregular. There was drowsiness alternating with mild delirium. Gastric distress very marked, with frequent efforts at belching, but the abdomen was not distended.

Brandy and digitalis were given, and a single small dose of antipyrin. Within an hour the temperature had fallen to 101½, and the breathing was easier. But the cerebral symptoms became more and more marked, and the patient died comatose, 18 the hours after attack began.

CHAPTER II.

PATHOLOGY AND MORBID ANATOMY.

Situated in the medulla oblongata, in the floor of the fourth ventricle, is an area which when irritated gives rise to glycosuria. This is the so-called diabetic area, and piercing this with an instrument in physiological experiments is called the diabetic puncture. The influence of this irritation is propagated through certain branches of the sympathetic to the liver, and acting through the vaso-motor nerves produces relaxation of its vessels and consequently hyperæmia. This hyperæmia is probably an invariable condition of essential glycosuria. The increased calibre of the vessels permits the blood to pass through the liver without coming into that intimate relation with the hepatic cells which is necessary for a proper regulation of the glycogenic function.

What is accomplished experimentally by the diabetic puncture, is probably brought about by pathological conditions involving irritation of the medulla or of its nervous connections with the liver. A persistent irritation of this kind would necessitate persistent glycosuria, or in other words diabetes.

This is but a surface-view of the subject. What lies deeper is being studied with much earnestness by many competent investigators, but definite results have not yet been obtained.

The only speculation which the writer will indulge in on his own account is: That in diabetes a vicious circle is established; irritation of the diabetic area inducing glycohæmia; and the presence of sugar in the blood inducing irritation of the diabetic area.

The first part of this proposition was long since demonstrated. The second derives probability from three facts. 1st. That dietetic glycosuria may lay the foundation for diabetes. 2nd. That excluding sugar producing substances from the urine not only controls glycosuria, but tends to remove its cause, effecting not infrequently a positive cure. 3rd. That evidence of irritation of nerve tissue by the circulation of sugar in the blood is found in the very frequent occurrence of neuralgia and even of neuritis in the clinical history of diabetes.

It is evident, however, that the diseased condition embraces more than the phenomena to which the name Diabetes has been given. The nervous derangement which produces glycosuria is but a part of a more general disturbance in which the vital principle relaxes the control which it normally exerts over chemical action, and permits a sort of chemical riot in every portion of the economy. The production of sugar is increased on the one hand, while its consumption is diminished on the other. Urea is formed in abnormal quantity. Acids which have no place in the healthy body are abundantly produced.

The nutrition of the tissues becomes defective, in fact the whole process of nutrition exhibits more of chemical reaction and less of vital function than in the condition of health.

Changes in the Urine.—The physical properties of the urine differ in a marked degree from those observed in health. Its color is light—a pale straw or greenish tint—and when freshly drawn it is remarkably transparent. The usual sources of turbidity produce little effect owing to the great degree of dilution. A short exposure to the air, however, especially in a warm place, induces chemical changes accompanied by more or less cloudiness. The odor is peculiar, and has been likened to that of sweet hay, apples, or chloroform. Its taste is said to be, and doubtless is, sweet. Its specific gravity is usually above the average of normal urine. The highest the writer has found recorded is 1,074, observed by Bouchardat. A bottle containing diabetic urine will often attract attention at once by its sensible weight. But when the quantity of urine is great, the specific gravity may be as low as 1,015, or 1,010. The quantity voided in twenty-four hours varies greatly in different cases. It may be scarcely above the normal amount, or it may reach 30, 40, or 50 pints or more. Indeed, one Italian author, quoted by Watson, declares that 200 pints have been discharged in 24 hours.

On chemical examination the urine is found to contain sugar, which is identical with glucose or

grape sugar. It may be obtained in a crystalline form by evaporating the urine to the consistence of a thin syrup, and allowing it to stand for some days in a shallow vessel.

The quantity of sugar passed daily varies from a few grains to 50 ounces, as in a case reported by Dickinson. The proportion may be as high as 15 per cent., but in the great number of cases it ranges between 1 and 10 per cent., with a total excretion in 24 hours of 300 to 4,000 or 5,000 grains. Slight variations in diet, exercise, temperature, mental conditions, etc., will materially affect the quantity passed.

In a case under the observation of the writer, the discussion of an important business project which was prolonged far into the night, was followed next day by the excretion of double the usual amount of sugar. A few days rest in the country restored it to the former quantity.

The occurrence of any febrile affection generally lessens the sugar production, and may cause its complete temporary arrest.

The diminished action of the system during sleep usually produces a corresponding reduction in the amount of sugar formed, and in mild cases it is not unusual to find the moring urine nearly, or quite, free of saccharine matter. On the other hand a restless night, with sleep disturbed by dreams, may result in an increase rather than a decrease of the amount

of sugar. As a rule the production of urea is increased, the increase bearing some proportion to the sugar excreted and amounting sometimes to five or six times the normal quantity. But the ratio of urea to the volume of urine is much reduced. Still after fermentation, even when the patient is passing 80 to 100 ounces of urine, the specific gravity will often be as high as 1.015 to 1.020.

Albumen is often found in the urine in diabetes, and where its presence is persistent it indicates that the kidneys have undergone structural change.

The urine may also contain alcohol, acetone, or peptones; and in some cases, in the later stages, oxybutyric acid in large amounts is present.

A great variety of tests have been employed for detecting sugar in the urine, and estimating its amount. Of these, Fehling's will be found the most convenient and satisfactory as a qualitative test, and the fermentation test best suited for quantitative estimation.

Fehling's solution is prepared as follows:

Copper sulphate, 90½ grains.
Neutral potassium tartrate, 364 grains.
Solution of caustic soda (sp. gr. 1.12),
4 fluidounces.
Add water to make six fluidounces.

This test is employed as follows: Put about a drachm of the solution into a small test-tube, heat to boiling, and add five to ten drops of the suspected

urine and boil again. If sugar is present there will be a reddish-yellow precipitate of copper. If the sugar is at all abundant, the precipitation takes place at once; if the quantity is very small, the change may take place more gradually.

It is objected to this test that the solution after a time undergoes changes that render it worthless. These changes may be avoided to some extent by covering the bottle with paper, so as to exclude the light. If the solution is clear, and there is no precipitate upon the inside of the bottle, it can be inferred that no change has taken place.

It sometimes happens that urine contains substances which prevent the reaction of the copper. This difficulty may be overcome by using a small quantity of urine as compared with the quantity of the test. On the other hand, when the solution is old, it will occasionally give with non-saccharine urine, a reaction somewhat resembling the reaction of sugar. In case of doubt, a fresh solution must be procured. A solution which changes in any way by boiling is unfit for use. The appliances for examining urine for sugar should include a bottle containing a solution of honey. Whenever a test gives a negative result, a few drops of this solution should be added to the contents of the test-tube, and the heat reapplied. If there is still no reaction, one of two conditions must be present; either the test solution has become worthless, or there is some substance in the urine

which prevents the reduction of the copper. If, however, the usual reaction takes place after the addition of the honey, the negative result obtained at first may be accepted as conclusive against the presence of sugar in the specimen of urine examined.

The bismuth, or Mylander's, test is thought by some to be rather more delicate than Fehling's test. It is prepared as follows:

Rochelle salt, 4 parts.
Solution of soda (10 per cent.), 100 parts.
Subnitrate of bismuth, 2 parts.

This is employed in the same manner as Fehling's test, and if sugar be present, a grayish deposit takes place as the liquid cools.

It being ascertained that sugar is present in a given case, it becomes important to know the amount excreted daily. For this purpose the urine passed during 24 hours should be measured, and the specific gravity obtained. A portion is then placed in a loosely corked bottle with a small amount of fresh yeast, and the bottle placed where the temperature is from 80° to 100° F. After 24 hours the urine is tested for sugar, and if none is found the specific gravity is again taken. Every degree of specific gravity lost indicates the decomposition of one grain of sugar for each ounce of the urine. Multiplying the decrease of the specific gravity by the number of ounces of urine passed in the 24 hours, will give the daily excretion of sugar in grains.

For example, if 40 ounces be passed and the specific gravity be 1.028, and after fermentation 1.020, then $40 \times 8 = 320$, represents the number of grains of sugar excreted.

ANATOMICAL APPEARANCES.

Post-mortem examination reveals no constant lesion as characteristic of diabetes. Most commonly there is extreme emaciation, often with the presence of bed sores. The skin frequently shows the remains of boils and carbuncles, sometimes of sloughs and gangrene.

Dickinson describes a peculiar lesion of the brain and medulla consisting of a cribriform condition of the white matter which gives to a section the appearance of being pierced with numerous holes of various sizes. These he has found chiefly in the optic-thalami, corpora striata, pons, and medulla. These holes, he believes, constitute the essential lesion of diabetes. But subsequent investigation by others has led to the general belief that these appearances are the result, not of disease, but of the methods employed in preparing and mounting the sections. Nevertheless, other observers have found in some cases small spaces filled with serous fluid around the arterioles in the gray matter in the floor of the fourth ventricle, and in the olivary bodies. Tumors and infarcts in the latter situation are not very rare. Occasionally colloid cells are found in the corpora striata and optic thalami.

Dickinson considers dilatation of the central canal of the spinal cord as one of the lesions, but it is so often absent in well-marked cases of diabetes, besides being occasionally found when diabetes is not present, that his view is generally not accepted.

In a large proportion (about one-third) of cases, the lungs are tuberculous, and the cavities are often remarkable for their size. It was at one time supposed that there was a special form of phthisis associated with diabetes, but more recent researches go to prove that it is not essentially different from that usually observed.

The tubercle bacillus was found, however, in only a portion of the cases examined by Riegel (quoted by Tyson), and there seems to be ground for believing that the diseased processes in the lung are not always the same.

Occasionally gangrene of the lung has been observed.

The liver is usually more or less enlarged, as might be expected from the congestion which is so generally present during life. This enlargement is partly due to an increase of liver cells, and so far constitutes a true hypertrophy. But there is also proliferation of connective tissue, which may be followed by contraction, with diminution of the size of the organ, the process being similiar to that observed in cirrhosis.

Minute examination shows evidence of pro-

longed hyperæmia. The capillaries are dilated and distended with blood. The acini are enlarged. The liver-cells are increased in size, their angles rounded off, and the margins indistinct. The nuclei are sharply defined. A wine color is developed by the application of tincture of iodine, which, according to Klebs, is due to a *post-mortem* change in the glycogen.

The kidneys in cases of short duration are not involved; but the functional activity implied in long continued polyuria, eventually leads to hyperæmia with corresponding changes in the renal structure. There is a proliferation of the epithelium which increases the size of the whole organ. The epithelium is prone to become detached, and a condition resembling desquamative nephritis may be found. In such cases albuminuria has been present during life.

But little interstitial change is observed, the parenchyma, rather than the stroma, being affected.

A catarrhal condition of the pelves of the kidneys, and of the ureters, may be present, due to the irritation caused by the sugar in the urine.

Quite recently, Fichtner has called attention to a degeneration or infiltration of the epithelium of Henle's tubes as one of the most constant of the kidney lesions in diabetes. In two cases of diabetic coma he found, in addition to this, very marked fatty degeneration of the cortical epithelium, the fat globules and particles being arranged along the

periphery of the cells just beneath the basement membrane; and only those tubes were affected which contained cloudy epithelium.

In seeking an explanation of this lesion, Fichtner remarks that both these patients died comatose, and had the peculiar odor of the breath indicating acetone and diacetic acid in the blood, and he is inclined to refer this special form of fatty degeneration to these or allied bodies (*Lancet*, 1889).

Atrophy of the testes is sometimes noted.

In a considerable proportion of autopsies of persons dying from diabetes (Senator thinks in one-half) the pancreas is found diseased. The lesion may be cancerous, or it may be a fatty degeneration of the gland-cells, or a hyperplasia of the connective tissue. Cystic dilatation of the ducts, or concretions may be present. Lancereaux has laid much stress upon this implication of the pancreas, which he considers to be the cause of a distinct form of diabetes characterized by suddenness of onset and rapidity of progress, and attended by the usual signs of deficient action of the pancreas.

Referring to this Tyson says: "Supposing the pancreatic disease to be primary, it is evident that it must operate through the cœliac plexus, which with its ganglion, is gradually encroached upon. On the other hand it is also possible that the disease of the cœliac plexus may be primary, and the co-existing pancreatic disease and diabetes mellitus both depend-

ent upon it. This can only be settles by more careful study of the cœliac plexus after death from diabetes, but up to the present time facts would seem to support the view of primary pancreatic disease." This latter conclusion would certainly accord better with the multiform character of the pancreatic lesions.

In well marked cases of diabetes nearly all the tissues of the body contain sugar. It is found in the blood, in the saliva, in the humors of the eye, and in effusions into serous cavities. In some instances the blood is found to contain free fat, and in sufficient quantity to render the serum opalescent. This opacity of the serum may at times be recognized with the ophthalmoscope in the vessels of the fundus oculi.

Pathology of Diabetic Coma.—More recent investigations, particularly by Naunyn, make it extremely probable that the real toxic agents in diabetic coma are certain fatty acids derived from the hydro-carbons, and of which oxy-butyric acid may be taken as the type. These acids have been found by Minkowski and by Stadelmann in the urine of patients dying of this affection. The quantity may amount to as much as three ounces per diem. These acids appear to act by withdrawing first ammonia, and then the fixed alkalies, from the system. When a similar effect is produced by administering hydrochloric acid to rabbits, death takes place, preceded by dyspnœa which is identical in its phenomena with the dyspnœa of diabetic coma

Minkowski, examined the blood of a patient before and during the coma, with reference to the percentage of carbon dioxide contained in it. The first examination yielded 17, and the second 3.34 per cent. In a comatose patient, not diabetic, the coma being due to meningitis, he found the carbon dioxide in the blood to amount to 28 per cent. (Lancet, Feb. 9, 1889.)

This diminution in the carbon dioxide corresponds with a lessened consumption of oxygen, and together with the low temperature indicates the extent to which the energy of tissue change is impaired.

CHAPTER III.

CAUSES, DIAGNOSIS AND PROGRESS.

Causes.—Diabetes is distinctly one of those diseases which may be transmitted by heredity. It is not uncommon to find in a given case, that the father, or one or more other blood relations, have suffered from the disease.* Doubtless in this affection as in phthisis, it is rather the predisposition to the disease than the disease itself which is hereditary. This predisposition, in the absence of an exciting cause, may remain dormant, but the occurrence of any condition capable of producing the necessary nervous disturbance, at once awakens it into activity. The practical lesson from this is, that where a father, for example, has suffered from diabetes as the result of prolonged nervous strain, his son should not be assigned to a walk in life which will necessarily subject him to a like exciting cause.

The disease occurs nearly three times as frequently in men as in women, probably because the former are more exposed to the exciting causes, to be mentioned hereafter.

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* The tables given by Cantani show that of 1108 diabetics 296 were nearly related to each other. Thus it happened 12 times that the mother was affected with the disease; 28 times the father; 179 times a brother or sister; 30 times an uncle or aunt, etc. (Deutsche Med. Woch., March 28 1889.)

Cantani, of Naples, from a comparison of 1,108 cases of diabetes, found that 915 of the subjects were males, and 193 females. The deaths in England and Wales for ten years, 1861–70, as quoted by Dickinson, show nearly twice as many males as females (4,271 M., 2,223 F.).

Cantani states that the greatest number of cases occur between the ages of 40 and 65, and this statement agrees essentially with the statistics given by other writers. It may occur during the first year of life, or it may develop in extreme old age.

Nationality seems to have little or no influence upon the frequency of its occurrence.

Syphilis is recognized as one of the causes of this affection, and some writers assign great importance to it as a causal factor. Syphilitic lesions involving the base of the brain, like other lesions in this situation, readily excite diabetes.

A special relation seems to exist between diabetes and excessive production of adipose tissue. Stout persons are more liable to diabetes than those of slender build, and in many cases the symptoms of the disease are preceded by a sudden increase of bulk. It is well known that very fat persons are generally small eaters, the deposition of fat in the connective tissue depending, not upon the consumption of an excessive amount of fat-producing, food, but upon a special direction given to the processes of assimilation and nutrition. Upon exactly the same

diet one person will produce fat, another muscle, and a third, uric acid.

Now, the fat-producing and the sugar-producing tendencies, are closely allied to each other, and seem sometimes to be interchangeable. Thus, in a family in which the diabetic tendency is strongly marked, certain members will be abnormally stout during a portion of their lives, and perhaps develop diabetes later, the tendency to obesity diminishing as the sugar formation increases, not simply because of the drain upon the system, but because the morbid impulse has changed its direction.

A similar predisposition to lithæmia is believed by some to co-exist with the tendency to glycohæmia. Arterio-capillary fibrosis, and contracted kidney, are often associated with diabetes, and perhaps occupy a relation to the disease similar to that held by poly-uria. Those who believe that lithæmia depends upon faulty assimilation of the carbo-hydrates will readily credit the theory of a pathological tripod of this kind; and the clinical fact that each of these three conditions is controlled by withholding the same class of articles from the diet, viz., the carbo-hydrates, lends probability to this view.

Among the exciting causes, mental impressions seem to be among the most powerful. These may be slight in degree, but of long continuance, or they may be intense, and of only momentary duration.

Long continued, habitual, severe mental effort,

such as is often the price of conspicuous financial success, very frequent has, as a consequence, the development of diabetes. It would be a great surprise to the public to know how many bank and railroad presidents, and large Wall Street operators, are victims of this affection, the existence of which they sedulously conceal. On the other hand, sudden, intense emotion, or mental shock, may be followed immediately by permanent glycosuria. Thus, the survivor of a duel may have this as a perpetual reminder of his folly. The writer has, at this moment under his care, a gentleman whose diabetes dates from a runaway accident, in which, for some minutes, it seemed certain that his carriage must be dashed in pieces.

Injuries to the head are often followed by diabetes. The effect may be observed within a few days, or not until weeks or months afterward. It occurs probably only in those cases in which there is a lesion in the vicinity of the diabetic centre. Such a lesion may be produced directly by the blow, or by *contre-coup*. It is to be feared, especially in those cases in which, after a blow upon the head, there is marked slowness of the pulse. This slowness indicates in most cases concussion, with probably minute hæmorrhages at the base of the brain. The proximity to the fourth ventricle exposes the floor of the latter to the consecutive irritation, and diabetes may be the result, especially if there be an hereditary tendency.

Tumors at the base of the brain are apt to

occasion glycosuria, and the diagnosis of obscure brain lesions may sometimes be facilitated by an examination of the urine for sugar.

Bruises and injuries accompanied by mechanical shock, as well as injury to large nerves, are sometimes the apparent cause of consecutive diabetes.

But in all these cases in which a direct involvement of the diabetic centre cannot be predicated, there remains the mental influence which a grave accident, with the fright and excitement accompanying, it must produce, and it is quite possible that this may have more to do with the result than the physical injury sustained.

Malaria is apparently the starting point in some cases of diabetes. The causal connection in this instance is not difficult to trace. The congestion of the liver which accompanies malaria may very readily interfere with the regulation of the glycogenic function; and clinically it is found that hepatic congestion from what ever cause, is accompanied in a large proportion of cases by glycosuria. For example, in a case observed by the writer at the Presbyterian Hospital, in which the menstrual epoch was regularly marked by great enlargement of the liver, the urine contained sugar on each occasion when the congestion was at its height.

The predisposition existing, it would only require a long continuance of the disturbance of the liver to convert temporary glycosuria into permanent diabetes, and this might be effected by chronic malaria.

The habitual long-continued use of large quantities of sugar or starch, beyond what can be appropriated by the system, seems sometimes to lay the foundation of permanent diabetes. At other times the glycosuria so induced is temporary, and ceases when the habit in question is relinquished.

This suggests the question whether the presence of sugar in the blood may not be a sufficient source of irritation to the medulla to cause diabetes in what would otherwise be merely a case of temporary dietetic glycosuria. This point has already been adverted to in another connection.

Diabetes seems to occur with more than average frequency in those who drink habitually to intoxication, just as temporary glycosuria is apt to follow a debauch. There may be an analogy between the effect of alcohol and that of ether or chloroform, anæsthesia from these agents being generally followed by transient glycosuria. How far the mental and nervous excitement incidental to the action of all these agents may be a factor in the production of the glycosuria, is a question yet to be determined. But if it be true as is alleged, that in the case of alcohol enough must be taken to induce intoxication, it would seem a fair inference that the effect is produced through the nervous system rather than through the irritation of the liver by the alcohol in the portal blood.

Of the other supposed causes, exposure to cold

and wet is mentioned by most writers. Inasmuch as such exposure falls more or less to every one, it would be difficult to establish a causal relation in a given case unless under very peculiar circumstances. Still as irritation or congestion in the neighborhood of the diabetic area is followed promptly by glycosuria, it is quite possible that cold and wet might so affect that region as to bring about a like result.

It has recently been brought to the writer's notice that locomotive engineers are exceptionally liable to diabetes. A member of the craft, a patient of the writer, and himself a diabetic, states that he can count no less than six subjects of the disease among his acquaintances in the fraternity. A reference to the mortuary statistics of a life insurance society for locomotive engineers, seems to confirm the belief that diabetes is especially liable to be induced by this occupation. A membership of 7,000 gave 367 deaths from all causes in five years. Of these eight were from diabetes, or a little more than two per cent. Probably all of these occurred in persons above 25 years of age. Now, in New York City, the percentage of deaths from diabetes, to the mortality from all causes is 0.13. Granting the most liberal allownce for deaths from all causes below the age of 25, we should still have not more than 0.30 as the ratio of deaths from diabetes during the period of life which yields a ratio of 2.18 in the case of locomotive engineers. It would seem, then, that this

occupation increases about seven-fold the liability to diabetes.

Mr. T. S. Ingraham, the Secretary of the company referred to, in a letter to the writer, gives it as his opinion that this special liability is the result of three factors: The constant jarring of the locomotives; the alternate heating and cooling of the system as the train is alternately at rest and in motion; and the unremitting mental strain which the responsibility of the duty necessarily involves.

According to von Moring, an artificial diabetes may be produced in dogs by administering phloridsin.

Diagnosis.—In well marked cases of diabetes the diagnosis is at once apparent. The large quantity of urine voided, with its high specific gravity, leaves little doubt as to the nature of the affection even without the application of the sugar test. But in the early stages, and in mild cases in which the sugar production is in excess of the volume of urine excreted, there is room for error in the absence of chemical examination. With such examination, properly conducted, the diagnosis is easily and certainly made.

Increase of volume of the urine may depend upon diabetes insipidus, or upon structural disease of the kidneys, such as cirrhosis, amyloid degeneration, hydromphrois, or pyelitis. In the first case the low specific gravity and the absence of sugar will decide

the nature of the affection; in the second case there will be in addition to these signs, those peculiar to the renal disease, such as albumen, casts, pus, etc., in the urine.

But it sometimes happens that without symptoms sufficiently marked to attract the attention of the patient, a diabetic condition is present which shows itself in the occurrence of boils, carbuncles, eczema of the genitals, or cataract. The presence of any of these affections should therefore lead to an examination of the urine for sugar.

But the presence of a small quantity of sugar in the urine does not of itself imply the existence of diabetes. Seegen and others have shown that it is common in gouty dyspepsia, and it may occur as a temporary condition after the ingestion of an excess of starchy or saccharin food. It is observed after chloroform or ether narcosis, and is a frequent accompaniment of acute hepatic congestion. Its occurrence in connection with injuries, and especially those involving the head, has been already considered. Indeed, without the other signs of diabetes, the presence of sugar in the urine must be persistent to warrant a positive diagnosis of that affection.

Prognosis.—The sketch given of the clinical history of diabetes applies to well marked and confirmed cases. Such cases are more apt to occur in young persons, and are generally fatal in a period varying from a few weeks to two or three years·

With regard to prognosis, cases may be divided into those in which the sugar production is controlled by diet and those in which it is not. In the first the effect of the disease is limited to the conversion of the carbo-hydrates into sugar, in the second it extends to the conversion of the proteids also. It will readily be seen that the latter is much the graver condition. Of 100 cases collected by Griesinger, 39 died in the course of the second year. But even of severe cases a small proportion recover absolutely, and a larger proportion improve to such a degree that the disease thereafter tends but little toward the abridgement of life.

This latter is the condition of a large share of the milder cases, in which the excretion of sugar is at no time very great, is often intermittent, and is to a great extent controllable by diet. Such cases are seen mostly in elderly people, and we are warranted in assuring patients belonging to this class that in all probability life will not be shortened by the disease. There is, however, this reservation to be observed, that in diabetes all acute intercurrent diseases assume additional gravity.

Diabetic coma has been considered as necessarily fatal, nevertheless instances of recovery from it have been recorded. Tyson mentions a case of his own, and also refers to one observed by Hardy. But such instances are so very rare as to afford but little ground for encouragement in any given case.

CHAPTER IV.

PREVENTION AND TREATMENT.

Prevention.—Prophylactic measures are important in families in which the hereditary tendency is marked. The selection of the occupations of the sons should have reference to the avoidance of prolonged and excessive mental strain, or intense business anxiety. An occupation requiring active outdoor exercise is to be preferred. The necessity for cultivating equanimity of temper should be enforced. Habits of temperance are very important, and late hours and revelling followed perhaps by exposure to cold and wet, should be interdicted.

A taste for nitrogenous in preference to amylaceous and saccharine food, should be encouraged.

Should there be the slightest trace of syphilis in the individual or of the family, a strict watch should be kept for the first manifestation of symptoms, and appropriate treatment applied if they appear.

Accidents involving concussion of the brain should receive special attention, and if such an accident should be followed for a considerable time by notable slowness of the pulse, suggesting minute basilar hæmorrhages, all mental excitement as well as exposure to excessive heat of the sun, should be avoided for at least a year after the injury.

Treatment.—The treatment of diabetes is hygienic, dietetic and medicinal.

The first embraces some of the measures already indicated under the head of phrophylaxis. In addition to these, a residence at or near the sea-level, is more favorable than at a greater altitude, as the denser atmosphere favors the oxidation of the sugar. (Demarquay.)

While business cares should be laid aside so far as possible, the mind should not be left unoccupied, and least of all should it be directed toward a minute scrutiny of the progress of the disease. For this reason, charging the patient with the duty of measuring the urine, taking the specific gravity, etc., and keeping a record of the changes that occur, is a practice to be deprecated. Under these circumstances everything which will bear an unfavorable interpretation is the source of renewed anxiety and increased mental depression, which exert a harmful influence on the progress of the disease.

On the other hand the cheerful side of the case should be presented as far as possible. If the patient is past middle life, he should have the benefit of knowing that the prognosis at his age is vastly better than when the disease occurs at an earlier period.

The heat-production being less than normal, it is necessary to meet this by warm clothing.

The frequent passing of water is apt to result in carelessness as to perfect cleanliness, the last drops of urine being allowed to wet the clothing and the adjacent skin. Much irritation and even excoriation

may result. Washing after each micturation is advised, but aside from the difficulty and annoyance which this entails, it is apt to excite and keep up a troublesome eczema. The better way is to use extreme care to void all the urine, and then to remove any drops that may adhere with a soft handkerchief carried for that purpose. Protecting the surface with vaseline or cold cream is of great service.

Dietetic Treatment.—If it were a question merely of the loss of nutritive material which the excretion of the sugar involves, the dietetic management would require nothing more than that sufficient carbohydrates should be taken to provide for the waste in addition to supplying the wants of the system. This has, in fact, been proposed as a method of treatment. But the excretion of sugar is only a measure of the amount of sugar circulating in the blood; and the presence of this foreign substance in every tissue and organ of the body, produces such derangement of function, and ultimately in some organs such change of structure, as must eventually compromise the life of the patient.

It is therefore of the first importance to check the formation of sugar. This was recognized as early as 1787, when Rollo began the treatment of diabetes by excluding vegetable substances from the diet. It was not, however, untll 1823 that it was shown by Tiedemann and Gmelin that the carbohydrates were the principal sources of the sugar, and

that vegetables not containing these in any considerable quantity might be allowed.

Our object then is to furnish a diet for the patient which shall be sufficient for full nutrition, and yet afford the minimum of starchy and saccharine material. A further requisite is that the diet shall be reasonably palatable, otherwise the repugnance of the patient will soon reach a degree that will break over all restriction. Indeed, it is remarkable to what an extent the appetite for forbidden articles of food will dominate even the most intelligent persons. It is often the case that a full realization of the danger of indulgence does not afford a sufficient motive for self-restraint, and the watchfulness of friends and attendants becomes a necessary supplement. To circumvent this, deceit and falsehood may be resorted to; and a complete counterpart is afforded to the moral condition so familiar in morphine habitués.

Animal food and such substances of vegetable origin as contain the smallest possible proportion of starch and sugar must furnish the diet. All forms of meat, except liver, may be allowed; but sauces sweetened with sugar or thickened with flour must not be served with them. Fish of all kinds, both fresh and salted, or dried, are to be used under like restrictions as to sauces. Eggs are a valuable resource, and in various combinations will serve to make other less palatable articles fairly acceptable.

Among vegetables, such as are known generically as green vegetables, are so far free from starch and sugar that their use may be allowed. These include celery, cabbage, Brussels sprouts, cauliflower, string-beans, asparagus, lettuce, dandelion, spinach, mush-rooms, radishes, cucumbers, endives, young onions, water-cresses, turnip tops, beet-tops, etc.

Acid fruits, such as tart apples, lemons, cran-berries, strawberries, gooseberries, plums and cherries, are permissible. They may be stewed with saccharin instead of sugar, or with sodium bicarbonate which renders them less acid to the taste.

But the most harmful of the articles of food, and at the same time the most difficult to do without, is bread. No one who has not personally experienced the deprivation of it can realize the force of the adage that "bread is the staff of life." No matter how varied the diet may be in other respects, the ab-sence of bread in some of its forms is soon found to be an almost intolerable privation. Hence some sub-stitute which shall meet in a measure the longing for bread has been eagerly sought. Naturally, attention was early directed to the removal of the starch from flour. This of course can readily be accomplished, but the gluten remaining is not capable of being made into anything resembling bread, or which will answer in the slightest degree as a substitute for it. To make it eatable, therefore, it is necessary to retain a portion of the starch; and in all the so-called gluten

or diabetic flours a proportion of starch will be found ranging from 66 to 72 per cent. (ordinary wheaten flour contains about 90 per cent.). The use of such flour, therefore, simply reduces the amount of starch consumed, and thus far is of value, but it is misleading in that the article is not what it purports to be.

A tolerably fair substitute for flour is made of wheaten bran. The bran is not wholly innutritious as it contains about 15 per cent. of nitrogenous material. Some of the starch will adhere to the scales of the bran, but this can be removed by washing. Bran as it comes from the ordinary flouring mills contains a large amount of grit, consisting mostly of silex. This comes from the nibs at the ends of the kernels and from the thin, almost glassy, external coating of the grain. It may be removed by passing the wheat through a machine contrived for that purpose, and as it is destitute of nutriment and imparts unpleasant qualities to the flour made from the bran, this preliminary treatment of the wheat adds materially to the value of the product. When thoroughly pulverized, bran made from wheat thus prepared will yield a flour from which a reasonably palatable, if not very nutritious, bread can be made. This bran flour may be added to gluten flour to give the lightness necessary in bread-making. The addition of eggs thoroughly beaten contributes to the same result.

By a special process in milling, it is possible to separate the embryo from the other portions of the wheat

kernel, and to prepare a flour from it alone. This flour is supposed to possess special nutritive properties. Recently, Henri Douliot, botanical curator in the Museum of Natural History in Paris (An. Univer. Med. Sciences, 1889), has investigated anew the composition of the embryo, and finds that it contains about 42.75 per cent. of albuminoid matter. Nearly twelve per cent. of moisture is present, and to preserve from fermentation this must be expelled by long exposure to a temperature of 100° Fah.

The embryo is free from starch and sugar. The proportion of albumen is said to be double that contained in the blood and in meat.

The flour produced from the desiccated embryos he calls *fromentine.* Most palatable buiscuits are made from fromentine, and white of egg, and at the suggestion of Dujardin-Beaumetz, saccharine has been added as a sweetening material.

Fromentine may prove to be a valuable resource for those whose means are equal to so costly an article of diet, but for general use the expense attending its production will be a serious objection.

A very palatable flour is made from almonds from which the sugar has been removed in the process of blanching. Bread, or rather cakes, made from this are generally well relished for a time, but are too rich to enter largely into the diet for any considerable period. They disagree with some patients even from the first.

In practice it will generally be found that all of these substitutes for bread fail to satisfy for any length of time the desire for an article of food which habit has made necessary to our comfort. Nor is it a matter of habit only; there seems to be a want which starch alone can satisfy, such a want as the lower animals exhibit for salt, and which amounts to a constant solicitation which will not be denied.

Fortunately, it is only in severe cases that rigid abstinence from the carbo-hydrates becomes necessary. For milder cases it will suffice to use the flour already referred to, from which only a portion of the starch has been removed. In still milder cases, rye bread may be employed instead of wheaten bread, a substitution to which few persons seriously object, but which effects a considerable reduction in the proportion of starch ingested. Stale bread, in which the process of fermentation has destroyed a portion of the starch and glucose, is less objectionable than fresh bread. Beans and peas, which contain less starch and more nitrogenous matter than the cereals, may be allowed in cases in which a strict diet is not necessary or desirable.

It is often desirable that the physician should be able to determine for himself the percentage of sugar-producing elements in a given article of diet. This may be done approximately by the process suggested by Charles A. Doremus, as given in the Annual of Universal Medical Sciences, 1880: "Five grammes (77

grains) of bread, or other article of food, a slice cut to give the average of crust and crumb, are digested in a closed flask—a patent rubber-stopper beer or soda bottle answers the purpose admirably—with 100 c. c. (3 ounces and 3 drachms) of water, and 10 c. c. (2 drachms and 45 minims) of pure, strong hydrochloric acid. The flask is kept at 100° C (212 F.) for at least three hours, say, in a saucepan of boiling water; neutralize the liquid after cooling it, with sodium-bicarbonate, and dilute to 500 c. c. (1 pint). To test the amount of sugar, use Fehling's standard solution; 10 c. c. (2¾ drachms) of this, when completely decolorized, indicates the presence of 0.5 grammes ($\frac{7.7}{100}$ grain) of sugar, and therefore of .045 gramme of starch. If the bread contains 10 per cent. of starch, then there will be 0.5 gramme ($\frac{7.7}{100}$ grain) in the 500 c. c. (1 pint), and 10 c. c. (2¾ drachms) when filtered should decolorize 2.2 c. c. (36 minims) of Fehling's solution, which should be used in the usual manner—complete decoloration indicating 10 per cent. of starch, or over. Several tubes containing 2, 4, and 6 c. c. of the Fehling's solution, may be heated simultaneously, and thus an approximate knowledge of the quantity of starch be easily arrived at."

The question of permitting the use of milk, is one which has given rise to much discussion. It seems conclusively proven that sugar of milk is much more readily disposed of by the liver than is glucose. In

the early stage of diabetes, at least, it can be given in considerable amounts without increasing the excretion of sugar by the kidneys. Indeed, Dr. Tyson of Philadelphia recommends that a diet exclusively of skimmed milk be the main element of the treatment of all recent cases, and claims that by it the sugar-production can be arrested in most instances, He employes skimmed milk in preference to ordinary milk simply because it is, as a rule, more easily digested, many persons being unable to assimilate the fat of cream. Casein appears to be perfectly digested in most cases, but if it is not, the milk can readily be peptonized, wholly or partially, as may be found most desirable. The combination of milk with Vichy water overcomes in many cases the inability of some patients to take plain milk.

Most patients find that the continued deprivation of sugar for sweetening purposes adds a considerable element of unpalatableness to the diabetic diet. The diet, at the best, becomes after a time so distasteful that this point is of importance. To meet it *glycerin* has been employed; and it is illustrative of the difficulties which beset the whole question of dietetic management that observers of large experience differ in regard to the effect off this article upon the sugar-production. By some it is contended that the use of glycerin is promptly followed by an increase of the sugar, while others claim that it is not only innocuous, but that it is positively useful in checking the

conversion of the glycogen in the liver into glucose. Clinical evidence is still conflicting in regard to these points, and it is probable that further observation will show that the effect of glycerin varies in accordance with certain conditions not as yet established. In the meantime each case will have to be a rule unto itself, and glycerin given or withheld in accordance with its observed effect.

But the practical importance of this is greatly lessened by the introduction of *saccharin*. This agent supplies the place of sugar much more perfectly than glycerin. From a considerable experience in its use, the writer is inclined to regard it as perfectly harmless in the quantity required for sweetening purposes. He has given it to patients for long periods, not only in diabetes, but also as a means for acidifying the urine in cystitis, and has used it himself in tea and coffee for weeks at a time without the slightest inconvenience. On the contrary, he has found that it diminishes in a remarkable manner the tendency to acid eructations after meals. In no instance has it caused irritation of the stomach or interfered with digestion in the slightest degree.

When used for tea or coffee the saccharin should be added before the milk, as otherwise its strongly acid property will cause coagulation of the casein. A single grain is sufficient to sweeten a cup of coffee. For convenience it may be made into a tablet with an equal weight of sodium bicarbonate, which insures

solution even when the fluid is cold, and does not sensibly affect the taste.

Saccharin may also be employed for sweetening stewed fruit, making custards, etc.

But saccharin is not only useful as a substitute for sugar, it is claimed that its action as an anti-ferment is of decided value in restraining the formation of sugar. As it is not decomposed by the action of the digestive fluids, but circulates in the blood unchanged, there is nothing improbable in the assumption that it may modify the process of sugar formation in the liver as it modifies the fermentative processes in the stomach.

In the matter of diet, it must be borne in mind, that while the exclusion of starch and sugar is the measure which gives us the most control over the disease, yet it is by no means paramount to every other consideration. There are conditions in which its rigid observance is inadmissible, and in no case should its efficacy in lessening the production of sugar lead us to a blind adherence to it. The object of treatment is to promote the general health and well-being of the patient, and the reduction of the out-put of sugar is to be regarded only as a means to that end, and never as an end in itself. It is a much more serious thing to the patient to have his digestion thoroughly disordered; his nutrition and strength impaired; and his morale broken down as the result of too strict a diet, than to pass an ounce or two more of sugar per

diem. As a rule, improvement in the general health coincides with reduction in the amount of sugar, but this is not always so; and if, under a rigid diet, there is loss of appetite and general falling away of flesh and strength, with mental depression and nervous disturbance, the diet should be made more liberal, no matter how gratifying the condition of the urine may appear to be under the stricter regimen.

Treatment by Drugs.—While the dietetic treatment holds the first place there is still room for the employment of drugs. As might be expected from the prominence of the neurotic element in the natural history of diabetes, the class of drugs found most beneficial are the nervous sedatives. *Opium* was early resorted to, and in its various forms still holds the foremost rank. Its exhibition nearly always results in some degree of improvement, although the benefit may not be lasting. It directly antagonizes that state of nervous susceptibility which supplies at once the predisposing and exciting causes in such a large proportion of cases. If the diabetic centre is unduly sensitive, a sedative lessens the sensitiveness, and with it the morbid predisposition. If, on the other hand, the general nervous system is subjected to strain or shock, the drug lessens the force of the disturbing agent, and in so far prevents its acting as an exciting cause.

Nearly the whole range of sedatives, including antispasmodics, have been employed with more or

less success. *Morphine* is probably the most efficacious of the list. Unquestionably this remedy will cause, as a rule, a very marked decrease both in the volume of the urine and in the quantity of sugar excreted. In connection with a restricted diet it will often bring about for a time an almost total disappearance of sugar from the urine. The dose should be small at first and gradually increased. Large amounts may be required, the equivalent of 60 to 90 grains of opium has been given in the 24 hours, the disease seeming to confer a remarkable tolerance of the medicine.

These large doses, however, produce constipation; and the danger of forming the opium-habit is great. These objections are less valid when *codeia* is employed, and this drug has grown much in favor since it was originally suggested by Pavy as a substitute for morphine. In the hands of the writer it has done good service. In one case in which about 1,700 grains of sugar were excreted per diem, a moderate restriction of the diet together with five grains of codeia daily caused the disappearance of every trace of sugar at the end of a month. The codeia was then omitted, and for the three months during which the patient remained under observation, only faint traces of sugar could be obtained.

From observations by Dr. Mitchell Bruce it seems evident that opium acts upon the liver directly, as well as through the nervous system. He found

that the effect of morphine was much greater when given by the mouth than when introduced into the general circulation by hypodermic injection. In the former case the whole amount of the drug would be taken into the portal blood, and would circulate immediately through the liver; while in the second case it would be diffused through the whole mass of the blood, and the liver would receive only its proportionate amount, and that through the hepatic artery where the drug would have only an indirect effect upon the hepatic function.

In the opinion of the writer the use of opium or its derivatives should be restricted to two conditions —first, in the early stages of the disease, when there would be a prospect that if the formation of sugar could be arrested for a time the tendency to its production might disappear, and second, in the advanced stage, when there is evidence that the system is greatly over-taxed by the formation of sugar, and it becomes justifiable to incur a less danger in order to avert a greater. But especially in the latter case, it is always to be borne in mind that we are concerned with a choice of evils, and we should be careful lest we overestimate those arising from the disease and underestimate those connected with the remedy.

Many other remedies having more or less affinity with opium in effect have been useful to some extent, among these may be mentioned *belladonna*, *valerian*, the *bromides*. Among these may also be classified the

recently introduced remedies from the phenol and the aromatic series, antipyrin, acetanilid, phenacetin, exalgin, etc., whose effect seems to be exerted principally through the nervous system.

In regard to *belladonna*, Villemin believes that in combination with opium it exerts a special influence, and that greater remedial effect is obtained than from either drug alone. His experiments were very carefully conducted, and his conclusions seem to be warranted by the results.

Antipyrin first suggested as a remedy in diabetes by Dr. Gormer in 1887, has been studied in this relation by Drs. Huchard, Robin, Germain Sée, and Panas. A resumé of the results obtained by these observers is contained in the Therapeutic Gazette for June, 1889. The subject is so important that the article is quoted almost entire.

Dr. Huchard reported in Nov. 1888 a case in which 753 grammes (23½ oz.) of sugar were excreted daily, which quantity was reduced in a few days by the use of antipyrin to 271 grammes, the urea being reduced at the same time from 96 to 26 grammes (3 ozs. to 6½ drs.) He was induced to employ this drug from its marked action in other neuroses of medullary origin.

Recently an entire session of the *Academie de Medecine* (Paris) was devoted to this subject.

M. Panas reported that he had experimented with two cases of diabetes, and that they appeared

to show incontestably the power of antipyrin to reduce the excretion of sugar. 3 grammes (45 grains) caused complete disappearance of sugar from the urine, while glycosuria reappeared as soon as the medicine was discontinued or the dose diminished. Accorping to Panas, the use of antipyrin will permit the enjoyment of moderate quantities of starchy food, and had succeeded in his hands even when in connection with absolute diet various other remedies had failed to reduce the quantity of sugar.

Germain Sée could report 18 similar observations, the antipyrin even suppressing entirely the excretion of sugar, and reducing the quantity of urine, although the use of starchy food was persisted in. If, however, the sugar amounted to more than 100 or 150 grammes to the litre of urine, the treatment was unsuccessful, as was the case also in phthisical patients.

Dujardin-Beaumetz stated that he had recognized more than a year before the value of antipyrin, and that all the substances belonging to the same series possessed anti-glycogenic properties.

Robin on the other hand is more guarded in his conclusions. He writes that since Oct. 1887 he has treated a large number of cases with antipyrin, and he concludes that while energetic in reducing glycosuria, it has never in his experience, cured a case of diabetes. Nevertheless with reduc-

tion of sugar and lessened thirst there has been improvement of the general condition of the patient.

He regards the proper daily dose as 45 grains, but if the urine contain albumen the dose should be reduced to 30 grains. Larger doses than 45 grains are apt to excite albuminuria. When this is observed the medicine should be withheld, though in cases in which albuminuria is present at the beginning of the treatment, 30 grains may be given with safety.

In beginning treatment Dr. Robin would give antipyrin for a week without restricting the diet. The amount of sugar being then greatly reduced an antidiabetic diet will at least keep it so, if it does not cause a further reduction. The antipyrin may then be stopped, to be resumed again for a short time whenever the patient finds the monotony of the diet insupportable. The use of the drug will thus permit relaxation of the diet from time to time, without danger of increasing the glycosuria.

If antipyrin does not at once produce reduction in the amount of sugar it is useless to continue it. If the appetite diminishes or there is feebleness, paleness, puffing of the eyelids or a sensation of tension in the face, these are symptoms that the drug is doing harm rather than good.

Dr. Worms thinks, on the other hand, that no more improvement will follow the use of antipyrin in diabetes than from a large number of other rem-

edies, or even any change of treatment. He claims that quinine has been found quite as effective. Arsenic, opium, valerian, and potassium-bromide, will succeed better, and be longer tolerated.

More recently, Dujardin-Beaumetz says: "Into a glass of Vichy water, sweetened with saccharin, and flavored with a little rum or kirsch, I dissolve one of the followiug powders, and order the whole to be taken at one dose: Antipyrin, 3 v.; divide in chart. No. xx. One powder three or four times a day. I have never seen any ill result from this treatment, however long continued." *

Dr. Carreau, of New York, reports three cases successfully treated with antipyrin, the sugar disappearing entirely from the urine in from six to sixteen days. The daily dose was from 40 to 90 grains.†

The writer has had no experience with antipyrin in the treatment of diabetes, but from the clinical evidence in its favor, and from analogy, he would expect benefit from its use. Possibly it acts in two ways—by its influence upon the nervous system, and as an anti-ferment. This latter action, as is shown in the use of remedies specially belonging to that class, is of great importance in the treatment of diabetes. As already observed, underlying the phenomena of the disease is a relaxation of the control normally exercised by the vital forces over chemical action. This

* N. Y. Medical Record, July 6, 1889.

† N. Y. Medical Record, July 13, 1889.

latter is restrained, in a measure, by antiseptics and antiferments. *Carbolic acid*, *salicylic acid*, *creasote*, *iodine*, *iodoform*, *thymol*, have been employed. Not only are such agents supposed to act upon the contents of the alimentary canal, and thus to influence primary digestion, but they are believed to enter into the circulation, and to modify the secondary chem ical processes which are characteristic of the disease.

Of their value in combating the indigestion which forms so troublesome a complication in advanced diabetes, there can be no doubt. But there is also much evidence to show that, while they do not change the fundamental condition upon which the disease depends, they are capable of restraining its manifestations, in many cases, to a considerable extent.

Iodoform, originally proposed by Moleschott in 1882, has been employed by a number of observers, with a generally favorable result, It appears to lessen thirst, and to cause a diminution of the sugar and urea, and a gain in weight. It is given in doses of half a grain to two grains, three times a day, or a single maximum dose may be given at bedtime, which causes less annoyance from eructations and less disturbance of the appetite.

Dr. Sansom, of the London Hospital, has great confidence in the value of the *snlpho-carbolate of sodium*. In a personal note to the writer under date of July 11, 1889, he gives the following case as an example: "Miss C. W., aged 67, Nov. 23, 1887, on

diabetic diet. Urine, sp. gr. 1044; sugar in large amount; considerable albumen. Ordered sod. sulphocarbol. gr. xx, t. i. d. Gradual diminution of sugar and of albumen. Dec. 14th, sp. gr. 1032. Jan. 13th, 1888, sp. gr. 1018, no sugar, trace of albumen. Saw her the other day; no sugar, no albumen; *quite well.*"

Ergot is given a high place as a remedy in diabetes, by several writers, and especially by Tyson. He considers that it stands next to codein. It is probably by its physiological action upon unstriped muscular fibre, and its consequent power to diminish the calibre of vessels, that its beneficial effect is produced. It is given in doses of half a drachm to a drachm, three times a day. If it produces nausea when taken into the stomach, it can be given in fluid form by the rectum. In view of its action upon the liver, this is preferable to its use by hypodermic injection.

Arsenic has been used with some degree of success in the treatment of diabetes. Its use was first suggested by Salkowski, who found that in poisoning with arsenic as well as with phosphorus, the glycogen in the liver was diminished.

It may be given in pill form in doses of $\frac{1}{20}$ to $\frac{1}{10}$ of a grain three times a day after meals. The quantity recommended by Leube, 1 grain daily, is certainly excessive.

The *bromide of arsenic*, as suggested by Clemens, gave a very satisfactory result in one case in the

hands of the writer. The patient had become so reduced as to be confined to his bed. All restriction in diet was removed, and Clemens' solution* administered. The sugar was reduced until a mere trace remained; and the patient gained strength and left the hospital at the end of three months feeling nearly well.

In another case under his observation, in which the amount of sugar was small, and the general health not affected, the arsenic produced little or no change. A combination of *arsenic* and *lithia* suggested by Rouget, and advocated by Martineau, has attracted a great deal of attention. Tyson describes the treatment as follows: "Add to a quart of water, in the upper globe of a Briette apparatus for making aërated water, 3 grains of lithium carbonate, and a tablespoonful of the following solution: distilled water, 1 pint; arsenite of sodium, 3 grains. This quantity should be drank during meals, mixed with wine, and the apparatus-full should last for at least three meals. Between meals, if the patient be thirsty, he should drink nothing but this water. The diet need be modified only so far as to limit the use of starches, fruit, and sugar. Martineau adopted this

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* The formula for Clemens' solution is as follows:

Arsenic	1 part.
Potas. carb	1 part.
Bromine	2 parts.
Water	96 parts.

Dose, 2 to 4 drops.

treatment in 1875. Since then, he has collected 70 cases, in 67 of which he made a 'rapid cure,' in 3 he failed. The 67 cases were of diabetes occurring in arthritic patients, the condition manifesting itself either in the arthritic form, or in the shape of biliary or urinary lithiasis, or as cutaneous eruptions. In the three cases in which he failed the arthritis was wanting."

Martineau considers the lithia the active agent, since it is found in nearly all mineral waters which have a reputation for the cure of diabetes.

The same ingredients in solid form are contained in the pill recommended by Vigier: ℞ Lithii carb., gr. 1½; sodii arsenat., gr. $\frac{1}{20}$; ext. gent., gr. ¾; for each pill. One to be taken morning and evening. Dujardin-Beaumetz says: "The most simple way of using Martineau's remedy is: Take before each meal, in a tumblerful of Vichy or Vals water, one of the following powders, adding to the mixture two drops of Fowler's solution of arsenic: Carbonate of lithia, ʒ iiss; divide in chart, No. xx." *

The alkalies which have been more or less employed on the authority of Mialhe, who claimed that that they had the power of destroying sugar in the blood, are now coming forward again as the means of neutralizing the fatty acids which Stadelmann, Naunyn and others claim to be the cause of diabetic coma. We shall refer to this again under a special

* Medical Record, July 6, 1889.

heading. Aside from this use, alkalies are valuable aids in correcting the tendency to lithiasis which seems to be present in so large a proportion of cases of diabetes.

Jambul seeds have recently been recommended by Saundby and others, and a number of cases have been reported in which the quantity of sugar has been greatly reduced by the use of this remedy. It is given in doses of 5 grains of the powder three or four times a day (*Am. Jour. Med. Sci.*, '88).

Potassium or Sodium iodide is useful in some cases, probably those chiefly which have a syphilitic basis. It should be given in large doses whenever symptoms of syphilis of the nervous system have preceded or accompanied the glycosuria. The sodium salt is to be preferred as less depressing.

Aside from the syphilitic dyscrasia, the apparent benefit derived from the iodide is doubtless due, as suggested by Dickinson, simply to the diminished appetite and general depression of function which it occasions, and with which a reduction in the sugar excretion naturally coincides.

Tonics, such as iron, quinine, phosphorus, cod-liver oil, and strychnia, are of great value in the general management of the disease. Dickinson considers strychnia the most serviceable of all, and among the various preparations of iron, gives the preference to the tincture of the chloride.

It is the opinion of the writer that, for the treat-

ment of diabetes, the natural chalybeate waters surpass in value any of the artificial preparations of iron. The iron is more readily assimilated in this form and the water serves to assuage the thirst.

Dr. J. H. Kellogg reports a case in the *Journal of the American Medical Association* for Aug. 25, 1888, in which enemata of oxygen gas, given after the method of Bergeon for sulphuretted hydrogen, induced very marked reduction of the amount of sugar excreted. Under nitrogenous diet the amount excreted daily at the beginning of treatment was 152 grammes. Two litres of oxygen were administered each day, and in three weeks the excretion of sugar had fallen to 3.1 grammes.

This method appears likely to be of service in the treatment of diabetes, as the blood in the veins of the colon being venous in character would readily take up oxygen and thus be in a measure arterialized before reaching the liver. Sub-oxidation being such an important item in the pathology of diabetes, it is easy to see that the presence of an unusual proportion of oxygen in the portal blood might be of essential service in preventing the excessive formation of sugar.

The retention of the oxygen in contact with the intestinal mucous membrane would insure the absorption of the entire quantity injected. The portal blood might thus be made to receive an amount of oxygen through the colon which would

bear a considerable proportion to the supply received by the same blood through the lungs.

In the same line is the method advocated by Le Blond, which consists in the use of aerated water charged with oxygen instead of carbonic acid. Here, the gas being absorbed from the stomach passes, as in the former case, directly into the portal blood. Le Blond reports three cases in which this treatment caused complete disappearance of sugar from the urine (*Annual of the Med. Sciences.*)

Treatment of Diabetic Coma.—In the advanced stages of diabetes, the practitioner should be constantly on the watch for symptoms of acid intoxication. These will probably appear first as gastric and intestinal derangement. More rarely the the nervous phenomena are first developed. The appearance of symptoms in either direction should be the signal for a change from the diabetic, to a mixed or even a farinaceous diet; as clinical experience has shown that a rigid exclusion of the carbohydrates has in many instances precipitated the toxic condition. This is explained by the results of recent investigations already referred to, which show that the poisonous acids are derived, not from the sugar, but from the albuminoids.

With the change of diet an effort should be made to saturate the system as rapidly as possible with an alkali. Sodium bicarbonate is probably the most suitable, and this should be given very freely both by

the stomach and by the rectum, the object being to neutralize the abnormal acids in the blood, and restore the alkali which they have abstracted. In cases of emergency, from two to three drachms of bicarbonate may be injected into the vein (Hesse).

Aside from the use of alkalies, the treatment must be symptomatic. Crisp has suggested the administration of oxogen by inhalation, in the belief that the formation of the toxic agents is due to suboxidation. Certainly no justification for this measure can be found in the dyspnœa usually present, as this is evidently not due to diminished access of air to the lungs, but rather to an inability of the blood to take up oxygen.

CHAPTER V.

DIABETES INSIPIDUS, Polyuria.

A condition somewhat allied to Diabetes, and having probably a certain community of origin with it, is that in which a greatly increased amount of urine is passed, which may not, and usually does not, contain any abnormal substance. In simple polyuria the urine is merely diluted with an abnormal quantity of water. Traces of sugar, of inosite, or of albumen, may occasionally be present, but they are unessential and not permanent.

It has been thought that the disease consisted essentially in an increased thirst, the polyuria being merely the escape through the kidneys of an undue quantity of fluid taken into the stomach. But the history, in many cases, shows that the polyuria precedes the polydypsia. Moreover, if the theory in question were correct, the other emunctories, and especially the skin, would participate in the effort to rid the system of the surplus water; whereas, in fact, their action is rather diminished than increased. The conclusion is, therefore, inevitable, that the disease consists in an abnormal activity of the kidneys. That this is induced by disordered nervous action, is evident from the absence of renal lesions, and from the numerous instances in which disease or injury affecting the brain and nervous system is accompa-

nied by polyuria. A somewhat analagous disturbance of the renal function through the medium of the nervous system, is observed in the increased volume of urine which characterizes hysterical paroxysms, migraine, etc.

Clinical History.—The most prominent clinical features are the frequent calls to urinate and the large amount of urine passed. Thirst is urgent in proportion to the drain of fluids by the kidneys. So long as this is satisfied without stint, the patient is fairly comfortable — indeed, suffers only from the annoyance of being the sluiceway through which gallons of water must pass daily.

There may be an excessive appetite, such as is sometimes seen in saccharine diabetes, but this is unusual. Generally the digestion remains fairly good, but constipation from dryness of the fæces is common. Usually, but not always, the skin is dry and harsh. Boils and carbuncles, common in the saccharine form, are not a feature of this affection; nor is opacity of the crystalline lens. There is no special tendency to phthisis or to renal disease, except that the intra-renal pressure may bring about sacculation of the kidney. Fecundity does not seem to be lessened, if we may judge from a case cited by Dickenson, in which a woman, while drinking four pails of water daily, became the mother of eleven children. Indeed, it is remarkable with how little disturbance to the general health a patient may go

on from early youth to advanced age. The disease, however, being very often secondary to some other affection, this latter may at any time become the leading factor, and perhaps bring about a fatal result. If not, in a considerable number of cases the wear and tear incident to the affection at last exhaust the powers of life, and the patient dies from this cause and not from the direct effect of the disease.

Pathology.—Irritation of a locality in the floor of the fourth ventrical somewhat above the area for saccharine diabetes, will cause an increased flow of urine without inducing the formation of sugar. This was pointed out by Bernard more than forty years ago. In a very considerable proportion of cases of polyuria, a source of irritation is found in this vicinity at the autopsy. But this is far from being an invariable rule, and the numerous exceptions suggest that there are other areas having the same peculiarity, or else that the evidences of irritation in the polyuric area sometimes elude our present methods of examination. Nevertheless, there is sufficient evidence derived from this source to show an unmistakable analogy between the origin of this affection and that of diabetes mellitus, the kidneys in the one case, and the liver in the other, being the seat of the disturbance of the function. But, as Bernard has shown that division of the sympathetic is followed by increased flow from the corresponding kidney, it may be that disease at some point in the course of this nerve is sometimes the cause of polyuria.

The *morbid anatomy* of diabetes insipidus is extremely meagre. Beyond lesions of the brain or nervous system, which may be regarded as causative, and which are in no wise characteristic, there is little to be found on post-mortem examination. The kidneys usually exhibit changes which indicate excessive functional activity rather than structural disease. They are apt to be injected and to some degree hypertrophied. In old cases, sacculation of the kidneys may be found as the result of long-continued intrarenal pressure. (Dickinson.)

The quantity of urine voided varies in different cases, from an amount but little above the normal to several gallons in the 24 hours. Marvellous instances are related in which the patients claim to have passed water by the pailful. Doubtless there is much exaggeration in these statements, but Dickinson mentions a case in which, under the observation of a scientific commission, a patient passed 14 quarts in 10 hours.

It is a singular fact that the quantity of the urine passed sometimes is greater than that of the fluids taken into the body, both as food and drink. A temporary excess of this kind might result from a withdrawal of fluids from the tissues of the body. But both Watson and Dickinson have demonstrated that there may be an actual increase in the weight of the body during an interval in which no food or drink has been taken. There are only two ways in which this can be accounted for: first, by the oxydation of hy-

drogen in the tissues, as supposed by Lavoisier, in which case the weight gained would represent the oxygen thus fixed; and, second, by the absorption of moisture from the atmosphere through the skin and lungs. As regards the latter, it implies that the flow from the kidneys may so drain the body of water as to render it actually hygroscopic.*

It has been suggested that an increase of the general arterial tension is the intermediate link between the basal irritation and the polyuria, such increase being well known to have as a sequence a larger flow of urine. This idea derives support from the near correspondence of the vaso-motor centre, as located by Owsjannikow, with the diabetic and polyuric centres. But physiological experiment shows that the irritation which produces polyuria does not increase aortic tension, and clinically we do not always find the signs of vascular tension especially prominent in polyuria.

The urine is naturally of low specific gravity in

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* Dickinson, in the case of a child weighing less than 28 lbs., found that between one urination and the next, no food or drink being taken in the interval, the gain in weight was as follows: In the first observation, in 3 hours, 15½ ozs.; in the second, in 5⅓ hours, 19¾ ozs.; in the third, in 3¼ hours, ¼ oz.; in the fourth, in 3½ hours, 3¾ ozs. Watson's observations had a similar result.

The differences occurring in different observations are probably to be explained by varying degrees of moisture in the atmosphere.

proportion as the quantity is great. In some instances it has been found to be less than 1.001; more generally it is from 1.002 to 1.004. Still the quantity of solids excreted by the kidneys is, as a rule, actually increased, however much it may be decreased in relation to the quantity of urine. This includes both the urea and the phosphates.

The urine is extremely pale, often resembling pure water, but sometimes having a slightly greenish tint. It is nearly free from odor, and the acid reaction, if present, is very feeble. Decomposition takes place on exposure to the air, and the urine becomes turbid.

Causes. The causes of diabetes insipidus are in part the same as those of the saccharine form. Of these heredity is well marked. Weil (quoted by Edes), in a family connection numbering 91 persons found 28 who had polyuria. Males are more subject to it than females in the proportion of three to one. It occurs more frequently in children and young people than in mature life. It is oftener met with in infancy than is its congener, diabetes mellitus. Persons of a nervous temperament, and those hysterically inclined, are peculiarly liable to it. It seems not to be influenced so much by mental causes as is the case with true diabetes, but it sometimes follows a severe nervous shock.

The chief exciting causes are those which operate upon the brain and nervous system. Among

these, injuries to the head, cerebellar tumors, hæmorrhage, especially at the base of the brain, meningitis, etc., are prominent. Kahler (quoted by Senator) in 22 cases associated with cerebral disease, found tumor in 10; atrophy of the right half of the medulla in 1, congestion of the floor of the fourth ventricle in 1, softening of the same area in apoplectic clot in 1.

Among other causes are noted, exposure to cold, taking large draughts of cold fluids, excessive muscular effort, severe tax upon muscular endurance in the way of privation and fatigue. It is occasionally the sequel of fevers of severe grade or long duration. It seems to be associated with spirit-drinking more frequently than can be accounted for by mere coincidence.

Diagnosis.—The diagnosis involves discrimination from diabetes mellitus on the one hand, and from the many forms of kidney disease attended by increased flow of urine upon the other.

From the first it is readily distinguished by the low specific gravity of the urine, and by the absence of sugar in any appreciable quantity. A mere trace of sugar may occur for a time, but it is not essential nor persistent. From structural disease of the kidney the diagnosis may for a time be somewhat difficult. Occasionally, in contracted kidney the quantity of urine voided may reach 100 ounces or more daily, and the specific gravity may be very low.

Albumen may not be present at all times, and many specimens of the urine may be examined before a cast is found. Now in simple polyuria an occasional trace of albumen is common, and now and then a cast is present. It may therefore not be easy to discriminate at first sight between a mild case of polyuria and a severe one of contracted kidney. The history of the case, the period of life (contracted kidney occurring generally after 40 years of age), the absence or minor degree of arterial tension and of hypertrophy of the left ventricle in diabetes insipidus, the absence of the eye-changes of chronic nephritis, these will seldom leave the differential diagnosis long in doubt.

Surgical affections of the prostate and bladder, and surgical kidney, though giving rise to increased secretion of urine, have their own distinctive features which can scarcely be overlooked.

Prognosis.—Diabetes insipidus is rarely cured, though it sometimes ceases spontaneously. It has been known to cease during pregnancy and not to recur after delivery. A severe pneumonia has in more than one instance had a like happy result.

Death when due directly to the disease occurs by exhaustion. This may take place in as short a period as four months, or only after many years. Those cases in which excessive appetite is developed show a more profound derangement of the vital processes and are more fatal. Usually life is terminated by some inter-current affection.

Treatment.—While so much can be accomplished by treatment in diabetes mellitus, very little is effected by it in the disease we are now considering.

To begin with, in this nothing is gained by any special form of diet. While in the saccharine form, aside from any effect upon the sugar production, withholding the farinaceous and saccharine elements from the food produces a reduction of the volume of the urine, no such reduction follows a similar restriction in the case of diabetes insipidus. From this it would seem that in saccharine diabetes the presence of sugar in the blood supplies the irritation to the polyuric centre which in the non-saccharine form results from some other cause.

In the way of regimen nothing more can be done than to allow such food as is best assimilated, and to permit the use of as much water as is required to assuage thirst. Restriction in this particular serves no good purpose, unless to diminish somewhat the frequency of micturition. On the other hand it increases the thirst, and adds in this way to the discomfort of the patient.

About the same list of drugs has been employed as in the treatment of diabetes mellitus, but with much less apparent benefit. Valerian is much lauded by Trousseau, but other authorities have failed to obtain from it the satisfactory results which he describes.

Edes gives the preference to large doses of

ergot, and believes that they have a decided beneficial effect.

Opium, it is generally admitted will reduce the quantity of urine, at least for a time, but its bad effect upon the digestion, together with the danger of forming the opium habit, more than counterbalance any advantage from its use.

Antipyrin has been useful in some recently reported cases.

Dr. M. Opitz, of Dresden, reports (*Deutsch. Med. Wochenschrift*, Aug. 8, '89) three cases in which this drug, in doses ranging from 2 to 6 grammes daily, produced rapid decrease of the urine, effecting a permanent cure in one case, and great temporary benefit in the other two. These cases were treated in the City Hospital, under the care of Dr. Fiedler, the circumstances being favorable for careful observation.

Tonics are valuable in improving the digestion and keeping up the powers of the system.

Indeed any of the drugs employed in diabetes mellitus may be used, and will occasionally produce at least temporary benefit.

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