THESIS

on

DIABETES MELLITUS

for the degree of

DOCTOR OF MEDICINE

of the

UNIVERSITY OF EDINBURGH

by

JAMES HERBERT MCKEE

[M. B., Ch. E.Edin., 1900]

1, Victoria Ovenue,

Horrogate.

1909.
CONTENTS

PAGE

Prologue .......................................................... 1
Nomenclature .......................................................... 2
Definition .......................................................... 2
History of .......................................................... 2
Etiology .......................................................... 6
Pathology .......................................................... 31
Theories of .......................................................... 36
Pathological Anatomy of ................................................. 38
General Clinical Course of ............................................. 47
The Urine in Diabetes .................................................. 50
Digestive System in .................................................. 54
Skin in .......................................................... 57
Nervous System in .................................................. 59
Respiratory System in ................................................ 65
Circulatory System in ................................................ 66
Reproductive Organs in ............................................... 66
Lymphatic System in ................................................ 66
Diabetes in Association with Other Affections ................. 66
The Course, Duration and Termination of Diabetes ............ 67
Diagnosis of .......................................................... 69
Prognosis of .......................................................... 75
Treatment of .......................................................... 76

Prophylaxis in .................................................. 76
Drugs in .......................................................... 78
Diet in .......................................................... 85
Complications .......................................................... 101

************
LIST OF CHARTS AND DIAGRAMS.

Tables showing the Percentage of Diabetes with Reference to Sex ........................................ 7

Tables showing the Relation of Diabetes with Reference to Age ..................................................... 8

Chart showing the Temperature in a Case of Acute Rheumatism .................................................. 17

Chart showing the Temperature in a Case of Relapsing Acute Rheumatism ................................... 18

Chart showing Sugar Excretion ................................................................. 83

Chart showing Sugar Excretion ................................................................. 84

Chart showing Temperature in a Case of Diabetes .............. 107

Chart showing Temperature and Excretion of Urine in a Case of Diabetes ................................. 109

Chart showing Temperature and Excretion of Urine in a Case of Diabetes ................................. 110
LIST OF AUTHORITIES.

A.
Ablemann, 24
Abram, 36, 81
Aldehoff, 23
Albertoni, 51
Ambrosiani, 3
Anselme, 46
Apt, 100
Aretius, 2
Argyll-Robertson, 63
Armanni, 40
Auger, 42
Auché, 64
Auerbach, 64
Auréli, 7
Ackerin, 87
Baron, 21
Barral, 25
Baylis, 35
Beale, 40
Benedict, 100
Bernard, 33, 37, 45
Bock, 16
Bouchard, 61, 95, 57, 62
Bouchardat, 15
Brandt, 27
Bremer, 46
Brücke, 41
Bunge, 37
Bussière, 51

C.
Cavazzani, 42
Cawley, 3, 23
Celsus, 2
Chauffard, 44
Chaveau, 41, 46
Cloison, 55
Cruickshank, 3

D.
Davy, 45
Davis, 6
Devic, 59
Dickinson, 44, 40
Dobson, 3
Donkin, 100
Dompelin, 29
Dreschfeld, 63
Dufour, 31
Duncan, 342

E.
Ebstein, 40, 59, 87
Edel, 48
Edie, 36, 81
Einhorn, 90
Ehrenberg, 27
Ehrenreich, 41

F.
Fichtner, 47
Flecker, 18
Fletcher-Worley, 1
Foster, Sir W., 4
Frerichs, 67, 81, 90, 42, 45, 63, 79
Fürbringer, 51
Fleming, 57

G.
Galen, 2
Geelmuyden, 53
Gerhardt, 4
Gilbert, 44
Giovanni, 29
Griesinger, 630
Grube, 78, 91, 64
Guthrie, 60
Ganis, 55
R.
Recklinghausen, 29
Reynolds, 103
Rollo, 345
Romberg, 45
Rosen,
Rosenstein, 56.44
Rubner, 44
Robert, 72

S.
Salles, 51
Satta, 52
Saunby, 6.7.14.39.42.43.85.90.86
Schein, 440
Schenk, 45
Schäfer, 26.37
Schnee,
Seege, 6.7.8.11.18.29.32.43.44.45.49.56.85
Senator, 6.39
Stadlemann, 51.53.60.61
Starling, 55
Startz, 51
Stern, 6.7.92
Straus, 440
Strasowski, 45
Strumpeil, 36
Schmitz, 6.15.37.51.56.89.67
Schull, 12.79

T.
Thiroloix, 24
Thompson, 3
Torok, 100
Trambusti, 51
Traube, 44.45
Trousseau, 18.80

U.
Underhill, 35

V.
Velisch, 23
Voit, 51

W.
Weintraub, 25
West, 80
Weyg, 440
Whitla, 80
Williamson, 6.7.39.42.43.44.46.65.68.80
Willis, 3

Y.
Yeo, 103

Z.
Zaleski, 440
Zenker, 29
Ziemssen, 64
Zimmer, 18

**********
PROLOGUE.

The author of this Thesis has been influenced in his choice of a subject by reason of the number of cases of diabetes mellitus which have come under his observation during the past two years; but more especially by the fact that several of these patients demonstrated points which were of more than passing interest, both from the etiological and the pathological standpoints.

Further, the disease is apt to be overlooked - not only in children, as pointed out by Morley Fletcher, but also in adults: a fact which has been verified by the writer; the absence of a routine examination of the urine will probably account for this.

Finally, the disease is a widespread one, being met with in every country - though not to the same extent in all; it is undoubtedly on the increase, whilst the effect upon the death-rate is more pronounced each succeeding year.
NOMENCLATURE.

Diabetes (dia - through, bainen - to go).
Polyuria; Hydrops ad Matulam;
Diarrhoea Urinosa; Mellituria;
Saccharine Diabetes; Glycosuria.

DEFINITION.

Diabetes mellitus is a somewhat obscure constitutional disorder characterised by the persistent presence of grape sugar in the blood, and consequently in the urine, with its commonly attendant polyuria, polydipsia and polyphagia, and resulting from deep-seated metabolic changes in the patient's system.

HISTORY.

The earliest reference to diabetes is to be found in works of Celsus - a Roman who lived in the beginning of the Christian Era.

Mention is also made of polyuria in the papyrus Ebers, a copy of an Egyptian compilation old in the time of Moses.

Aretæus of Cappadocia, and his supposed contemporary Galen, speak of an affection which was accompanied by the passage of enormous quantities of urine, unquenchable thirst, and emaciation.
Unmistakable references to the disease are found in the writings of ancient Indian physicians, who, for ages, have been acquainted with a disorder characterised by the passage of a sweet-tasting urine.

Centuries later, the sweet taste of the urine was first noticed by Thomas Willis, an Englishman, in 1674.

In 1775, W. Dobson, of Liverpool, was the first to demonstrate that this sweetness was due to a variety of sugar, which he obtained from the urine by the evidence of vinous fermentation. Dobson also affirmed that sugar was present in the blood of diabetics, as well as in the urine.

In 1788, Cawley recorded a case of diabetes in which the pancreas was atrophied and contained calculi.

The first really chemical test to demonstrate the presence of sugar in diabetic urine was suggested by Cruikshank. Hollo, who was the greatest authority on diabetes at the beginning of the century, also accepted the existence of sugar in the blood of diabetics; and, by observing the restriction to an animal diet checked the elimination of sugar, he concluded that the disease was due to faulty digestion of vegetable foods.

The presence of sugar in the blood was, however, afterwards disputed.

In 1818, Duncan described the sympathetic trunk as greatly enlarged in a case of diabetes.

Ambrosiani and Waitland, in 1835, were successful in separating sugar from the blood; and McGregor, about the same time, was able to obtain evidence of fermentation with yeast.

In 1842, Percy described the semilunar ganglia, the splanchnic nerves, and the vagi as thickened.

In 1845, Thompson, by fermentation, effected a determination of the sugar in the blood of fowls.

At the close of the forties, Claude Bernard conducted his important investigations on this disease. He discovered sugar in the liver after death, and his inference that the liver is therefore a sugar-forming gland has withstood all the criticism to which it has been subjected. He found that the liver stored up carbohydrates in the form of glycogen, and thought that this substance was converted into sugar by a ferment in the blood. He also demonstrated the fact that a glycosuria of several hours' duration could be produced in animals by a puncture of the floor of the fourth ventricle.
at the extremity of the calamus scriptorius.

At a later date, Bernard's views were opposed by Pavy, who held that glycogen is transformed into substances other than sugar; and he denied that the post-mortem formation of sugar from glycogen is a true picture of what occurs during life, maintaining that it is due to a ferment which is only formed after death.

In 1848, Traube discovered the difference between the mild and severe forms of diabetes by observing that sugar disappeared from the urine of a diabetic patient when carbohydrates were omitted from his food, but that later the glycosuria persisted in spite of the withdrawal of carbohydrates.

Between 1860 and 1863, Bence Jones and Brücke demonstrated small traces of sugar in normal urine; and Lawes and Gilbert by their classical experiments on the fattening of sheep, proved the physiological fact that the body fat may arise from carbohydrate food.

Gerhardt, in 1865, discovered that a solution of ferric chloride caused a wine-coloured reaction with the urine of patients suffering from diabetes: this observation has proved of great diagnostic value.

In 1874, the special features of diabetic coma were first described by Küssmaul; and, in 1877, Sir Walter Foster read a paper in this country in order to draw special attention to this subject.

Dickinson, in his work on "Diseases of the Kidneys," 1875, treats of diabetes mellitus; and many well-known authorities held the opinion that diabetes is a primary affection of the kidneys.

Kühnert, about 1885, published his calorimetric tables of the nutritive value of different articles of diet, from which a rational dietary for diabetics was framed.

In 1886, von Mering announced that after the administration of phloridzin to dogs and rabbits there was an excretion of a large percentage of sugar in the urine. The same result can be obtained in the human subject.

In 1889-90, von Mering and Winkowski discovered that severe diabetes can be produced by complete extirpation of the pancreas. Simultaneously and quite independently, an Italian scientist, de Dominicis, arrived at practically the same results.

Within recent years the amount of work done upon
diabetes and its metabolism has been enormous. Yet we are still without any unanimously accepted theory explanatory of its protean manifestations.

Fortunately, the observations already made are not in vain, but ensure for the diabetic patient a prolonged and more comfortable existence.
GENERAL ETIOLOGY.

HEREDITY.

Heredity is not without influence in the causation of this disease, although to a much less extent than in such affections as gout and obesity. Hereditary influences are much more frequently met with amongst private than amongst hospital patients, by reason of the greater prevalence of diabetes in the families of the rich and well-to-do.

Klein says: "In fully a quarter of all cases of diabetes there exists a direct diabetic hereditary predisposition!"

It is very rare to find that the father or mother have had the disease; but when we take into account the morbid history of other relatives (uncles, aunts, and cousins), the influence of heredity becomes much more apparent.

The disease is prevalent amongst the Hebrews, and it is not unusual for children of the same family to be attacked by diabetes.

Morton records a family history in which four children were affected.

Frerichs has demonstrated the influence of heredity in 10 per cent. of his cases; R. T. Williamson in 13 per cent., Seegan in 14 per cent., Schmitz in 20 per cent., and Bouchard in 25 per cent. Naunyn obtained a family history of diabetes in 35 out of 200 private cases.

Saundby quotes an example in which diabetes occurred in eight members of one family, the same extending over three generations.

Stern has analysed 117 cases in children in which hereditary influences were very marked.

SEASON.

Davies holds that season has something to do with the occurrence of the disease.

Diabetes seems to be more prevalent in cold than in mild and warm climates; and the mortality amongst diabetics seems to be greater during the cold than the warm months.

Exposure to cold, if severe or often repeated, is generally considered to be one of the etiological factors; and Griesinger had 40 cases in which the affection was believed
to be produced by such exposure.

According to Purdy, Vermont, a place remarkable for its cold winters, shows a death-rate 6.3 per 1000 from diabetes higher than that of any of the other states.

Sugar has been demonstrated in the urine of dogs and rabbits, by Araki and others, after the application of ice around the body.

**SEX.**

Diabetes is more common among males than females, in the proportion of about 3 to 2 — except during the first decades of life, when it is more evenly distributed.

Stern, amongst other investigators, finds that diabetes in children affects the female more than the male sex in the proportion of 5 to 3.

Amongst 400 diabetic patients seen by Freriohs, 118 were women.

Seeger records 232 women out of a total of 938 diabetic patients.

R. T. Williamson, in the following table, gives the age and sex of 100 cases of diabetes in Manchester (mostly hospital patient):

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-20</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>20-30</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>30-40</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>40-50</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>50-60</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>60-70</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>29</td>
</tr>
</tbody>
</table>

Robert Saundby, in Allbutt's "System of Medicine," gives the following statistics for England and Wales:

| All Ages | Under 1 year | 1 year | 2 years | 3 years | 4 years | 5 years | 6 years | 10 years | 15 years | 20 years | 25 years | 30 years | 35 years | 40 years | 45 years | 50 years | 55 years | 60 years | 65 years | 70 years | 75 years | 80 years | 85 years | 90 years | 95 years | 100 years |
|----------|--------------|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Males    | 1142         | 3      | 4       | 1       | 1       | 11      | 3       | 50      | 44      | 47      | 116     | 150     | 192     | 236     | 233     | 67      | 67      | 7       |
| Females  | 869          | 1      | 3       | 4       | 7       | 28      | 34      | 48      | 104     | 84      | 125     | 188     | 177     | 52      | 52      | 3       |
| Total    | 2011         | 3      | 4       | 2       | 2       | 4       | 16      | 10      | 58      | 78      | 95      | 220     | 214     | 517     | 460     | 410     | 124     | 10      | 7       | 67      | 67      | 7       | 7       | 7       |

Exclusive of the ages under 20, Pavy had 928 male and 373 female patients; and Grube had 157 male and 40 female cases.
There can be no doubt that the reason why the disease is so much more common amongst the male sex is the severe struggle for existence and man's greater proneness to excesses of all kinds.

AGE.

Diabetes is more common in adults, and is most frequently met with between the ages of 40 and 60. No age, however, is exempt: for cases have been observed in infants a few weeks of age and in aged persons over 80.

The percentage at various ages, as recorded by Grube, Seegen and Frerichs, is as follows:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Grube</th>
<th>Seegen</th>
<th>Frerichs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10</td>
<td>1.7</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>10-20</td>
<td>2.8</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>20-30</td>
<td>11.2</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>30-40</td>
<td>22.1</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>40-50</td>
<td>39.5</td>
<td>30</td>
<td>26</td>
</tr>
<tr>
<td>50-60</td>
<td>18.1</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>60-70</td>
<td>3.4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>70-80</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pavy's table shows:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>10-20</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>20-30</td>
<td>60</td>
<td>28</td>
</tr>
<tr>
<td>30-40</td>
<td>164</td>
<td>70</td>
</tr>
<tr>
<td>40-50</td>
<td>260</td>
<td>79</td>
</tr>
<tr>
<td>50-60</td>
<td>281</td>
<td>157</td>
</tr>
<tr>
<td>60-70</td>
<td>128</td>
<td>44</td>
</tr>
<tr>
<td>70-80</td>
<td>26</td>
<td>9</td>
</tr>
<tr>
<td>80-90</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

The disease is stated to be rare in childhood: that is, it is not nearly so common at such an early age as it is in persons of more mature years is evident. But is it so rare as reports make it out to be?

Does the busy general practitioner make the same routine examination of the urine of his young as he does of his adult and older patients?

With a view to getting some answer to this question, the writer interrogated 100 medical men in general practice. The answers given would roughly cover a period of two years in each case. Only those cases in which there was a fatal termination, and in which the diagnosis was doubtful, are included. In children under 5 years of age, not one of the number had tested the urine for sugar. 11 per cent. had examined for blood, pus and albumin, and the remaining 89 per cent. had not examined the urine for any abnormal constituent. Between the ages of 5 and 10, 7 were found who had endeavoured to establish the presence of glucose in the urine in cases in which a
diagnosis could not be arrived at - negative results being obtained in each case.

Looking at it from a personal standpoint, there are several reasons to account for the absence of an examination for sugar in a child’s urine. Thus, there is the difficulty of securing a specimen; there is the fact, stated in all the text-books, that the disease is very rare amongst children; and added to this, the examination requires a little time, some trouble, and freshly-prepared chemicals, which are probably not at hand; further, it is known that other copper-reducing substances, besides glucose, are to be found in the urine of infants and young children, such as lactose in the case of breast-fed babies, - so that, having found one to be present, it is necessary to prove that it is dextrose.

Undoubtedly many cases of diabetes in young children remain undiagnosed from want of a routine examination of the urine. The disease in children is of a more severe type than in adults; it begins more abruptly, and runs a very rapid course to an invariably fatal termination - the majority dying within one year from the onset of the symptoms. Indeed, Stern reports 7 cases in which death occurred within one month.

Cases of diabetes in young adults, although not so severe as in children, are usually unsatisfactory: they either get a false impression as to the necessity for constant care of themselves, or they are very apt to become careless.

**RACE.**

The Hindu is the most susceptible of all races to diabetes; and, according to the "Indian Medical Gazette", almost every family belonging to the upper classes has lost one or more of its members from the disease. This susceptibility is attributed to their sedentary life, their nervous constitution, and to the large amount of carbohydrates contained in their diet.

The Jews are also susceptible to the disease, and they rank probably next to the Hindus in the scale of frequency. They are likewise a neurotic race, and they lead an intellectual and sedentary life.

Negroes are comparatively immune to the disease; and the lower we go down the scale of intellectual and nervous development, the rarer the disease becomes.
SOCIAL CIRCUMSTANCES.

The disease has a distinct preference for the rich; and von Norden states that the statistics for London and Berlin show that the number of cases in the upper ten thousand exceeds that in the lower hundred thousand inhabitants.

On the other hand, as Klein points out, a far greater percentage of cases of diabetes of a severe kind occurs amongst the lower than the upper classes of society.

PSYCHICAL INFLUENCES.

Intense psychical influences have proved to be, in many cases, the immediate occasion of the disease, or have aggravated it following a temporary improvement in the patient's condition.

Numerous instances are on record of diabetes following fright or joy, violent passion, emotion, prolonged mental strain and worry: this is especially the case in individuals whose temperaments are of the nervous type, and whose equilibrium mental is easily upset.

Osier mentions a case in which the symptoms of diabetes came on suddenly after the patient had been nearly suffocated by smoke from having been confined in a cell of a burning jail. Shock and the toxic effects of the smoke may both have been factors in this case.

One patient, under the care of the writer during the past summer illustrates well the effect of such influences in the causation of the disease.

Mr. A, an Australian gentleman of independent means, aged 58, married and the father of 9 children—8 girls and 1 boy.

His parents were both dead—the father having been thrown off his horse and receiving fatal injuries, and the mother having died of pneumonia consequent upon a severe drenching. He has one brother and one sister, both living and in good health. There is a history of gout on the paternal side, and his mother was, according to him, a very high-strung and nervous woman.

He himself was gouty and had suffered from it for a considerable number of years. He had had influenza on several occasions.

Both he and his wife were devoted to their only son; this boy, whose age was 14, had enjoyed good health and was strong
and well developed for his age.

He was out fishing one day in a small stream, distant about one mile from his home; the day was warm; and, feeling thirsty, he drank deeply from the stream, with the result that typhoid fever developed – death occurring within two months from the onset of the symptoms.

M. A... had a serious break-down consequent upon the shock, and was troubled greatly with insomnia and depression; he began to lose weight, and in the course of four months had developed all the symptoms of diabetes.

He was carefully dieted and sent off to Europe for a holiday and change of scene, his surroundings having become very distasteful to him.

He was examined by the writer three months after his departure from Australia; during that time he had most carefully carried out his doctor’s orders, and he had in consequence improved considerably in health, in addition to having gained ten or eleven pounds in weight.

The morning urine – the first specimen examined – contained no trace of sugar; the specific gravity was 1018; and there were no abnormal constituents present. The after-dinner urine contained sugar, but rather less than 0.1 per cent. The total amount of urine passed in the twenty-four hours was 61 ounces.

All diabetic patients react badly to psychic disturbances, and show a marked intolerance to carbohydrates at such times.

Diabetes following upon psychic disturbances is probably produced by some derangement of the innervation of the liver, and possibly also of the pancreas.

Pavy has suggested vasomotor paralysis and dilatation of the small vessels of the liver; this view has been criticised by Seegen, who points out that Pavy was able to produce diabetes experimentally by injury to the nervous system after ligature of the hepatic artery.

**OCCUPATION.**

Occupations, predisposing to the disease, are such as necessitate great mental activity, strain and excitement; and it is acknowledged that diabetes occurs amongst city dwellers to a larger extent than amongst those resident in the country.

A large number of diabetics are to be found amongst
scientists, merchants, speculators, teachers, statesmen and musicians. On the other hand, diabetes is especially prone to attack those leading an idle and luxurious existence.

**CHRONIC AFFECTIONS.**

Such chronic affections as syphilis, alcoholism and gout have undoubtedly a marked influence upon the etiology of diabetes.

SYPHILIS, by attacking the organs engaged in the metabolism of the carbohydrates, may occasionally be an indirect cause of the disease. Again, if it be admitted that the lesions of the central nervous system can produce diabetes, then syphilis may stand in a very close casual relationship to glycosuria.

Schull, amongst other writers, insists that diabetes is a syphilitic disease, and that all cases of the disease are associated with hereditary syphilis; this extreme hypothesis must, of course, be rejected, as it is opposed to the results of the careful analysis of the majority of diabetic cases. Evidence of syphilis has, however, been found in very many cases of diabetes, both during life and post-mortem.

There is under the care of the author at the present time a Mr., who was sent over to Harrogate from Ireland, early last December, suffering from syphilitic disease of the tongue — the only other abnormality being a trace of albumin in the urine.

He is 54 years of age, married, and the father of one child — a girl of 4.

The disease was contracted about eighteen months ago. For a long time subsequently he paid no attention to his condition; the state of his tongue, however, becoming so painful, he consulted a medical man, who told him that it was due to the bad condition of some of his teeth: he was ordered a mouth-wash, and forthwith had the offending teeth removed.

No improvement resulting, he sought the advice of another doctor, who also failed to arrive at a proper diagnosis of his condition, and a consultant was called in.

Mercurial inunctions were ordered, and for six days the ointment was rubbed into the skin by the patient: profuse salivation resulted, and this has continued without intermission up to the present time; the mercury was stopped and has not been used since.

His weight six months ago was 16 st., 1 lb. During the
past two months he has complained of severe and persistent headache; and notwithstanding a large appetite, the loss of weight has been out of all proportion to the severity of the disease,—so the writer thought that the key to this loss of weight might be found in the urine.

The result of examination was as follows: total quantity in twenty-four hours—67 ounces, specific gravity—1.026, a trace of albumin, sugar rather less than 0.50 per cent.

His diet was now altered, and carbohydrates were given in small amount; but notwithstanding, the sugar still persisted.

The stools were carefully examined for traces of fat, but with negative results.

There is no apparent pathological condition of the liver: so that it would appear as if the glycosuria were due to some syphilitic lesion of the central nervous system. The headache remained, but no other signs or symptoms were present to point conclusively to any intracranial trouble.

Since his arrival, 7 weeks ago, he has been taking increasing doses of iodide of potassium; and two weeks ago, intramuscular injections of soamin (5 grains) were begun and given daily. Both these drugs were now pushed, and the patient’s condition began to improve; the headache has now almost disappeared, and is only present at intervals during the day; the tongue is much less painful, more movable, and is decidedly cleaner; the salivation has diminished, and the patient is now able to sleep more comfortably. No sugar can be demonstrated in his urine the past three days.

One is almost forced to the conclusion that the exhibition of glucose in this man’s urine was due to possibly a gumma in the neighbourhood probably of, or in a region to cause pressure on, the fourth ventricle, or to syphilitic disease of the cerebral arteries or brain itself.

Von Hoorden vaunts the opinion that neurogenous diabetes is most frequently curable and disappears coincidently with the subsidence of the cerebral affection.

The subsequent history of this case is interesting. After continuing soamin injection daily for a month, he began to develop symptoms of arsenical neuritis; the injections were discontinued, and he was kept on small doses of iodide of potassium.

His condition was not improving; he was losing weight and complaining of thirst. His appetite was very large; he asked for food every hour, took what was given him, and asked
for more. He complained of seeing objects double when at a distance from him, and he began to exhibit symptoms of hallucination, believing that large sums of money had been left him. His stools were markedly fatty, and sugar was present in the urine.

Iodipin was prescribed in doses of .02 grm. three times a day.

Both the pancreas and brain were evidently involved; and as mercury was not tolerated, even in the smallest dose, the prognosis is gloomy.

The patient returned to Ireland about this time.

ALCOHOLISM.

Alcohol in small quantities increases the power of the carbohydrate assimilation; in large amounts it has the opposite effect. A history of alcoholism is present in 17 per cent.

GOUT.

Gout undoubtedly constitutes a predisposition to diabetes, and is more often than any other disease associated with it. There seems to be some connection between the change in metabolism which results, in the one case, in gout and which, in the other case, gives rise to the presence of sugar in the blood and urine.

Probably no fact is of better prognostic import to the patient than the association of gout with diabetes. The cases are almost always of a mild type.

Such individuals are usually stout, healthy-looking persons, full of the joy of living. As a rule, they are not aware of the presence of sugar in their urine, except in severe cases; and to inform them, when ignorant, of such a fact would be to commit a very grave error, knowing what a bad effect worry and anxiety have upon the diabetic subject.

Generally the glycosuria has existed for years before some slight disturbance has led to an examination of the urine.

A large percentage of gouty individuals undoubtedly pass pathological quantities of sugar in their urine, sometimes in the twenty-four hours, and usually after dinner. The probability is that the liver, which in gout is not performing its functions properly, allows varying quantities of carbohydrates to pass unchanged into the blood.

From mild cases of gouty glycosuria, in which small amounts of sugar are excreted, there is every possible grade to the most severe types of diabetes. Again, attacks of gout
may alternate with glycosuria (diabetes alternans), or the attacks of gout may cease and glycosuria appear, or both may be present at the same time.

Bouchardat says that those cases in which diabetes existed first, the gouty symptoms appearing later, are not so favourable.

In two members of my own family gout existed for years before sugar was demonstrated in their urine. One, a female, is 68 years old and would undoubtedly enjoy good health, were it not for the fact that she indulges too freely in the pleasures of the table. The other, a male, is 59 and enjoys good health.

Diabetics frequently present an ancestral history of gout (hereditary alternating gout).

**Geographical Distribution.**

The disease is present in every country. In England, France, the United States of America and Denmark it is steadily increasing.

It is frequently met with in Southern Italy, India, Malta, Sweden and Germany. It is stated to be less general in China and Japan, amongst the Turks and Persians, than amongst Europeans.

Diabetes is relatively rare in Mauritius and British Guiana, where the people are employed chiefly in the manufacture of sugar; in Africa, where the sugar-cane and other sweet fruits form a large part of the diet of the natives; and in Ireland.

**Contagion.**

Although there is no evidence of any specific microorganism in the etiology of diabetes, still many remarkable cases are recorded which would seem to prove the communicability of the disease from one individual to another.

R. Saundby was the first to attract attention to this possibility; out of 2,320 cases of diabetes, he was able to collect 26 instances which he believed to be the result of contagion. He therefore brings forward the question as to whether there is not a special form of diabetes which can be conveyed from one person to another. In the 26 cases there was nothing else that could be set down as a cause; but, as von Noorden points out, the instances alleged by Schmitz are explained by the fact that persons living together are
naturally exposed to the same injurious influences.

Senator cites a number of examples which also seem to suggest possible transmission: amongst these is a case of diabetes in a woman whose husband's brother and his wife both had the disease. Also a case developing in a man after marrying into a diabetic family, both parents of his wife having diabetes. He records 19 cases of conjugal diabetes out of a total of 516 persons suffering from the disease. The total proportion of 3.7 per cent. is too small, Senator declares, to justify the assumption to date that diabetes can be transmitted from one person to another not a blood-relation.

**SPECIFIC FEVERS.**

Acute infectious diseases have proved to be the direct etiological factors in quite a number of cases of diabetes; this is not surprising in view of the number of organic affections which occur as sequels of such infectious conditions.

The probability is, as von Noorden points out, that such cases of diabetes are due to secondary affections of the pancreas, and likely produced in the same way as secondary organic affections involving such organs as the heart and kidneys.

Numerous examples have been recorded as sequels of influenza, typhoid fever, malaria, acute rheumatism, diphtheria, measles, cholera, pertussis, pneumonia, erysipelas and croup.

The following case is not without interest in this connection:

Miss G..., aged 17, was seized with illness one Saturday evening, and was seen by the writer the following morning.

She complained of only feeling very hot, and of a slight headache. No articular pains were present, even on movement. She was perspiring very freely and had a temperature of 103.4°F.

Examination of the various systems gave negative results, and the urine contained no abnormal constituents.

She was placed on fever diet, she was kept under the continuous observation of a specially-procured nurse.

The temperature rose in the evening to 105.2°F; still there were no signs of pain anywhere, no rash could be seen, and there was nothing to give a clue to the nature of the existing condition.

She was ordered large doses of sodium salicylate, and was sponged with tepid water when the temperature was
becoming high.

For eight days the temperature did not fall below 100°F., and, save for the temperature and the profuse sweating, no other symptom could be elicited until the morning of the seventh day, when a marked mitral systolic bruit was noticed.

On the morning of the ninth day, the temperature touched the normal for the first time, and, but for the slight rise, the same evening, remained so for six days. The left ventricle showed marked hypertrophy; the apex beat being one and a half inches outside the nipple line.

She was seen the next three days, and instructions were given for the medicine to be continued in diminished dosage. She was also warned not to leave her bed.

The patient was not seen again till three days had elapsed, when, on being sent for, she was found to have suffered a relapse.

On investigation, it was found that the medicine had been withheld, and that she had been allowed out of bed for several hours. She was now suffering severe pain in the joints of the hands and feet and knees; the joints were swollen, and the temperature was 104.2°F. There was again marked perspiration.

Sodium salicylate was again administered, and with marked and almost instantaneous benefit - the pains almost
Two days later, the mother drew my attention to the large amount of urine which was being passed. On examination it was found to contain sugar in quantity. The specific gravity of the urine was 1028; the amount passed in the twenty-four hours was nine and a half pints; and the sugar was estimated at 2.4 per cent.

On suitable diet the sugar disappeared, and the amount of urine passed fell to normal.

The urine was examined every day, but no sugar could be demonstrated — not even when a normal diet was resumed. This bears out what Klein says that the "prognosis of glycosuria due to infectious disease is decidedly more favourable than that due to any other cause."

Her urine has been examined once a month for the past six months, no sugar being found on any occasion.

**OBESITY.**

It is believed that fat persons have traces of sugar in their urine more frequently than others.

That diabetes and obesity are frequently associated is an established fact — such good observers as Trousseau, Sjöegång, Fleckless, Zimmer and others holding that obesity is a predisposing factor.

The following figures give some idea of the frequent
association of the two conditions: Frerichs had 59 cases of obesity among 400 diabetic patients, or 15 per cent.; Seegan 20 per cent.; and Bouchard 45 per cent.

The view is generally held that the obesity precedes the appearance of the sugar in the urine - this form of the disease being called "lipogenous diabetes." Von Noorden has shown there may be a "diabetogenous obesity," in which the adiposis masks the diabetes - such patients not excreting sugar in the urine, but rather into their adipose tissue.

The lipogenous variety is of the mild type, and is not of grave import: for a considerable glycosuria may exist for years without affecting the patient's powers to any appreciable degree. The diabetogenous form, on the other hand, develops in early life, and is of very serious moment.

Kisch is of the opinion that diabetes arises from the muscles becoming infiltrated with fat so much that they are thereby unable to do their share in the destruction of sugar. He believes that in about 50 per cent. of cases of heredity, and in 15 per cent. of cases of acquired, obesity pathological excretion of sugar takes place sooner or later.

The probability is that obesity and diabetes are both the outcome of similar conditions: for how otherwise can one explain cases in which persons of middle age suddenly become corpulent and at the same time begin to pass traces of sugar in their urine - more especially after meals. These obese individuals who excrete glucose in their urine rarely suffer from ravenous hunger, excessive thirst or extreme polyuria, and on the withdrawal of carbohydrates from their diet, lose their glycosuria. Their condition is quite consistent with long life, although their resisting-powers are much less than those who do not exhibit glucose in their urine.

Four of the writer's patients suffered from lipogenous diabetes, and in each case the obesity had been present for some years before the presence of sugar was discovered.

Mrs. M., aged 64 years, had grown extremely stout since the menopause at 42. She took little or no exercise and lived an indolent and luxurious existence. She came from a gouty family and had herself suffered from irregular gout. She was free from any known hereditary predisposition or other etiological influence worthy of mention, other than two attacks of influenza, - one five years ago and the other two years later, - and the gouty condition already mentioned. Two years since she began to be troubled with pruritus
vulvæ; and on consulting her medical attendant, the presence of sugar in her urine was forthwith demonstrated. The sugar, however, disappeared after a course of dietetic treatment. She has spent one month each year, for the past two seasons, in Harrogate, and on each occasion glucose, though absent from the morning was always present in the urine passed after dinner— to the extent of about 0.2 per cent. on an average.

Mrs. W., aged 53 years, had for the past ten years or so been fat— for over six years her weight being close on 13 stones, and her height being 5 ft. 5 in. She had hereditary adipose tendencies, led a sedentary life, and was of a markedly nervous temperament. About two years ago, she began to notice a marked increase in the amount of water she passed; this was especially noticeable at night, and it disturbed her rest to such an extent that she at last sought advice on the subject. Sugar was found to be present in the urine, but to what extent is not known. She underwent a course of treatment for close on six months; during that time the sugar disappeared, she lost over 2 stones in weight, and she felt better in every way. She has ever since paid great attention to her food; and though her urine has been examined every month, no trace of sugar can be found. She enjoys good health and weighed 11 st. 12 lbs., when last seen by the writer.

Mr. R., a stockbroker, aged 53 years, knew of no hereditary cause for his condition. He is a bachelor, and for the last twenty years has not failed to gratify any and every desire that may have possessed him. He had been stout as a boy—the only stout one in a family of five. During the past seven years his weight has increased greatly; he is now 15 st. 5 lbs., and 5 ft. 9 in. in height. Nine months ago an attack of furunculosis drew the attention of his doctor to the urine, and glucose was found present, but in small amount: this disappeared on dieting. When seen last summer, there was a suspicion of sugar in the after-dinner urine, but in a few days no trace of it could be demonstrated.

Miss M., aged 59, was a remarkably stout woman, and weighed between 16 and 17 stones for many years. Her father and mother were both stout, but she knew no case of diabetes in the family. She had no idea that sugar was present in her urine until, four years ago, she requested her doctor to examine a specimen for sugar: it was found to contain a faint trace of glucose. Her reason for this request was due to the fact that her most intimate friend had developed
a mild form of diabetes.

**miscellaneous factors.**

Amongst other factors in the production of diabetes may be mentioned sexual excesses, ingestion of ices and iced drinks, climatic disturbances, pregnancy; and Eshner says there is evidence to show that the power of assimilating carbohydrates is diminished in conjunction with pregnancy, abscess of the breast, injuries (more especially of the head), violent muscular strain, lightning-stroke, exophthalmic goitre [Bar: Brit. Med. Jour., 1904, Vol.i., No. 332], abscess of the liver, acromegaly, malignant disease of the abdomen not involving the pancreas, and starvation.

**cryptic origination.**

In many cases of diabetes, about 15 per cent., the most careful enquiry fails to reveal any exciting cause.
The pancreas is a tubulo-racemose gland closely resembling the salivary glands in structure, the principal differences being that the alveoli or acini are more tubular in character; the connective tissue between them is looser, and in it are small groups of epithelium-like cells, which are supplied by a close network of capillaries. The secreting cells are polyhedral, and when examined in the fresh condition, their protoplasm is seen to be filled in the inner two-thirds with small granules; but the outer third is clear.

During secretion the granules are discharged. These granules indicate the presence of zymogen, called trypsinogen, that is, the precursor of trypsin, the most important ferment of the pancreatic juice.

In the centre of each acinus, spindleshaped cells (Langerhan's centro-acinar cells) are often seen, whose function and origin are at present unknown.

Quantitative analysis of human pancreatic juice gives the following results: Water 97.6 per cent., organic solids 1.8 per cent., and inorganic salts 0.6 per cent.

The organic substances are:-
(a) Ferments — four in number:
   1. Trypsin, which acts like pepsin, but in an alkaline medium.
   ii. Amylopsin, or pancreatic diastase, which converts starch into maltose.
   iii. Steapsin, a fat-splitting ferment, which decomposes the fats and fatty acids into acids and glycerine.
   iv. A Milk-Curdling Ferment.
(b) A small amount of Proteid matter.
(c) Traces of Leucine, Tyrosine, Xanthine, and Soaps.

The inorganic substances are:-
(a) Sodium Chloride.
(b) Potassium Chloride.
(c) Sodium Phosphate.
(d) Calcium Phosphate.
(e) Magnesium Phosphate.

The duct of the pancreas is called the canal of
The vagus contains the secretory nerves of the pancreas.

The blood-supply is derived from the splenic artery.

In 1788, Cawley recorded a case of diabetes in which the pancreas was atrophied and contained calculi. Since then the important etiological bearing of this organ has to diabetes has been elaborated by many others; but no opinion as to the casual relation between the pancreas and diabetes was clearly formulated until, in 1877, Lancereaux described a special form of diabetes under the name of "diabète pancréatique" or diabète maigre."

This form was said to be characterised by a sudden onset, rapid loss of strength, progressive emaciation, unusual malignancy and a special tendency to pulmonary tuberculosis.

During the following twelve years or so, many experimenters tried, with little or no success, to produce glycosuria by extirpation of the pancreas, division of the nerve-supply, and ligature of the pancreatic duct; and the subject was on the point of becoming neglected when, in 1889–90, von Mering and Minkowski communicated to the Association of Natural Sciences of Strassburg their great discovery that total extirpation of the pancreas gives rise to severe diabetes, characterised by glycosuria under all dietetic conditions, polydipsia and polyuria, rapid loss of weight, the presence of acetone, diacetic acid, B-oxybutyric acid, an increased amount of ammonia in the urine, and death in diabetic coma,—their experiments being carried out upon dogs, cats and hogs.

Diabetes following extirpation of the pancreas has also been observed in hawks (Langendorf), falcons (Weintraud), geese (Kausch), turtles and frogs (Aldehoff, Marceuse, Velisch).

The French experimenters have usually injected paraffin, asphalt, &c., into the pancreatic duct, causing atrophy and induration of the gland, and some weeks afterwards have removed the pancreas. The glycosuria usually begins a few hours after the operation and reaches its maximum on the third day, with from 10 to 12 per cent., or more, of glucose in about 1.5 litres of urine. The hyperglycosuria rarely exceeds 0.5 per cent.

It was at first suggested that the solar plexus was
damaged during the operation and a nervous diabetes set up. That this is not the case has been conclusively proved by the experiment independently performed by Minkowski, Hédon and Thiroloix, of grafting a portion of the extirpated gland in the muscles of the abdominal wall with the result of preventing the occurrence of diabetes; but if this engrafted portion of the pancreas is removed later, by a now insignificant operation, the disease manifests itself.

Minkowski found that if any considerable portion of the pancreas is left, about one-tenth part, with power of performing its functions, no diabetes ordinarily results; but if this remaining portion becomes subsequently obliterated, then diabetes follows. If less than a tenth part is left in a functionating condition, a mild form of diabetes ensues.

Hédon found the retention of such a small portion as one-thirtieth sufficient to prevent the development of glycosuria.

After removal of the pancreas the animals quickly lose flesh; and Abelmann found 45 per cent. of fat ingested in emulsion, almost all the fat and 56 per cent. of ingested protein in the faeces of Minkowski's dogs after the operation.

Chauveau and Kaufmann found that if the spinal cord is divided in the lower cervical or upper thoracic region, after extirpation of the pancreas, the operation is not followed by glycosuria, though the hypoglycemia continues - the stimulating centre for the formation of glucose in the liver being cut off. If, however, the pancreas is first removed, the same section being made after the beginning of diabetes, hyperglycemia and glycosuria continue. They explain this by a certain autonomy on the part of the sympathetic centres in the abdominal cavity, which continue to exercise stimulating functions after these have been assumed.

Hédon and Thiroloix are of the opinion that a gradual and slow destruction of the pancreas - by injections of various substances into it - may take place without causing glycosuria.

After extirpation of the pancreas the deposit of glycogen in the liver and muscles does not normally take place. The animals may be fed abundantly with starchy materials without more than traces of glycogen being found in these organs; the one exception to this is when the animals are supplied with levulose.

Many endeavours have been made to get a better understand-
ding of the way in which these results of extirpation of the pancreas are brought about. It is not due to the action of the pancreatic juice: for diabetes does not occur in cases of simple shutting off of this secretion from the intestine, nor yet when the fluid escapes through a cutaneous fistula.

Lépine, of Lyons, has afforded, up to the present, the best solution of the problem. He believes the pancreas produces a ferment destructive of the sugar, which enters the circulation and causes a breaking up of the grape-sugar molecule; after extirpation of the pancreas this ferment is not present, and sugar therefore accumulates undestroyed, producing hyperglycemia with its resulting glycosuria.

The experiments upon which Lépine bases this opinion were conducted, with barral, in the following way:—He abstracted a certain amount of blood from the vascular system, and immediately heated the half of it to 129.2°F., thereby destroying the glycolytic ferment; he then put this portion of the blood, as well as the remaining portion, which had not been heated, into an incubator in a temperature of 102.2°F., and examined both samples for sugar after the lapse of an hour. When he used the blood of healthy animals and man, he found a much smaller percentage of sugar in the non-heated than in the heated sample of blood; but when the blood of an animal from which the pancreas had been removed was taken, the difference in the proportion of sugar contained in the two samples was slight. He reasoned from this that there was a decrease in the amount of glycolytic ferment after extirpation of the pancreas. He found the conditions were the same in individuals suffering from diabetes mellitus as in dogs without the pancreas.

Many well-known investigators, such as Seegan, Kraus, Minkowski, &c., have repeated Lépine's experiments without obtaining his results; and it is further held that we cannot argue from the results of test-tube experiments as to the conditions present in the blood circulating in the vessels of the living body. Furthermore, no one has yet succeeded in obtaining such a ferment from the pancreas, and pancreatic extracts, however administered, have failed to control glycosuria.

Kaufmann has suggested a modification of Lépine's hypothesis, namely, that the secretion controls the sugar-forming function of the liver.

Von Noorden, on the other hand, denies the extra function
production of sugar, and holds that the cause of diabetes is diminished destruction in the tissues, loss of power to store carbohydrates as fat, and incompetency of the glycogen reservoirs of the liver and muscles.

Opie regards the presence or absence of diabetes as dependent on the destruction or integrity of the islands of Langerhans in the pancreas, and the intimate relation of these columns of cells to the rich network of blood-vessels suggests, as advanced by Schäfer, that they furnish the internal secretion of the gland.

Investigations have shown that two forms of interstitial fibrosis of the pancreas may be recognised — interlobular and intralobular; and according to Opie's results, it is the intralobular variety which is peculiarly associated with diabetes; for in this form the islets of cells undergo degeneration.

Osler records a case of diabetes in a woman, aged 24, who died of tuberculosis of the lungs. At the post-mortem examination Opie found the glandular tissue of the pancreas well preserved and healthy, but the islands of Langerhans were everywhere represented by a sharply-circumscribed hyaline structure composed of particles of homogeneous material. In two other cases, lesions of the islands were found, but there was also chronic pancreatitis (Opie: Jour. Exper. Med., Vol. V.).

From the foregoing it is evident that the removal of the pancreas either causes something to disappear from the blood that is essential for the normal combustion and utilisation of sugar, or it causes something to remain in the blood that prevents such taking place. Many cases of diabetes associated with pancreatic disease are now on record; and there can be no doubt that diabetes is directly due to pancreatic disease in many cases.

Amongst the lesions of the pancreas most commonly associated with diabetes, atrophy and fibroid outgrowth stand out as the most frequent. Other lesions sometimes present are fatty degeneration, cystic disease, calculi, haemorrhagic and suppurative pancreatitis, carcinoma; and it is probable that arterio-sclerosis may cause diabetes by producing changes in the gland.

Further, if Lépine and Schäfer are correct in the theory that diabetes is a result of the stoppage of an internal secretion, is it drawing too much on the imagination to
suppose that diabetes following psychic disturbances is due to stimulation of the vaso-constrictor nerves, thereby causing a stoppage of this secretion as it does the pancreatic juice? 

McKendrick reports an interesting case of pancreatic diabetes in a man, aged 46, it being one of chronic inflammation of the pancreas giving rise to, in the first instance, dilatation of the stomach, relieved partly by gastro-enterostomy, and, in the second place, to severe diabetes mellitus. In this patient the diabetes is supposed to be due to an intralobular cirrhosis.

John nose Bradford reports three cases of diabetes, which are most probably due to pancreatic disease:

(1) A woman, aged 62, was operated upon for a large and painful swelling in the epigastrium; this was found to be a hard mass in the region of the pancreas, which could not be removed. Three years later, the patient came again under observation, suffering from severe diabetes; and on examination, no tumour could be detected in the abdomen. It is possible that this is a case of chronic pancreatitis.

(2) The second case, also a woman, had a large abdominal tumour causing sufficient pressure on the pylorus to necessitate gastro-enterostomy; the tumour itself was not capable of being removed. Eighteen months after the operation, the patient presented all the signs of very severe diabetes, and the tumour was no longer to be detected.

(3) The third patient was a woman, aged 30, suffering from jaundice. When the jaundice had subsided, severe diabetes developed. Some cases of catarrhal jaundice have been attributed to swelling of the head of the pancreas as a result of pancreatitis, and it is possible that the illness from which this woman suffered was of this character.

The writer records the following case as of interest:

A lady, aged 64, was seriously ill during practically the whole of last year. She was a spinster, and had lived a very quiet and uneventful life. There was no history of any hereditary disease, with the exception of rheumatism. She consulted the writer in October, 1907, for pain in the back and lower part of the abdomen, as well as for a slight vaginal discharge.

On examination, a hard mass, about the size of a walnut, was felt growing from the cervix uteri; the vaginal wall was implicated, and the broad ligament infiltrated; a diagnosis of carcinoma was made. The other organs seemed normal, and the
urine contained no abnormal constituents.

A surgeon was asked to see her a week later, but found the disease too extensive to warrant operation.

The disease advanced slowly, and nine months later a secondary deposit was felt in the liver. Shortly after this she began to complain of difficulty in swallowing, so the presumption was that the esophagus had become implicated.

At the end of eleven months the disease had eaten through the posterior wall of the vagina and invaded the rectum; the urethra was also involved, and urine was voided continuously in increasingly large quantities. There was a marked odour of acetone, and the urine on examination showed the presence of sugar in quantity.

The specific gravity of the urine was 1.026, and the amount of glucose in one ounce was seven grains; the test for acetone was positive.

Her weight was now 4 stones 10 and a half pounds, and she looked more like a lady removed from the grave than a living, though semiconscious, individual.

A distinct hard mass could be felt in the region of the pancreas. Unfortunately, no post-mortem examination was allowed; but the pancreas without doubt was extensively involved.

She died in a comatose condition six days after the sugar had been found to be present in the urine.

The amount of urine voided in the twenty-four hours could not be estimated.

**Diseases of the Liver.**

The post-mortem findings in the liver in diabetic cases are not such as to suggest definitely an important rôle for this organ in the production of the disease - no definite or constant pathological change being met with, although the organ is sometimes diseased; it is frequently enlarged, in other cases normal or diminished in size.

It is sometimes fatty, and often is congested. Cirrhosis is sometimes found. Abscesses and malignant disease have been encountered, but all these conditions are often seen unassociated with diabetes.
It has already been shown how diabetes may be set up through the medium of the nervous system, as a result of some violent emotion, such as sudden joy or fright, causing some derangement of the innervation of the liver and possibly of the pancreas.

Closely allied to these are the examples in which diabetes is actually associated with injury to, or disease of, the brain or spinal cord; but it must be remembered that every anomaly of the nervous system met with in diabetes is not to be considered an exciting cause, as it may be a consequence of the disease.

Diabetes of nervous origin is much more frequently due to cerebral lesions than to spinal or peripheral causes. In the case of the brain, the lesions are generally to be found in the medulla oblongata, or its immediate neighbourhood: such are tumour, softening, fatty degeneration, cysticercus, sclerosis, hemorrhage.

Hecklinghausen and others have found melituria in cases of tumour of the fourth ventricle; Dompeling, in a tumour of the medulla; Giovani, in sclerosis of the cerebellum; Zenker, in disease of the fourth ventricle; Naupyn, Mosler and others, in softening of the cerebellum; and Michael and others in cases of cysticercus. It is reported of these, and many other similar cases, that there were no evident pathological changes in other organs to account for the melituria.

The spinal cord is usually normal; but in a few cases gross lesions have been found, such as tumour or softening, and usually in the cervical region. Pathological quantities of sugar have also been discovered in the urine in cases of myelitis, spinal hemorrhages, fracture and contusions of the cervical and lateral dorsal vertebrae, and spondylitis.

Occasionally glycosuria, usually of a mild type, occurs in association with well-marked disease of the nervous system, such as tabes dorsalis, disseminated sclerosis, Graves' disease, cerebrospinal meningitis, epilepsy, chorea minor, paralysis agitans, general progressive paralysis, and insanity.

Besides the "diabetic puncture," glycosuria is said to follow certain experimental lesions of the nervous system, such as injury to the vermiform process of the cerebellum, section of the spinal cord at various levels, section of the
the anterior cervical nerve-roots, section of the posterior cervical nerve-roots, artificial neuritis of the first pair of dorsal nerves, destruction of the superior and inferior cervical sympathetic ganglia, of the first thoracic and of the abdominal ganglia, section of or ligature of the splanchnic nerves, irritation of the right vagus, section and stimulation of the central end of the an ordinary sensorimotor nerve, such as the sciatic.

Such lesions generally increase the glycogenic function of the liver, causing an amount of sugar to be poured into the general circulation far in excess of the consuming and storing powers of the tissues.

**INJURIES**

There are many cases on record of the occurrence of diabetes following mechanical injury. Of diabetic patients 6 per cent., show such an exciting cause; and in at least 50 per cent. of the cases of traumatic diabetes, the head has been the seat of injury. The diabetes may follow immediately after the accident, or not till some months have elapsed.

Griesinger was the first to call attention to the fact that contusions of various parts of the body, no matter how distant from the nervous centres, may lead to glycosuria; such cases are more frequently seen amongst children.

The glycosuria generally passes off in a few days, but it may become permanent.
In order to better understand the pathology of the excretion of sugar, it will be necessary to give some account of the physiology of sugar excretion.

Let us first consider the carbohydrates of the food and their absorption.

The most important is starch or amylum. Starch is a compound of several smaller carbohydrate molecules, and is therefore called a polysaccharide.

Before absorption can occur, starch must be broken down in the body; this division takes place through the action of the ferment diastase, which is contained in the buccal secretion and the pancreatic juices — the resulting dextrin and maltose, as they pass into the intestinal wall and portal vein, undergoing a further change, being almost entirely converted into grape-sugar.

Dextrose and Maltose, when taken as such in food or drink, undergo, of course, a like change.

Cane-sugar is split up into fruit-sugar (levulose) and grape-sugar, in the alimentary canal by the action of acids, enzymes and bacteria. If cane-sugar be taken in excess, it may pass into the urine directly, without being split up. Fruit-sugar (levulose), present in ripe fruits and honey, and milk-sugar (lactose) pass into the blood unchanged. Cellulose is probably not absorbed.

From the intestinal wall these sugars pass through the portal vein to the liver, where they are converted into glycogen, and deposited in the form of flakes in the hepatic cells. The liver is therefore a reservoir for the storing of carbohydrates, and it may contain as much as 14 per cent of its own weight of glycogen. Recent physiological researches have rendered it probable that sugar-formation is a function of the liver cells, under the control of certain undetermined excitatory-sensory nerves, which, according to Morat and Dufour, are distinct from the vasomotor nerves. This glycogen the liver passes on into the circulation, as it is needed, in the form of grape-sugar.

Glycogen, however, is found in other parts of the body —
especially the muscles; but the quantity varies, being greater after the ingestion of large amounts of carbohydrates, and after long rest, than after abstinence from food and hard labour. The muscles are also, therefore, reservoirs for glycogen, which they themselves probably elaborate from grape-sugar which is always at hand in the blood.

Glycogen may also be produced from albuminates; for it has been found that, in animals which have been made glycogen-free, a new formation of glycogen takes place when they are fed exclusively upon albuminates; and our clinical experience of diabetes has frequently proved how large a quantity of sugar may be excreted by patients whose diet contains very little carbohydrates.

Where this formation of carbohydrate from albumin takes place is not known - it is supposed to occur in the liver, though some believe it takes place in the muscles.

The carbohydrates are burnt up by the muscle cells in the production of force and heat.

Now, supposing the supply of carbohydrate is not sufficient, the reserve store of glycogen is soon drawn upon: this, together with what is newly formed from albumin, will at first suffice to meet the demand. If the drain continues, the supply becomes finally exhausted; still, if the arterial blood be examined, the usual proportion of grape-sugar (0.12 to 0.13 per cent.) will be found present. It is evident from this that the organism does not suspend the production of sugar, but manufactures it from the only substance which can meet the deficit, the fat of the body and from that taken as food. This conversion of fat into sugar probably takes place in the liver.

When the carbohydrate material supplied is too great for the needs of the body, it is stored up in the liver and muscles; but the capacity of these reservoirs is limited - consequently, if the carbohydrates continue to be ingested in large quantity, the storing capacity is soon overtaxed, and the excess is converted into fat and deposited in the subcutaneous tissue and other parts of the body. When the supply is larger than can be disposed of by these methods of storing, the blood becomes abnormally charged with grape-sugar - a condition of hyperglycaemia resulting, and as soon as the percentage of sugar in the arterial blood exceeds about 0.2, glycosuria results. This is called "alimentary glycosuria."

Traces of sugar are present in normal urine; but in such
small amount that the ordinary tests fail to detect it. If sugar is ingested in large quantities at short intervals, it may appear physiologically in the urine, and is of the same kind as that ingested. If it be glucose, we have glycosuria, lactose-lactosuria, levulose-levulosuria, saccharose-saccharosuria. The amount necessary to be taken varies as to whether the individual is fasting or not, and it also varies with the individual.

According to von Noorden, sugar appears in the urine after a simple ingestion of:-

- Milk-sugar more than 120 grms.
- Cane " " " 150-200 grms.
- Fruit " " " 200 "
- Grape " " " 200-250 "

These figures are only approximate, and represent the amounts taken when the individual is fasting; the limit is higher when the stomach contains food.

The sugar appears in the urine usually about one hour from the time of ingestion.

Any amount of starch may be taken without causing sugar to appear in the urine, provided the individual be healthy; but when sugar is excreted after starch ingestion, there must be a morbidly-depressed assimilation limit, and the existence of diabetes is to be strongly suspected.

Milk-sugar may at times be found in the urine of nursing women, when there is an interruption to the withdrawal of milk, or when there is an abundant supply of milk too great for one child to consume.

We have now come to the consideration of what happens when these carbohydrate reservoirs become changed through DISEASE; and in order to arrive at a proper understanding, it is necessary to recall the facts observed from EXPERIMENTAL RESEARCHES.

Claude Bernard demonstrated the fact that injury to the floor of the fourth ventricle in animals produced a glycosuria of several hours' duration; but this injury is only effective in its results when the liver contains glycogen, and cannot be produced in an animal whose store of glycogen has been depleted by fasting or by inducing a pyretic condition, ligation of the ductus choledochus, or other means.

This injury produces a disturbance of the vasomotor mechanism—but this form of diabetes cannot be regarded as purely vasomotor in origin, since a fall of blood-pressure
produced in other ways, is not accompanied by a diabetic condition.

There are experiments recorded which show that the liver nerves have a direct influence on the liver cells, apart from their influence on the blood-vessels; and, as Halliburton points out, it may be that puncture diabetes is due to injury to, or stimulation of, a centre controlling the action of this secretory nervous mechanism.

In puncture diabetes, as in alimentary glycosuria, there is no fundamental disturbance of the power of the organism to burn sugar, but simply a diminution, or overstraining, of the sugar-holding capacity of certain organs.

Transient glycosuria may also follow certain nervous injuries, such as painful stimulation of peripheral nerves, destruction of certain of the sympathetic ganglia, lesions of various parts of the brain, and possibly sudden injury to any part of the nervous system.

Certain poisons are also capable of producing a like condition: such are curare, morphia, strychnine, amyl nitrite, carbonic oxide, nitrobenzol, and carbon disulphide. An abundant supply of glycogen is presumed to be present in the liver in all these and similar conditions. The glycosuria resulting from the injuries mentioned is produced much in the same way as that following puncture of the floor of the fourth ventricle.

All these forms of glycosuria have been termed "hepatogenous" by von Noorden, since the liver especially enters into consideration.

Closely related to the foregoing results of experiments on animals belong the transitory glycosurias following concussion of the brain, cerebral apoplexy, severe neuralgia, and disturbance of the mental balance: also those which follow poisoning by such substances as morphine, hydrocyanic acid, amyl nitrite, arsenic, chloralamid, anilin, ergotin, and phosphorus — chloroform and ether narcosis likewise occasionally producing temporary glycosuria.

As already stated, certain poisons are capable of producing temporary glycosuria; but the most powerful and interesting of these is phloridzin; this substance is a glucoside (C_{21}H_{24}O_{20}) obtained from the bark of apple, pear, cherry and plum trees.

In 1886, v. Mering proved that, after the administration of this substance to dogs and rabbits, there was a large
excretion of sugar in the urine, and the glycosuria persisted as long as the administration of phloridzin was continued. The sugar passed in the urine is too great in amount to be accounted for by the small quantity of sugar in the drug; moreover, phloretin, a derivative of phloridzin which is free from sugar, produces the same results.

In the human subject, the same results are obtained, and the ingestion of phloridzin produces no injurious consequences.

The sugar appears in the urine whether carbohydrates have been previously taken or whether the individual is fasting or living on a flesh diet. This form of diabetes is therefore analogous to those severe forms in which the sugar must be derived from protoplasmic metabolism.

A curious feature of phloridzin diabetes is the absence of an increase of sugar in the blood; and, if phloridzin is directly injected into one renal artery, sugar rapidly appears in the secretion of that kidney, and later in that of the other kidney.

There can be little doubt that this drug acts primarily upon the kidneys, changing the renal epithelium so as to destroy its normal power of keeping back the sugar.

The study of phloridzin in diabetes has established the certainty that the albuminates may become a source of sugar-production; but whether or not fat also acts in a like manner is not yet definitely determined.

Mention may here be made of adrenalin, a drug which, after administration, produces both glycosuria and glycemia. It largely depends upon the amount of carbohydrate in the food; but there is an increased decomposition of protein material in metabolism leading to an increase of urea and ammonia in the urine.

How this drug acts is not known: some think it acts through the pancreas, others, such as Noel Paton, that it does not,- whilst Underhill and Closson regard the condition as nervous.

As already stated, extirpation of the pancreas leads to a variety of diabetes; and the experiments on animals are paralleled by many cases of diabetes in man, produced by pancreatic disease. In these cases, it is assumed that the diabetes is due to the loss of an internal secretion; and as it has been discovered, by Bayliss and Starling (Progressive Med., Vol. ii., 1907, p.321), that pancreatic secretion proper
is effected through the agency of a substance, secretion elaborated by the mucous membrane of the duodenum [strictly speaking, the mucous membrane elaborates a prosecretion which is converted into secretion by the influence of the hydrochloric acid present in the duodenal contents], it was hoped that it might also be effectual in causing an internal secretion.

Moore, Edie and Abram point out that if the duodenum yields a chemical excitant for the internal secretion of the pancreas, and that if in the absence of this secretion glycosuria results, there are three ways in which diabetes may result:—(1) The duodenum may fail to yield the secretion; (2) although the secretion is formed, the cells of the pancreas may not be capable of excitation; or (3) although the duodenum and pancreas are normal, yet there may be changes in the various tissues of the body, such as the liver and muscles, and as a result of these glycosuria may ensue.

Hence, under the most favourable conditions, all cases of diabetes would not be benefited by treatment with secretion: in fact, it is only the first type of case that may be expected to improve.

Our authors record the treatment of three cases of diabetes with acid extract of duodenal mucous membrane—the results in two of the cases being decidedly encouraging.

THEORIES AS TO THE CAUSATION OF THE DISEASE.

Terrier thinks that the glycosuria results from interference with normal oxidation processes in the pancreatic cells. He found the direct application of an aqueous solution of adrenalin (a powerful reducing substance) produced glycosuria in 22 out of 25 animals experimented upon.

Strümpell holds that some cases are entirely, or almost entirely, endogenous in origin, and due to some developmental abnormality.

Pavy affirms that diabetes is due to diminished formation of glycogen from the sugar of the portal blood. He maintains that in health the intestinal villi also, as well as the liver, stop the carbohydrates and convert them into fat—consequently, when the liver and villi fail in their sugar-eliminating function, sugar accumulates in the blood and glycosuria results.

This theory explains the mild forms of diabetes in which
the sugar disappears from the urine upon restricting or stopping the carbohydrates in the food.

The severe forms of the disease in which sugar still continues to be excreted in the urine, even on a carbohydrate-free diet, Pavy explains by the supposition that the sugar is derived from the proteins of the body.

Bernard's theory is that the disease is due to an increased formation of sugar from glycogen—the excess of sugar being poured into the circulation more quickly than it can be burnt up, or destroyed by the tissues.

The different nervous theories of the origin of diabetes, in which the central nervous irritation leads to a greatly increased flow of blood through the liver, come in here.

The view is gaining ground that diabetes is the result of diminished sugar destruction, and it is here that the pancreatic theory comes in.

The internal secretion, supposed to be produced by the pancreas, according to Lépine and others, and manufactured, as Schüfer believes, in the cells of the islands of Langerhans, if this theory be accepted, possesses the power of breaking up the sugar in the blood.

The microbic theory, first advocated by Schmitz, is exceedingly rare, and it is questionable if such a mode of origin ever does occur.

The phloridzin theory, in which the kidney plays such an important part, has already been described.

The alimentary-glycosuria theory embraces those rare cases in which, when sugar is given in larger amounts than can be dealt with by the liver, glycosuria results—the condition being most readily produced when the metabolic functions of the liver are "below par."

Finally, diabetes has been attributed, by Bunge and others, to pathological chemical changes commencing in the muscles.
PATHOLOGICAL ANATOMY.

It would be impossible, at the present time, to diagnose diabetes mellitus solely from the pathological changes present, without taking into account the clinical history or making a chemical examination of the urine and blood.

The disease has no definite pathological anatomy, though numerous pathological changes have been described; the changes met with are usually secondary to the diabetes, or are the result of complications which have arisen in the course of the disease.

In many cases, especially if of short duration, the post-mortem appearances differ little, if at all, from the normal.

APPEARANCE OF THE CADAVER.

As a rule, there is wasting, whilst in other cases there may be extreme emaciation, though at times the body is well nourished and possessed of a quantity of fat.

The skin is generally thin and harsh, and it frequently bears traces of rashes or the scars of boils and carbuncles.

The hair is scanty and dry, and the teeth are defective.

PANCREAS.

Gross changes in the pancreas are frequently met with; and it is said that pathological processes are found in more than a half of the subjects dying from diabetes.

It has been suggested that the changes in the gland are secondary to disease of the celiac plexus; but Mustig and Peifer have shown that removal of this plexus is not followed by atrophy of the pancreas.

Probably the most important change found is the intralobular form of chronic pancreatitis, in which the islands of Langerhans undergo degeneration.

Karakascheff reports nine cases of diabetes terminating in coma, and in all found fatty degeneration and atrophy of the pancreas, with outgrowth of the connective tissue.

The islands of Langerhans were less numerous than normal, and the major portion of their number showed signs of transformation into normal pancreatic acini.
The condition of the pancreas, in 24 cases examined by R. T. Williamson, was as follows:

(a) Extensive changes (marked cirrhosis 2, cancer 1, atrophy 1) in 4 cases.
(b) Well-marked changes (cirrhosis 2, lipomatosis 1, atrophy with fatty degeneration and infiltration) in 4 cases.
(c) Slight changes (atrophy with fatty degeneration 1, atrophy, out of proportion to the general wasting 2) in 3 cases.
(d) Atrophy, but only corresponding to the general wasting, in 5 cases.
(e) Normal in 8 cases.

Robert Saundby reports the condition of the pancreas in 27 consecutive cases as follows:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophied</td>
<td>13</td>
</tr>
<tr>
<td>Large and hard</td>
<td>5</td>
</tr>
<tr>
<td>&quot; soft</td>
<td>1</td>
</tr>
<tr>
<td>Large</td>
<td>1</td>
</tr>
<tr>
<td>Congested (mottled)</td>
<td>1</td>
</tr>
<tr>
<td>Normal</td>
<td>6</td>
</tr>
</tbody>
</table>

Cysts and calculi and arterio-sclerosis of the pancreatic vessels have been found present, as well as such acute lesions as haemorrhage and suppurative pancreatitis.

In many cases of diseases of the pancreas, glycosuria is absent; and in connection with this fact it must be remembered that, in experimental extirpation of the pancreas, no diabetes follows if a small portion of the gland is left.

**LIVER.**

From the results of physiological experiments it would appear that one would be justified in expecting some clear relationship between diabetes and pathological changes in the liver; but no definite or constant pathological change is met with.

So far as clinical investigation goes, the usual state of the organ is normal, though in some cases there is enlargement, and perhaps some tenderness on pressure.

The elaboration of the bile does not seem to be interfered with.

Gall-stones are frequently met with, especially in corpulent persons.

The organ is frequently enlarged, weighing from sixty to eighty ounces; in other, and rare, cases it is small, pale
and soft.

It is sometimes fatty, often congested, and it may be abnormally firm. It may be cirrhotic, and, as Hamot and Schachmann have shown, this cirrhosis may be accompanied by bronzing of the skin. Bronze-coloured diabetes generally appears in men of from 40 to 60 years old, and in most cases there is a history of malaria or alcoholism; the dark brownish-gray colour of the skin is most pronounced in the face and on the extremities and genitals. Naunyn records 22 cases of incipient, and 2 cases of advanced, cirrhosis of the liver amongst 152 diabetics. Abscess of the liver is occasionally met with, as is carcinoma.

Dickinson has described thrombosis of the branches of the portal vein, and angiomas formed of dilated capillaries near the radicles of the hepatic vein.

According to Weyl and Apt, the diabetic liver does not contain excess of fat; and absence of this substance, from the hepatic dells, has been noticed by Beale and Frerichs.

Quincke thinks that iron is in excess; but Zaleski points out that we have no data to enable us to say whether it is in excess of the normal or not.

KIDNEYS.

Albumin is often present in the urine of diabetic persons, but usually in small quantities or small traces. It has been attributed to catarrh of the bladder, excess of nitrogenous food, and to the mixture of pus with the urine, owing to balanitis in the male or eczema of the vulva in the female; in other cases it is associated with nephritis. In some cases it is due to stasis in the kidneys resulting from a weak heart; whilst in severe cases of diabetes it may be dependent upon toxic conditions.

Slight albuminuria in diabetic individuals is usually considered as of less clinical and prognostic significance than under other conditions.

The changes found in these organs are secondary, and, though variable in extent and degree, are always present. The most characteristic and only distinctive lesion is the hyaline transformation of the epithelium of Henle's tubules, first described by Armanni and called by him "hyaline metamorphosis; to the same condition Hbstein gave the name "hyaline necrosis", Straus "vitreous degeneration", and
ehrlich glycogen clods. It is not constantly present.

Slight fatty degeneration is not uncommonly present; and, in 1883, Richter described a collection of fat granules arranged in rows in the peripheral parts of the epithelial lining of the convoluted tubes and of the ascending portion of Henle's tubes.

The kidneys may be enlarged and congested; sometimes the cortex is thinned and the organ contracted, lardaceous disease and gangrene have been found, as also have such affections as diffuse nephritis.

NERVOUS SYSTEM.

The brain, spinal cord, cerebrospinal nerves, sympathetic nerves and ganglia may present interesting and significant lesions in diabetes, though in certain very rare cases symptoms may be encountered, which one is accustomed to refer to disease of the spinal cord or central nervous system, such as hemiplegia, aphasia, hemianopsia and localised convulsions, without any disease or lesion of the nervous system being found post-mortem.

The brain shows no constant lesion, it is often normal. The most common change is congestion and edema, with thickening of the membranes. In other cases it is found anemic, and sometimes the sulci are widened and the convolutions wasted.

The lateral ventricle and the iter have been found dilated and cavities been exposed in the brain tissue. The choroid plexus may contain cysts, and may be congested or thickened.

Tumours of the fourth ventricle and medulla have been recorded, which have undoubtedly been the cause of the diabetes; in the same region of the brain examples have been observed of sclerosis, softening, fatty degeneration, cysticercus and congestion.

Hemorrhage into the brain substance is rare.

Glycogen is present in large amount in the medulla, and the sheaths of the vessels of the cortex.

In the spinal cord glycogen is present in the sheaths of the vessels and spinal membranes. The extension of disease from the cord into the medulla accounts for a certain number of cases of diabetes; and when this occurs, changes characteristic of locomotor ataxia, insular sclerosis, and like lesions are present.
R. T. Williamson has recorded two cases in which there were changes present in the posterior columns of the cord in diabetic persons; in both cases the changes were easily seen with the naked eye; the degenerated tracts occupied Goll's columns in the cervical region in both cases; they extended to Bourdech's columns in the dorsal region in one case, in the lumbar region in the other. Microscopically, the changes were much less distinct, and consisted of slight degeneration of the fibres of the posterior columns.

In very few cases, lesions of the spinal cord's cervical region (tumour or softening) have been found.

Several examples are recorded of diabetes following tumours growing from the right vagus nerve (Feriches, Anger and Neumann); and Lubinoff has described a case of diabetes in which atrophy and pigmentation of the inferior ganglion of the vagus were present.

The peripheral nerves may be found to have undergone inflammatory changes, characterised by increase of the connective tissue, with secondary destruction of the axis cylinders; the nerves of the lower extremities are chiefly affected and well-marked clinical symptoms result.

Changes in the sympathetic nerves and ganglia have often been found.

In 1816, Duncan found the sympathetic trunk in the abdomen greatly thickened.

In 1842, Percy described the semilunar ganglia, the splanchnic nerves and vagi as thickened and of cartilaginous hardness.

The celiac plexus has been found atrophied by Cavazzani; Saundby reports four cases in which the semilunar ganglia were enlarged, one case in which they were atrophied, and one case in which they were embedded in a mass of fibrous tissue.

LUNGS.

The lungs show frequent and important changes: they are often congested and edematous.

Pulmonary tuberculosis, according to von Noorden, is present in at least one-fourth of all diabetic subjects in Germany; and when diabetes attacks youthful subjects, it is the rule that they become tuberculous, unless coma or some accidental intercurrent disease carries them off earlier - older, and especially corpulent and gouty subjects being in
m u c h less danger of this complication. Tuberculosis attacks diabetics of the poorer classes much more frequently than those in better circumstances.

LOBAR and BRONCHO-PNEUMONIA are sometimes met with, and small foci of SOFTENING, ABSCESSES, HEMORRHAGIC INFARCTS, FAT HEMOLISMS, PLEURISY and EMPYEMA are found present at times. GANGRENE is occasionally noticed.

Seegen's table, from the post-mortem room of the Vienna General Hospital (given in Williamon's monograph on the disease) of the findings in 92 autopsies on diabetics, is as follows:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>40</td>
</tr>
<tr>
<td>Croupous Pneumonia</td>
<td>9</td>
</tr>
<tr>
<td>Lobular Pneumonia</td>
<td>8</td>
</tr>
<tr>
<td>Oedema</td>
<td>15</td>
</tr>
<tr>
<td>Hyperpyrexia</td>
<td>4</td>
</tr>
<tr>
<td>Diffuse Gangrene</td>
<td>2</td>
</tr>
<tr>
<td>Localised Gangrene</td>
<td>1</td>
</tr>
<tr>
<td>Hæmorrhagic Infarct</td>
<td>1</td>
</tr>
</tbody>
</table>

HEART AND ARTERIES.

No uniformity in the post-mortem changes found in the heart and arteries can be looked for; and it is probably on account of this absence of uniformity that Seegen, after examining 52 cases of diabetes on which autopsies had been made, although he mentions the condition of many other organs, passes over the heart and arteries.

HEART.

In diabetes the cardiac affections are most likely to be present are those which depend upon impairment of the nutrition of the muscular fibre of the nerves of the heart by the presence of sugar in the blood.

The organ may be hypertrophied; Israel found hypertrophy of the left ventricle in 40 per cent. of his cases, Mayer in 13 per cent., and Saundby in 13 per cent.; Mayer found hypertrophy of the heart in 27 per cent. during life.

The cardiac muscle may also show fatty infiltration, atrophy and dilatation; pericarditis and endocarditis, with coincident valvular disease may be encountered.

Glycogen granules may be found between the muscular bundles.

In young patients, in whom diabetes is not complicated
with other diseases, the muscular tissue of the heart is frequently found to be flabby or atrophied.

**ARTERIES.**

Arterio-sclerosis is common, and diabetics are very liable to suffer from premature arterio-sclerosis; diabetics under middle age at times exhibit a pulse which is large, hard and of increased tension, even when there are no evidences of kidney disease.

**INTEGUMENT.**

As already mentioned, the skin is dry and harsh. A variety of xanthoma, which occurs in association with diabetes, was described by Malcom Morris in 1885 - the lesion being distinguished from those of ordinary xanthoma by the presence of a red and raised area around the yellow spots. Hanot and Chauffard's description of a bronze-coloured diabetes - "le diabète bronzée - has been referred to.

**ALIMENTARY TRACT.**

The STOMACH is found to be dilated in a few cases, and especially in those who have remained without treatment for a long time, and have taken large quantities of food to cover the unrecognised loss of sugar.

Evidences of chronic gastritis may be present; and the mucosa may be congested or contain hemorrhages, and is at times thickened.

The INTESTINES share in the congestion and catarrh found in the stomach; hemorrhages may be found in the duodenum.

The colon is generally filled with hardened faces; and it may show signs of dysenteric inflammation or desquamation of its epithelial lining.

**SPLEEN.**

We know little of the behaviour of the spleen in diabetes.

Like the other abdominal organs, it is often hyperemic and enlarged; in other cases it may be small and flabby.

Glycogen has been found in it, and sometimes tuberculous lesions and hyaline degenerations of the vessels are present.
REPRODUCTIVE ORGANS.

Straynowski mentions atrophy of the uterus and ovaries as occurring in diabetic women; and testicular atrophy has been described by Romberg and Seegen.

The seminal vesicles usually present no abnormalities. Frerichs, however, dwells upon the fact that in one of his patients, a man of 40 years, they contained, in addition to innumerable spermatozoa, a pea-sized reddish and transparent secretion, as well as some grayish liquid.

BLOOD.

Normal blood contains only a very small amount of sugar — from 1 to 1.7 per 1000 (Pavy, Seegen); but, unlike the glycogen of the liver, which varies greatly under different dietetic conditions, the amount of sugar in the blood normally undergoes but little variation. It increases somewhat after the ingestion of large amounts of carbohydrates (Bernard, v. Mering), and after copious hemorrhage (Edel, Schenck), and decreases during continued starvation (Bernard, Eick and Hoffmann, Otto, Seegen, Chaveau), during the febrile state, after extirpation of the liver, and as a result of phloridzin poisoning.

In diabetes the percentage of sugar in the blood is greater than normal: Pavy reports from 1.54 to 5.76 per mille; Seegen, in grave cases, from 2.3 to 4.8 per mille.

As soon as the sugar in the blood reaches a certain amount, which Bernard found to be about 0.25 per cent. in the dog, it begins to pass into the urine. Seegen's figures indicate that glycosuria in man may exist with less glycaemia than 0.20 per cent.

The percentage of water has been found both increased and diminished; the kidneys irritated by the sugar draw such a volume of water from the blood that a certain amount of thickness may result. In such cases the proportion of solid constituents is increased, and examination shows a larger amount of hemoglobin and red blood-corpuscles than normal; in other cases the fluid portion may be normal or increased.

The specific gravity was found by Hammerschlag to be increased to 1.064; by Davy to be 1.061, and by Nasse to be diminished to 1.048.
According to James and others, the number of red blood-corpuscles is usually high, except in bronze-coloured diabet­es, in which the number is much diminished. According to others, the red corpuscles are diminished; they are sometimes broken down into a granular material.

Anselme, amongst others, considers the disintegration of the red corpuscles from some unknown cause responsible for diabetes by invading the pancreas and inducing cirrhosis.

Almost all the organs contain a deposit, ochre-coloured, derived from the hemoglobin of the blood; and this substance, according to Hanot and others, increases up to several thousand per cent. the amount of iron of the tissues.

Williamson, Bremer, and others have found that the red corpuscles in diabetic blood are obtained in a different way by methylene-blue and other dyes than those in normal blood.

Habershon found marked leucocytosis in diabetic blood—the number of white corpuscles diminishing with restriction of carbohydrates, and increasing during coma.

The appearance of the blood is generally normal; but at times it is loaded with fat, which, after the blood is shed, floats on its surface in a cream-like layer.

Microscopically, the fat is present as a very fine emulsion, and the condition is spoken of as "diabetic lipemia."

After a rich meal, the percentage of fat in the blood may reach a high figure in healthy persons; but the lipemia in diabetics may, according to Naunyn, occur on an empty stomach.

The alkalinity of the blood-serum is reduced in consequence of the presence of acids of doubtful identity—

B-Oxybutyric and diacetic acids being the most probable.

The presence of acetone has been observed, but is not constant.

***************
SYMPTOMATOLOGY

GENERAL CLINICAL COURSE.

(A) ACUTE FORM.

This form, although it may occur in the aged, is usually met with in persons under 40 years of age, and not uncommonly in children and young adults.

It is characterised by a more sudden onset, a more rapid course, and frequently fatal termination. Thirst, the frequent passing of an excessive quantity of water, increased appetite, and general weakness are complained of. The frequent micturition, interfering as it does with sleep, is one of the chief causes of the great constitutional depression; and, in spite of the voracious appetite, wasting rapidly sets in.

At times, cases are met with amongst children in which there is no obvious wasting, the patient presenting a healthy and well-nourished appearance, which is sometimes retained to the end.

The face is commonly flushed, the skin dry, the lips parched, the tongue red and dirty or covered with fur, and the bowels constipated. The secretions of the mouth are diminished, the breath may have a sweet odour, and there is often a nauseous and sweet taste in the mouth.

Attacks of vomiting may come on suddenly without apparent cause, and they are sometimes attended by drowsiness.

The temperature is frequently subnormal; the sexual appetite is usually lost.

The quantity of urine varies from 5 to 15 pints or more; it contains up to 10 per cent. of sugar, though higher percentages have been recorded.

As stated, the termination of such cases is usually fatal—some dying in a few months, others living a year or two from the onset of the symptoms.

One such acute case came under the observation of the writer, which, as already reported, followed a severe attack of rheumatic fever.

The girl passed large quantities of urine, her sleep being greatly disturbed by the constant desire to pass water. The appetite was not excessive, but marked thirst was
complained of. The skin, in marked contrast to its condition during the fever, was dry and harsh, the tongue coated with a brown fur, and the bowels obstinately constipated. Aceto-acetic acid was not present in the urine, and the sugar and polyuria disappeared under dietetic treatment without recourse being had to drugs.

(b) CHRONIC FORM.

There is no essential difference between the acute and chronic types of the disease, except that, as stated, the former has a more rapid course.

The chronic form is to be observed usually in elderly individuals, and not infrequently in those who have been decidedly obese. The symptoms come on gradually, and it may be very imperceptibly. Such individuals complain of bodily weakness, mental depression, frequent micturition, impotence, some loss of flesh, and disturbance of the digestive organs. Constipation is usually present, though in some cases there is a marked tendency to diarrhœa, and the stools have a fœtid odour.

As this type of the disease usually begins in a gradual way, it is apt to be overlooked, or to be mistaken for nervous dydpepsia, overwork, and such like conditions.

In other cases, diabetes is only recognised when disease of some other organ, or organs, develops—such as visual disorders, impotence, neuralgia, pruritus, furunculosis, tuberculosis; and the variety of forms under which the disease appears is often responsible for the fact that the diagnosis is made only when serious destruction has already been wrought in the body through defective nutrition, complications, or sequelæ of the primary disease.

The quantity of urine varies from 3 to 6 or more pints, and the sugar from 2 to about 10 per cent.

The course of the disease varies also, as follows:

1. In consequence of regulation of the diet, good nursing, avoidance of any tax to the mind or body, and careful treatment of any complications, the patient may increase in weight and his strength return. The tolerance of carbohydrates increases slowly, and he may live for many years—finally succumbing through inability to take and assimilate sufficient nourishment to maintain strength, or by reason of some intercurrent disease, such as heart failure, tuberculosis,
or finally death may result suddenly and unexpectedly from coma.

(2) In contrast to these relatively favourable cases are those with a rapidly fatal course. In spite of every care and attention, severe complications and sequelae attack them; they suffer from grave cardiac weakness, gangrene, neuritis, tuberculosis, and death occurs within the short period of one or two years.

In the severe forms of the disease the sugar in the urine is evidently not dependent simply on the carbohydrates of the food, since the glycosuria persists when carbohydrates are withheld from the diet, and even when no food is taken.

Pavy believes that in these severe forms the sugar is derived not only from the substances taken as food, but from the tissues as well.

According to Seegen, in the severe forms the cells and tissues of the organism have lost their function of destroying the sugar in the blood.

(c) MILD FORMS.

The mild forms of diabetes compatible with long life are by far the most common; they belong to the middle and later periods of life, and usually affect obese persons and those suffering from the gouty diathesis.

Removal of the carbohydrates from the dietary causes the glycosuria to cease; and usually there is a tolerance of certain amounts of starch.

The onset of such mild cases is seldom known, and the condition may remain for years undiscovered.

The glycosuria may be found accidentally, or after an examination of the urine suggested by certain complications - such as furunculosis, pruritus, neuralgia, and impotence.

In these mild forms the sugar appears to be derived from the carbohydrates of the food in some way, directly or indirectly; and Seegen believes the liver cells are unable to assimilate the carbohydrates in a normal manner.

Such cases improve rapidly under dietetic treatment and proper surroundings; but dietetic abuse, overwork of mind and body, etc., will soon lead to a return of the glycosuria and a deterioration in the general condition, and, despite their benign tendency, to an unfavourable termination.

The amount of urine passed is slightly increased, because the excess of dextrose in the blood acts as a diuretic. The
quantity of dextrose passed in the twenty-four hours varies from a few grammes up to several hundred.

There are many intermediate forms between the acute, chronic, and mild types of the disease.

ANALYSIS OF THE SYMPTOMS.

THE URINE.

The QUANTITY of urine is increased - often to from 150 to 300 ounces in the twenty-four hours; but in milder cases the increase may be slight - 60 to 100 ounces: it being not unusual to find patients passing considerable quantities of sugar, and yet having no diuresis. The amount of urine is reduced by nitrogenous diet, and by intercurrent disease; it is often diminished before a fatal termination.

The COLOUR, in typical specimens, is a pale greenish-yellow; but it varies from all shades of yellow up to deep amber. The liquid is generally clear, but may be turbid from lithates, muco-pus, or torulae. When the amount of urine is not increased, in mild cases, the colour may be normal.

A MUCOUS CLOUD, when present, is often seen - not at the bottom, but at the upper part of the urine-glass.

The ODOUR is often sweet or aromatic; and in severe cases - especially before the onset of coma - the urine has a peculiar chloroform smell, usually attributed to the presence of acetone.

The TASTE of diabetic urine is said to be sweet.

The REACTION is nearly always acid, and it is often markedly so.

The SPECIFIC GRAVITY of the urine is usually high, varying from 1020 to 1050; several observers have found it as high as 1070, and Trousseau records it as great as 1074.

A low specific gravity does not exclude sugar, nor a high density prove its existence.

Saundby reports several cases in which it was as low as 1013, while phosphatic urine may be as high as 1040.

Diabetic urine does not tend to DECOMPOSE so deadly as normal urine.

UREA is excreted by diabetic patients in very considerable quantities - larger figures not being reached in any other disease.
Many authors have given the name of AZOTURIA to this symptom. This azoturia is due largely to the abundant ingestion of proteids; it is very large as long as the diabetic is left to himself to ingest the carbohydrates which are useless to him, but becomes slight, or ceases, when the diet consists largely of proteids and fat (Lusk, F. Voit, v. Noorden, Hirschfeld).

URIC ACID is present in normal, or only slightly increased, amounts in diabetic urine (Startz).

HIPPURIC and OXALIC ACIDS frequently occur.

CREATININ oftens appears in quantities that could hardly be reached in health; this is due to the diet.

ALBUMININ.- Statements concerning the frequency of albuminuria vary from 10 to 68.7 per cent. (Bouchard, Führinger, Schmitz, Salles, Eussière).

The albuminuria is nearly always slight. Pathological anatomy teaches us that sufferers from diabetes seldom have perfectly healthy kidneys.

Von Noorden thinks that the organ becomes diseased in consequence of the enormous tax put upon it by the excretion of such large quantities of water, nitrogenous substances, and sugar; others believe that the kidneys are poisoned by the definite products of metabolism in the diabetic organism.

Albertoni, Trambusti, and Nesti believe that it is due to aceto-acetic acid: nothing, however, that is definite is known regarding this point.

AMMONIA.- An excretion of from 5 to 6 grms. a day has been frequently observed; and Stadlemann found as much as 12 grms. The highest figures belong to the stage of diabetic coma.

Of non-nitrogenous organic substances, acetone, aceto-acetic acid, and E-oxylbutyric acid are the most frequently encountered.

It has long been known that ACETONE appears in the urine and breath of a diabetic patient who is progressing unfavourably. Its presence is probably a better guage of the patient's condition than the amount of sugar in the urine.

Chiefly owing to von Jaksch, it has been recognised that acetonuria appears in a great many other conditions, such as the recurrent vomiting of children, the pernicious vomiting of pregnancy, delayed chloroform poisoning, bronchopneumonia, fevers, prolonged rectal feeding, carcinoma of the digestive organs, and other diseases; it is also said to
occur in uræmia.

Acetone is derived from the unstable diacetic acid; if this abnormal acid is being excreted slowly, it will all break down into acetone, but if more than half a gramme of acetone is being excreted in a day, diacetic acid is certain to be found also.

The odour, variously compared with that of hay or of apples, which is noted in these cases, is due to diacetic acid rather than to acetone, which has a more penetrating odour. It follows that the recognition of diacetic acid in the urine is of greater importance than the detection of acetone, its decomposition product; and this is convenient, as diacetic acid is very easily tested for: on the addition of ferric chloride, a claret colour results, which does not appear if the urine has been previously boiled.

Acetone is best detected by the addition of a few drops of a freshly prepared solution of sodium nitro-prusside, and then excess of sodium nitro-prusside - when a ruby-red colour is developed, which is intensified and turned purple on the addition of acetic acid.

Acetone is very volatile, and the reaction can be prevented by previous boiling.

Diacetic acid is usually derived from β-oxybutyric acid. There is no convenient clinical test for this body; but it is probably present when the diacetic reaction is well-marked, though it sometimes cannot be found in diabetic coma. β-Oxybutyric acid yields diacetic acid by oxidation, while diacetic acid is converted into acetone by the loss of CO₂.

So far as is at present known, the immediate precursor of acetone is a fatty acid.

The sudden and complete withdrawal of carbohydrates from the diet of a diabetic person is followed by nausea, vomiting, loss of weight, the odour of acetone in the breath, the presence of these acids in the urine, and an increase of the amount of ammonia in the urine, whilst signs of coma may occur: if carbohydrates are now given, the symptoms disappear.

From this it is evident that these bodies do not come from the carbohydrates, but must be derived from either proteid or fat. Both views have been held; but it would appear that proteid is not the main source, as their excretion is not accompanied by a proportionate increase in the excretion of nitrogen and sulphur (M. Levy Satta).
There remains the fat, and no acetone is derived from the decomposition of a fatty acid; this would involve but a simple change.

Geelmuyden and others produced acetonuria in healthy persons by a fatty diet.

Acetonuria results from starvation and defective oxidation, as in broncho-pneumonia; and von Noorden correlates these factors by referring the rôle of carbohydrates, in the prevention of acetonuria, to the relative abundance of oxygen they contain.

Acetonuria therefore becomes a symptom of incomplete oxidation, due to the absence of sufficient oxygen or of sufficient aldehyde groups to which the oxygen could attach itself.

The relation of these substances to diabetic coma has been considerably debated in the past; many authors (Stademann, Minkowski, von Jaksch) look upon diabetic coma as an acid intoxication, others regard it as the result of a specific poisonous action of E. oxybutyric acid or the substances allied to it, while other again would attribute to acetone and aceto-acetic acid an important rôle in the etiology of the comatose condition. But many observers, including von Noorden, have seen marked acetonuria and diaceturia continue in diabetics for weeks, and then disappear without any symptoms of coma becoming evident.

The appearance, however, of E-oxybutyric acid in the urine is always followed in time by coma, unless death is occasioned by some intercurrent disease. The views held concerning this substance are flatly contradictory; von Noorden inclines to the opinion of Klemperer, according to which, in some stages of diabetes, certain toxic substances are formed; these poisons act (1) after a certain accumulation has taken place, as paralysants of the brain inducing coma, and (2) as destroyers of protoplasm.

It may be asserted that acetonuria and diaceturia appear whenever for any reason a diabetic is unable to take as much nourishment as his need demands, and as a warning to attend carefully to the regulation of the diet; the excretion of oxybutyric acid is of the gravest prognostic import, as it renders the speedy onset of coma very probable.

MINERAL CONSTITUENTS of the urine,—sodium chloride, and sulphuric and phosphoric acids,—are usually present in increased quantities in the urine of diabetics.
PNEUMATURIA.—In rare cases of diabetes, air is voided with the urine in both sexes. It may be caused, of course, by the entrance of atmospheric air, or of intestinal gases into the bladder, when any lesion of these parts has led to the formation of a fistula.

In other cases it may arise from the formation of gas in the bladder itself, in consequence of decomposition or fermentation processes, due to the action of micro-organisms upon the sugar.

SUGAR.—The sugar which appears in the urine is dextrose. It is present in varying amounts: in mild cases it does not exceed one and a half or two per cent., but it may reach from 5 to 10 per cent. or more. The total amount excreted in the twenty-four hours may range from 10 to 20 ounces, and in exceptional cases from 1 to 2 pounds.

Sometimes the patient, before he has become aware of his condition, has been struck by the way flies have been attracted to his urine; also by the fact that if a drop has fallen on to his boot, or any adjacent object, and has been allowed to dry, a salt-like deposit is left behind.

The sugar increases after food, in mild cases, and diminishes during fasting: hence the excretion is less during the night,—indeed, it may be absent from the urine passed before breakfast.

Muscular exercise diminishes the sugar excretion in well-nourished patients suffering from a mild form, or early stage of the disease; but when the case is a severe one and the patient is wasted, the sugar excretion is increased by exercise.

DIGESTIVE SYSTEM.

MOUTH AND THROAT.

One of the most distressing symptoms in diabetes is THIRST, and large quantities of water are required to keep the sugar in solution and for its excretion in the urine. Instances are on record of pronounced cases of diabetes in which the thirst was not excessive. The amount of fluid consumed bears a definite ratio to the quantity excreted. The thirst is most intense an hour or two after meals.

Excessive HUNGER—polyphagia or bulimia—is a common symptom in the severe stage of diabetes, and is a favourable manifestation, as it enables the patient to make good the loss of glucose and helps to mitigate the consequences of the
protoplasmic disintegration taking place in the tissues.

In certain mild cases the appetite is not increased, whilst in severe cases at a late stage it fails.

The SALIVA is, as a rule, scanty and poor in ferment, and the mouth shows an obstinate tendency to become dry; in others the secretion is normal, and in some cases even excessive. Sugar is said to have been found in the saliva. The buccal secretion gives, as a rule, an acid reaction.

Weakness, and even total loss, of the function of TASTE has been noted.

The TONGUE is frequently dry in mild cases, or it may be little changed from the normal: in severe or advanced cases it is dry, and marked off by deep furrows and rectangular areas. The base is often covered with a brown or black coating, while the apex may be abnormally red.

The TEETH are, as a rule, carious; they become loose, and readily fall out.

The GUMS are frequently affected, and little whitish patches - due to colonies of the Oidium albicans - are often seen; gingivitis is not infrequently present, as is also alveolar periostitis.

Evidently the cause of these troubles of the teeth and gums is due to the lowered power of resistance of the tissues to attack by the schizomycetes.

STOMACH.

As already stated, the APPETITE is frequently excessive. Some patients are liable to periodical attacks of GASTRITIS; and GASTRIC CRISIS, resembling those of tabes dorsalis, are not rare.

DILATATION OF THE STOMACH is not infrequently observed; there is usually a simple enlargement - the evacuation of the stomach not being delayed or interfered with, though sometimes there is weakening of the muscular coat leading to motor insufficiency. Gastric dilatation is especially present in those who have gone for a considerable period without treatment, and who, in order to cover the loss of sugar, have taken enormous quantities of food.

GASTRIC ULCER is seldom present.

The SECREATION OF HYDROCHLORIC ACID has been examined by Honigmann, Rosenstein and Gans in 28 cases of diabetes, but without the enunciation of any law; they found the secretion of gastric juice usually below the normal; and a diminution, if it occurs, is to be referred, according to Rosenstein,
to nervous influences

In most cases, in the absence of intestinal catarrh, the bowels are regular; there may be a slight tendency to constipation; a loose condition of the bowels is not uncommon; and here it must be remembered that the diabetic diet is not very digestible and contains a large amount of vegetable material, which acts as a mechanical irritant to the gastro-intestinal mucous membrane.

Frequent attacks of diarrhoea may occur in consequence of acute intestinal catarrh: this interferes with nourishment, and it is known that coma is a frequent sequel of acute catarrhal enteritis. Opinions differ as to whether (a) the diarrhoea is the first symptom of the threatening coma, or (b) the toxic substances formed in the intestinal canal during a catarrhal attack are absorbed, and induce coma, or (c) the coma is a result of the general depression and interference with nutrition associated with enteritis.

On the other hand, Schmitz has drawn attention to the fact that coma is a frequent sequel to long-continued constipation.

The faeces may contain much fat, and then the stools are frequent, pulpy, of a dirty-gray colour, and very offensive. This condition of fatty stools may happen in disorders of the pancreatic secretion, and in stoppage of the biliary passages; microscopical examination shows the presence of large fat globules, crystals of soap, and fatty acids and muscular fibres.

Hirschfeld recorded an average of 35.2 per cent. ash, 51.8 per cent. nitrogenous substances, and 34.8 per cent. fat, which had been taken in by the mouth, in the faeces: the normal figures are from 6 to 7 per cent.

Anatomical changes in the intestinal walls are very rare; catarrhal lesions of the mucous membrane and brown atrophy have been observed in the muscular coat.

LIVER.

Mention has already been made of the rarity of morbid phenomena on the part of the liver, although the organ not infrequently shows a moderate enlargement in corpulent persons. In these instances there is nearly
always, besides the fatty infiltration, some venous hyperemia which is probably due more to the disturbance of the circulation caused by the obesity than to any influence of the diabetes.

Jaundice is present in some cases.

Gall-stones are frequently met with in corpulent persons; Bouchard observed them in 10 per cent. of his cases.

Naunyn does not believe that there is any intrinsic relation between gall-stones and diabetes.

Marie has seen a pigmentary hypertrophic cirrhosis, regarding which he publishes 9 cases.

**PANCREAS.**

The etiological significance of pancreatic changes has already been demonstrated; and here it is necessary to see whether pancreatic diabetes betrays itself by any special signs.

In this connection von Noorden lays stress upon the following symptoms: (a) Existence of a pancreatic tumour; (b) severe colic which cannot be referred to the kidney or the liver, but which by its location raises the suspicion of a calculus in the duct of Wirsung (Fleiner, Lichtheim, Holtzmann; (c) excretion of maltose in the urine - a symptom only being observed on one or two occasions by le Nobel and von Ackeren; (d) steatorrhoea without jaundice; (e) azotorrhoea or the passage of large quantities of nitrogenous substances in the faeces.

The occurrence of the symptoms and a diagnosis of the condition presuppose not only that the internal secretion of the pancreas is interfered with, but that there are also gross anatomical changes present.

**SKIN.**

The secretion of the sebaceous and sudoriferous glands is diminished, and the skin itself, as a result, is dry and harsh; it is also, in advanced cases, atrophied and thin and glossy-looking.

Diabetics are especially prone to certain forms of skin disease: these are either local affections or general dermatoses.

The local lesions affect the orifices of the urinary
passage, the external genitals and the neighbouring parts of
the skin. In males the meatus is often abnormally red;
erythema may occur and affect the glans, prepuce and penis,
and may spread to the scrotum and thighs.

In the female the condition of affairs is well
illustrated by the following case:

A lady, aged 64, had occasion to come under the
writer’s observation. She was very stout, and had led an
indolent and luxurious life. The family history was of a
gouty nature.

She had, for some time before consulting her medical
attendant, noticed redness and swelling of the external
genitals, and had suffered considerably from itching, which
at times was so severe as to prevent her leaving home. She had
tried many remedies, powders, ointments, lotions and baths;
but, deriving no benefit therefrom, she at last sought
advice.

The external genitals were swollen, red and excoriated,
and the erythematous condition had spread over the skin
round the perineum, involving the contiguous aspects of the
thighs.

The itching is due to a growth of hypomycetes.
The general skin diseases associated with diabetes are
numerous, and such as erythema, eczema, herpes,
lichen, psoriasis, urticaria, thrush, seborrhoea, and acne.

Davies Pryce has described an erythematous oedema,
which he refers to the existence of a neuritis.

Diabetics are more susceptible to these diseases than
other people; and when the disease occurs, it is apt to be
accentuated in its severity and of longer duration.

Of all the skin lesions boils and carbuncles
are the commonest; furunculosis occurs in both
mild and severe cases, in the early and late stages, when
the patient is on an animal as well as a carbohydrate diet.

Carbuncles are not quite so common, and have
their origin in cracks of the skin.

A point of importance in the cutaneous affections of
diabetes is the possibility of gangrene resulting;
this may come on suddenly from a trifling cause in persons
to all appearance in good health; it may occur in the form
of small areas of superficial necrosis, or may involve a large
surface and give rise to serious destruction of tissue.
Gangrene is usually found in persons about 60, and it may occur spontaneously and spread from a pre-existing ulcer; it may attack any part of the body, but usually the lower extremities.

The nails sometimes show distinct alterations. Paronychia is not rare, and may cause the nails to fall out; they may become thick, brittle and discoloured.

NERVOUS SYSTEM.

DIABETIC COMA.

This condition was first described by Küssmaul in 1874; it may occur in both sexes and at any age, but is more common in the young.

It is the most frequent termination of diabetes, which is not dependent upon any gross lesion of the organs.

The direct causes are fatigue, excitement, exposure to cold, and any intercurrent acute disease; great muscular exertion, mental worry and excitement are also excitants. A sudden change of diet, and a very rigid diet, are thought by many [Abstein, Naunyn, Schmitz and Grube] to favour its development when the patient is suffering from a severe form of the disease, and when the urine gives a marked reaction with perchloride of iron. Prolonged constipation is a likely predisposing cause, and many cases are on record in which surgical operations have appeared to be exciting causes.

Von Noorden regards E-oxybutyric acid as the true cause of the coma; but Hogue, Devie and Hugueneng failed to find any trace of this body in the exhaustive examination of their case.

Küssmaul's original suggestion, that it is due to poisoning by acetone, has not been proved.

Latham thought that the poison might be paraldehyde; Senator has advocated trimethylamine as the cause; but neither poison has been demonstrated.

Other investigators regard the condition as uræmia; but the classical symptoms of uræmic coma are different in many respects.

Fat embolism has been suggested as a cause; and, according to Schmitz, the symptoms are due to a ptomaine formed in the intestine owing to obstinate constipation.

The almost universal opinion now is that the coma is due to an acid intoxication, or, as Naunyn
terms it, an acidosis; and the offending agent is believed to be \( \text{B-ox} \text{ybut} \text{yric acid} \), which accumulates in the tissues and blood in large quantities, and is eliminated in the urine with various base-forming elements, but never free.

Acidosis may occur in all cases in which the liver is excessively fatty; and as acetone bodies are chiefly formed from fat, it is, as Guthrie points out, reasonable to suppose that their origin in these cases is in the fat in the liver and tissues.

In 1884, Stadelmann, Kulz, and Winkowski almost simultaneously found this acid in the urine of patients with diabetic coma.

The amount of the acid excreted in the twenty-four hours may be enormous: Kulz found in 3 cases 67, 100, and 226 grammes respectively.

The symptoms of diabetic coma often commence with lassitude, epigastric pain, nausea, and occasional vomiting; in other cases shortness of breath is the earliest symptom, and it has occasionally preceded the other symptoms for several days.

Headache may occur at the onset. Often the patient is anxious, restless, or excited at first, then drowsiness gradually develops, and passes into coma; the pulse becomes rapid and feeble,—and Lépine regards rapidity of the pulse as an important early sign of commencing coma.

Dyspnoea is usually a prominent symptom, and the breathing has a peculiar panting or sighing character; the number of respirations per minute is normal, or but slightly increased, the inspiration and expiration being deep rather than rapid; Küssmaul termed the condition "air-hunger."

The skin becomes pale and cold, and cyanosis of the nose, lips, ears, hands and feet may be present.

The temperature is generally subnormal, but in a few cases it is raised.

The breath has a chloroform-like odour usually, and acetone has been found in the expired air.

The acidity of the urine is increased, but the quantity of urine and the amount of sugar excreted usually diminishes with the onset of coma; the urine voided smells of chloroform.

A trace of albumin is invariably present, according to some writers, in the urine; and we have it on the authority of Kulz that casts are always found, and that they denote
the onset of coma; they are finely granular or hyaline.

The urine gives a dark reddish-brown colouration with perchloride of iron in coma (Gerhardt’s reaction).

Acetone is present, the amount of ammonia is increased, and, according to Stadlemann, B-oxbutyric acid is always to be found.

The alkalinity of the blood is said to be much decreased, and the blood decolourises with an alkaline methylene-blue solution, as mentioned before.

The knee-jerks are absent in the majority of cases.

The coma may be complete, or the patient in other cases can be roused up to the last.

The description just given represents the common, or Kussmaul’s, form of diabetic coma.

The following are the notes made by the writer in a case of diabetic coma under his care:

The patient, a man of 35 years, had suffered from diabetes for close on six months; he was losing flesh rapidly, as much as 20 lbs., having been lost during the two weeks prior to the writer seeing him. His chief complaint was of extreme weakness and of intense thirst; the appetite was rather above the normal. The mouth was very dry, the tongue coated, and the teeth nearly all carious; the skin was dry—otherwise it presented nothing abnormal.

The bowels were constipated, and the temperature was normal.

The amount of urine passed daily was from 114 to 115 ounces, and it contained 26 grains to the ounce of sugar.

There was no sign of pulmonary disease.

It was, after a month’s treatment, evident that neither diet nor drugs had any marked effect on the quantity of his urine or the sugar contained therein.

He complained, four months later, of pain in the left side; and on examination friction sounds and râles were audible over the left upper front, and the left apex was found to be solid. Tubercle bacilli were present in the sputum.

Ten days later, marked failure of strength was noticeable, and the patient showed signs of drowsiness; he took no interest in anything, and he could with difficulty be aroused.

There is a marked odour of acetone near the bedside, and the urine gives Gerhardt’s reaction. Temperature 101.4°F.

There is a good deal of hiccough, and he is markedly
dyspnoeic; the pulse is 122 and weak, but there is no cyanosis.

Eight hours later, the coma is deepening, and the dyspnoea increasing - the patient cannot be roused and the conjunctival reflexes are absent.

About four pints of saline solution, at a temperature of 105°F., were then injected into the median basilic vein; the pulse at once became much stronger and decreased in frequency; the dyspnoea almost disappeared; he came out of the comatose state, and was able, half an hour after the operation, to talk and answer simple questions.

The temperature, which rose immediately after the injection to 102.2°F., fell rapidly to 99°F., and the respirations decreased from 42 to 30 per minute.

This improvement was maintained for six days, when he began to pass his motions and urine in bed; delirium appeared, and his temperature was 99°F.

He was still delirious on the following day, again becoming dyspnoeic, and still passing his urine and faeces as he lay. Three pints of saline solution were injected into the other median basilic vein: this was again followed by improvement, but not so marked as after the first injection. The temperature again rose after the operation to 102.6°F., but subsequently fell to 98.2°F.

The delirium continued for from five to six hours, but kept decreasing during that time; and at the end of eight hours he was almost rational, the dyspnoea had gone, and he could retain his urine, though still continuing to pass his motions in bed.

The next day he again relapsed, and in the evening his temperature rose to 104°F.; on examination of the chest, it was found that the tubercular process had extended over the whole of the left lung.

The dyspnoea was more marked than at any previous time, and he was gradually losing consciousness; the pulse was 124 and very feeble.

Five pints of saline solution were again injected, and this procedure was followed by a pulse-rate of 160, a temperature of close on 105°F., and respirations 58 per minute.

Sodium bicarbonate and sodium salicylate were given in large doses every two hours: the temperature, pulse and respirations gradually fell towards the normal, and eight hours after the operation there was neither dyspnoea nor
coma present.

The patient died the following evening, having had no return of the dyspnoea or coma.

There are two SUB-VARIETIES of Kössmaul's diabetic coma:—

(1) The ALCOHOLIC FORM, in which the patient is very excited at the onset and behaves like a drunken man. The pulse is rapid, coma develops, and soon death occurs. Gerhardt's reaction is present, the breath has the acetone odour, but dyspnoea is absent or slight.

(2) DIABETIC COLLAPSE, - a condition described by Dreschfeld and Frerichs, - is that in which the patient suddenly becomes drowsy, the extremities and face turn cold and livid, the pulse becomes quick and small, and coma develops. The temperature is subnormal, the acetone odour of the breath is absent, and the urine does not give Gerhardt's reaction.

PSYCHICAL DISTURBANCES.

Psychical symptoms are commonly present; and it is usual to meet with listlessness and depression of spirits, weakness of mind, and irritability of temper; melancholia with suicidal tendencies may occur, and it is said that depression occasionally alternates with the glycosuria; profound melancholia may be present just before the coma sets in.

In certain rare cases of diabetes, symptoms arise that resemble those due to disease of the central nervous system - such as hemiplegia, aphasia, hemianopsia, localised convulsions (similar to those due to Jacksonian epilepsy), ptosis and strabismus. These disturbances may subside or lead to a fatal issue - in the latter case post-mortem examination revealing little or no lesion.

Diseases of the brain and spinal cord, due to a central lesion or systemic disease, are hardly ever immediately dependent upon diabetes.

Symptoms of spinal cord disease, - such as lightning pains, girdle sensation, gastric crises, and even the Argyll-Robertson pupil, - may be present.

In some cases of true tabes dorsalis, glycosuria has been noticed.

When we take into account the recent observations of Williamson, who found sclerotic changes in the posterior
columns of the spinal cord of patients dying from diabetes, it is not to be wondered at that such symptoms arise now and then.

The most important form of peripheral nervous disease is neuritis; its significance was first appreciated by von Ziemssen and Auché, and others have confirmed the clinical diagnosis by autopsial findings.

These sensory symptoms are the earliest, and in mild cases the only ones: they are paraesthesia, hyperaesthesia, and anaesthesia of varied degree and location, pains and cramps in the calves of the legs, especially at night, and neuralgia.

The diabetic neuralgias are often very obstinate and painful, and occur most frequently in the lower limbs; the upper extremity may be affected and the trunk, and when this is the case the pain may closely resemble the girdle pain of tabes and other spinal cord diseases.

In many cases there are muscular wasting, tender nerve trunks, glossy skin, loss of hair and nails, and altered electrical reactions pointing to a definite peripheral neuritis affecting mixed nerves.

Other disturbances noticed are local oedema, hyperidrosis, herpes, pemphigus and gangrene.

The rectum and bladder are not affected.

The knee-jerks are often absent in diabetics; the absence thereof was noted by Bouchard in 37 per cent., by Maschka in 30.6, by Auerbach in 35 to 40, by Williamson in 50, and by Grube in 7.6 per cent.; but this is of no value in a prognostic sense (Rosensen, Grube).

ORGANS OF SPECIAL SENSE.

OCULAR MANIFESTATIONS are rarely met with in the early stages of diabetes, but are not uncommon in the acute and chronic cases; the common symptoms are cataract and retinitis — the latter being the rarer finding.

Oedema of the retina may be present in acute cases, and vitreous opacities are not infrequently observed. There is a tendency to hemorrhages.

Optic neuritis may be noticed, and amblyopia also; paralysis of the ocular muscles is said to occur in 7 per cent. of diabetics.

Other conditions are rare.

Blunting of the senses of SMALL and TASTE have been
DEAFNESS, due to otitis media or to edematous swelling of the Eustachian tube lining, may occur; diabetic otitis may develop, and is characterised by severe pain in the mastoid region, tinnitus, and deafness.

In some cases nerve-deafness has been observed.

**RESPIRATORY SYSTEM**

The odour of acetone is important in denoting a severe stage of the disease.

Statistics published by Seegen show that, out of 32 cases of diabetes, pulmonary complications were present in 73.

Tuberculosis is by far the most common complication. It is more frequently met with amongst hospital than amongst private patients; it is rare in the old and gouty and in the milder cases, but is a frequent accident in the young and in severe cases. When it occurs, extensive caseation is common, and the evidence of efforts at repair - so prominent in most cases of chronic tuberculosis - are wanting.

Miliary tuberculosis is said to be rare in diabetes.

Non-tubercular phthisis is very rare and quite exceptional.

The site occupied is usually that typical of tuberculosis. Cough is not a marked symptom, expectoration is usually scanty, fever is slight, and haemoptysis is rare.

In the case, already recorded, of coma there was practically no cough present, there was no haemoptysis, little expectoration, and moderate fever.

Gangrene, according to von Noorden, is not uncommon, and is at times a cause of death. He recognises two types: (a) an acute form with high fever, and (b) a subacute or chronic form in older people.

In the acute form, the physical signs are those of pneumonia; the sputum is bloody, but rarely fetid.

In the chronic type, fetor may be present. The physical signs are those of catarrh.

Pneumonia complicating diabetes usually results in speedy death.
CIRCULATION.

The pulse is usually normal, though it is said to be increased in frequency in 75 per cent. of all cases of severe diabetes.

In elderly persons, often signs of arterio-sclerosis and high tension are met with; sometimes the pulse is large, hard, and of increased tension in diabetics under middle age, even when there are no evidences of kidney disease.

Usually there are no signs of heart disease, but in the late stages of the affection the heart's action and sounds are often feeble.

Diabetic endocarditis is rare, and it usually affects the mitral valves.

Heart failure, due to fatty and fibroid degeneration, is common, and it may be associated with attacks of dyspnea, faintness or angina pectoris.

REPRODUCTIVE ORGANS.

Atrophy of the uterus and ovaries and testicles has been noted in occasional instances.

In the male, diminution or loss of sexual power is not uncommon.

In females, sexual desire is said to be diminished greatly in severe cases; but in mild cases in elderly women it is said to be increased.

Amenorrhea may occur, and pregnant diabetic women not infrequently abort; whilst the disease often advances markedly during pregnancy and in the puerperal state.

LYMPHATIC GLANDS.

The lymphatic glands are often swollen, especially in the severe cases of diabetes. The glands are hard and painless. The etiology of the condition is not known.

DIABETES IN ASSOCIATION WITH OTHER AFFECTIONS.

Diabetics appear to be susceptible to the poison of enteric fever, but the attacks are mild; during the fever the sugar generally disappears.

Rheumatic pains are common in diabetes,
and Dupuytren's contraction of the palmar fascia has been repeatedly observed.

Some authorities believe that diabetes disposes to the formation of tumours, but when they occur, they grow slowly.

* * * * * * *

THE COURSE, DURATION, AND TERMINATION OF DIABETES

In mild cases, under the influence of a restricted or rigid diet, the symptoms may entirely disappear, but they usually return when ordinary diet is resumed.

In elderly people the disease makes slow progress, and it lasts for many years.

In children and young persons, diabetes is generally an acute and rapidly fatal disease, lasting in some cases but a few weeks or months, and at most one or two years.

In rare instances diabetes is associated with symptoms of nephritis, and the diabetic symptoms may gradually subside - those of the renal inflammation remaining.

Occasionally, but very rarely, the symptoms of diabetes mellitus give place to those of diabetes insipidus.

The fatal termination in diabetes mellitus is more frequently by coma.

Death occurs in many cases as a result of one or other of the complications already described, of which pulmonary tuberculosis is the most common.

In many cases the accidents that precede death come on more or less suddenly from some slight cause - such as fatigue, excitement or a chill.

Any acute infectious disease is very liable to terminate fatally in diabetes.

The disease generally proves fatal, though instances of alleged recovery are reported in which the disease appeared to have been induced by eating excessive quantities of sugar; in such individuals, however, the glycosuria tends to recur, so that there is probably some underlying tendency to diabetes.

Schmitz considers spontaneous sweating a favourable sign.

Cases which occur in women about the climacteric period end in recovery more frequently than other forms.
Klein reports three cases of recovery from diabetes, in which sugar had been excreted in pathological quantities.
**DIAGNOSIS.**

The diagnosis of diabetes mellitus is usually easy, and is made chiefly by the urine tests presently to be described. The diagnosis may be overlooked, and the patient treated for wasting or one of the complications Deception may be practised by the patient; and one case is on record in which a woman bought cane-sugar and injected it into her bladder.

As stated in the definition, the sugar must be grape-sugar, and its excretion must be continued for a certain length of time, and follow the ingestion of moderate amounts of carbohydrates.

More than one test must be used, and if any doubt is present, the fermentation, the most reliable single test, must be made.

If the patient is in a comatose state when first seen, and the urine cannot be obtained, the reaction of the blood with methylene-blue is diagnostic.

The TESTS FOR THE DETECTION OF GRAPE-SUGAR in the urine are provisional and positive:

The provisional tests are so named because the reaction may be caused by the presence of substances other than sugar; they are Trommer's, Nylander's, and Moore's.

If all three, especially Nylander's, give a negative result, then any further test is unnecessary; if they all give positive results, the presence of sugar is very probable; still it is better to have the evidence of other tests, and this is necessary when the provisional tests have given uncertain or contradictory results.

(a) Nylander's Test.

Nylander's solution is prepared by dissolving 4 grammes of Rochelle salt in 100 c.c. of a 10 per cent. caustic soda solution, adding 2 grammes of bismuth subnitrate, and digesting on the water-bath until as much of the bismuth salt is dissolved as possible. To 10 c.c. of urine add 1 c.c. of the Nylander's solution, and boil for a few minutes: if glucose be present, a black deposit of bismuth occurs.

(b) Trommer's Test.

To a dram of urine in a test-tube add a few drops of a dilute copper-sulphate solution, and then as much liquor potassae as urine. On boiling, the copper is reduced if
sugar be present, forming the yellow or orange-red suboxide.

There are certain fallacies in the copper test: for gluconic acid, which reduces copper, is met with in the urine after the use of chloral, phenacetine, morphia, chloroform, and other drugs. Alcaptonuria may also be a source of error.

(c) Moore's Test.

3 c.c. of a 10 per cent. solution of caustic potash and 10 c.c. of the suspected urine are mixed together; the upper portion of the fluid is then heated one minute. If sugar is present in the proportion of at least 0.5 per cent., the heated layer becomes of a brown colour, which grows darker with further heating. Normal urine shows under the same conditions only a dark-yellow colouration.

The following are the positive tests:

(a) Fermentation Test.

To 30 c.c. of the suspected urine a piece of ordinary yeast, the size of a pea, or better a small quantity of a pure culture of saccharomyces apiculatus, is added, and the whole well shaken. Then the urine is poured into a so-called "fermentation-tube" and set aside in a warm place (20° to 30°C.). If much sugar be present (0.5 per cent. or more), a large quantity of carbonic acid gas will have collected by the end of two hours at the upper extremity of the tube; if but little sugar is present, it will be necessary to wait from five to eighteen hours. The formation of gas is very evident when not more than 0.15 per cent. of sugar is present in the urine. The yeast fungus spits up the grape-sugar into alcohol and CO₂.

It is advisable for comparison to place another glass containing normal urine and yeast alongside the first one.

(b) E. Fischer's Phenylhydrozin Test.

10 c.c. of urine and 2 drops of a saturated solution of neutral acetate of lead are mixed and filtered; the filtrate is acidulated with one drop of glacial acetic acid, and to it are added a piece the size of a pea of phenylhydrozin, and one the size of a bean of sodium acetate. The test-tube is then placed in a water-bath for an hour and heated. At the end of this time, if sugar be present, there will be formed a yellow precipitate, in which there can be seen under the microscope a cluster of long, yellow and needle-shaped crystals, which consist of phenylglycosazon and
indicative of sugar.

(c) *Rubner's Test.*

10 c.c. of urine are mixed with an equal amount of a concentrated solution of neutral acetate of lead, and filtered; to the filtrate ammonia is added, drop by drop, until a thick cheesy precipitate is formed; it is then cautiously heated up to not more than 80°C. When grape-sugar is present the previously white precipitate is coloured a rose-red, and further heating changes the colour to a coffee-brown.

A positive reaction is obtained when sugar is present in the proportion of at least 0.25 per cent.

(d) The Circumpolarization Test.

Solutions of grape-sugar have the property of turning the plane of polarization — i.e., the polarized light is turned to the right. In order to examine the urine for this property, we may use either the saccharometer of Soleil-Ventzke, or the so-called half-shadow apparatus of Laurent, Lippich, and others. Marked dextrorotation of polarized light always points to the presence of grape-sugar; a slight dextrorotation may be caused by milk-sugar, by compounds of glycuronic acid, and by many medicinal substances. Saccharine urine may lose the property of dextrorotation when at the same time levorotatory substances are present in the urine, such as oxybutyric acid and many drugs, including such substances as levulose.

**QUANTITATIVE EXAMINATION FOR GRAPE-SUGAR.**

(a) By Means of Polarization.

The different saccharometers either indicate directly on a scale the percentage of sugar in the urine, or mark only the degree of rotation of the polarized light; in the latter case an accompanying table shows to what percentage of sugar the degree of rotation corresponds.

(b) By *Fehling's Solution.*

This procedure is carried out as follows:

1. A solution of 34.659 grammes of pure crystallised sulphate of copper in 500 c.c. of water, and
2. 173 grammes of sodium sulphate are dissolved in 350 c.c. pure caustic soda, of a specific gravity of 1.14, and water is added to bring the entire amount up to 500 c.c.
3. Before being used, a mixture is made of 10 c.c. of each of the two solutions.

Upon boiling a thin solution of grape-sugar with
Fehling's solution, the copper sulphate is reduced to red copper oxide — exactly 0.05 grammes of grape-sugar being necessary to reduce completely 10 c.c. of Fehling's solution.

To perform the estimation, 10 c.c. of Fehling's solution are measured off, diluted to 50 c.c. with distilled water, and boiled in a capsule. 10 c.c. of urine are now measured off, diluted, and well mixed with 9 volumes of distilled water; a burette is then filled with the diluted urine to zero on the scale. When the Fehling's solution begins to boil, the diluted urine should be run into it, drop by drop, until the blue colour entirely disappears and the whole of the copper is reduced.

The calculation is then made thus: Supposing 20 c.c. of diluted urine have been used to reduce 10 c.c. of Fehling's solution, which is equal to 0.05 grape-sugar, the percentage is $\frac{0.05 \times 100}{20} = 0.25$. But as the urine was diluted ten times, $0.25 \times 10 = 2.5$ per cent.

(c) By Means of Aerometry and Fermentation.

The specific gravity of saccharine urine is reduced by fermentation, as the heavy sugar is taken away, and light alcohol is formed in the fluid; Roberts and others have determined experimentally to what percentage of sugar a definite decrease in specific gravity following fermentation corresponds.

After the specific gravity has been ascertained, the yeast is added, and the mixture is set aside in a temperature of from 26 to 30°C.

The fermentation should be carried on until the urine gives no sugar reaction, and then the specific gravity is again taken.

The difference of specific gravity multiplied by 430 gives the percentage of sugar in the urine.

A C T I O N may be most readily detected in the urine by the Nobel's method: A few drops of a weak solution of nitro-prusside of sodium (1 per cent.), rendered alkaline by addition of ammonia, are added to the urine, which turns to an amethyst colour in the presence of acetone. On boiling and acidulation, this colour changes to a greenish-blue.

In Legal's test caustic potash takes the place of ammonia, and the resulting colour is red, which disappears on standing; on the addition of acetic acid a deep-violet colour is produced.
Lieben's test, as modified by Halfe, is performed by floating a drachm of urine upon a drachm of liquor potassa containing 20 grains of iodide of potassium, and previously boiled in the test-tube. In the presence of acetone the phosphatic ring, which forms at the point of contact, turns yellow, or is studded with yellow points from the formation of crystals of iodoform.

The ferric chloride reaction is the name given to the Burgundy-red colouration assumed by urines on the addition of a few drops of the solution of the perchloride of iron; it is probable that the cause of this reaction in diabetic urine is the presence of diacetic acid.

Many other, more or less nearly allied substances, also give this reaction; and the reaction of diacetic acid may be distinguished by boiling another specimen of the urine before applying the test; as this acid is driven off by heat, the reaction should fail.

In the quantitative analysis, not only the amount of already existing acetone, but also of that formed by the splitting up of diacetic acid has to be determined.

Add one drop of glacial acetic acid to 100 c.c. of urine and distil, the receiver and tube being kept very cool, until three-quarters of the entire amount has passed over; the distillate is treated with 5 drops of dilute sulphuric acid, and after a few crystals of urea are added, is again distilled - the receiver and tube being cooled as before. To the second distillate caustic potash is first added, and then compound solution of iodine in excess; a precipitate of iodoform is thrown down, which is collected at the end of six hours, on a weighed filter, and washed with distilled water. After the filter and precipitate have been allowed to dry on the air, they are placed in an exsiccator with sulphuric acid, and weighed at the end of one and a half to two hours. One grain of iodoform represents 0.147 gm. of acetone. By reason of the volatility of iodoform, the loss of a small amount cannot be avoided. Another source of error arises: for when the patient has been taking large doses of alcohol, a certain amount will always pass off in the urine, and will give the same reaction as acetone in the distillate.

Diacetic acid may be detected, as already shown, by Gerhardt's reaction: its presence is of more importance than is that of acetone, and is indicative of a severe form of the disease. It is usually found in cases of
diabetic coma.

In testing for diacetic acid perfectly fresh urine should be used, as it rapidly becomes broken up into acetone and carbonic acid.

**Beta-Oxybutyric Acid** is held to be the cause of diabetic coma by its power of lessening the alkalinity of the blood. If diacetic acid is not present, the absence of this acid may be inferred, as they always occur together.

The presence of this acid is rendered probable:

1. When Fehling's titrate method gives evidence of the presence of considerably larger amounts of sugar than does the polarisation test. Grape-sugar rotates the plane of polarisation to the right, oxybutyric acid to the left. When, therefore, oxybutyric acid is present in considerable quantity, a part of the dextrorotatory power of the grape-sugar is nullified, or it may be even that there is so much oxybutyric acid that the plane of polarisation is rotated to the left.

2. When the urine, after complete fermentation with yeast, is found to be levorotatory.

3. When the urine, after precipitation with basic acetate of lead and ammonia, is levorotatory.

The application of these methods, von Noorden says, when it gives a positive result, renders the presence of oxybutyric acid very probable.

The determination of the presence of this acid can only be performed with certainty by a difficult and prolonged chemical process.
The prognosis of diabetes mellitus chiefly depends on the form of the disease and the age of the patient, and is practically hopeless in young persons and in the severe forms of the affection.

Favourable prognostic signs are: the association of obesity or gout, as already pointed out; long duration of the disease, prior to the time of observation, without much wasting; onset of the condition late in life; mild forms of the disease, especially if the excretion of sugar can be checked by a rigid diet; gradually increasing tolerance of carbohydrates; the occurrence of the disease after injury or acute diseases; syphilitic origin of the diabetes; favourable social conditions; and freedom from worry.

Other points in the patient's favour are: early treatment; onset of the affection at the climacteric period in females; sufficiently strong will-power to enable the patient to adhere strictly to the regulated diet.

Unfavourable indications are: onset of the disease in early life, and especially in childhood; marked wasting and loss of strength; poverty which renders impossible the carrying out of dietetic treatment, or the avoidance of bodily and mental overwork; a family history of the disease; the appearance of secondary accidents and complications; signs of commencing coma; Gerhardt's perchloride of iron reaction; complete, or almost complete, intolerance of the carbohydrates; the presence of any marked amount of albumin in the urine, and especially if casts are found present; the absence of the knee-jerk is regarded by some as of grave import, but experience has disproved this opinion.

With the exception of the one case which died from pulmonary complication, all the writer's cases of diabetes, so far as recorded, have been of favourable import; they followed shock, acute infectious diseases, whilst others were associated with gout and obesity.
TREATMENT.

In the treatment of every case of diabetes mellitus it is necessary to bear in mind that adherence to any fixed routine may result disastrously for the patient: some are benefited by means which are harmful to others, and it becomes imperative to study the needs of each case individually.

It is not right, or just to any patient who comes for guidance and advice to supply a stereotyped diet-table from one of the text-books or pamphlets of one of the many firms manufacturing diabetic foods, and present along with it a prescription for some preparation of opium or one of its alkaloids - a course of procedure which seems only too common amongst medical men engaged in general practice.

PROPHYLAXIS

Prophylactic measures may be adopted with advantage by members of families in which there is direct diabetic hereditary predisposition. In such cases it is a wise precaution to limit the ingestion of carbohydrate food, though whether this has, or has not, any effect in preventing the development of the disease is not known.

In such families proper hygiene should be insisted upon; outdoor games should be encouraged; over-fatigue and catching cold are to be guarded against; the living-rooms must be plentifully supplied with fresh air; sources of worry should be avoided; and a quiet and even life, in as equable a climate as possible, ought to be led.

Personal hygiene is of great importance. The body must be suitably clothed, and preferably in light woollen garments; these garments should be changed at least once a week, and the socks or stockings every day, if possible. If, from any cause, the body gets overheated and the flannels become moist from the absorption of perspiration, the entire under-garments should be removed and fresh ones put on. Every care should be taken to promote a healthy action of the skin; a lukewarm or, if fairly robust, a cold bath ought to be taken every day, and an occasional Turkish bath - about once a month - will be found most beneficial. When the patient's instinct of cleanliness cannot be relied upon, strict orders should be
given concerning the care of the skin.

A daily evacuation of the bowels is important, and any tendency to constipation is to be overcome by bodily exercise; a well-regulated diet, and, if necessary, suitable doses of castor-oil, calomel, and similar drugs may be prescribed; and a regular time each day should be set aside for the purpose of evacuation of the bowels.

In individuals who, on account of their social position, live luxurious lives, and who, in the prime of life, show a marked tendency towards corpulence, and in whose family history there is a diabetic taint, a gradual withdrawal of carbohydrates from the diet is to be recommended; but a too-energetic reduction-treatment ought not to be carried out for fear of weakening the resisting powers of the patient unduly. Muscular exercise in such individuals is of great importance, but should in all cases be short of fatigue: such exercise may consist of walking, cycling, rowing, riding, gymnastics, golf, and tennis. If active exercise cannot be undertaken, passive movements and massage may be employed.

Muscular exercise often causes an increased tolerance of carbohydrates — not only during the performance of the exercise, but perhaps for months afterwards.

In members of families with a neuropathic predisposition, prophylactic measures,— on the lines of prevention of shock and fright, especially amongst children, strains of all kinds, overwork, fatiguing and enervating pleasures, and too early or excessive sexual activity,— are more or less necessary.

For those who are able to afford it, change of climate, in the winter to a warm and sunny country, is desirable; here the patient should avoid large cities and enclosed places, and the more the climatic conditions permit of sitting and walking about in the open air, the greater will be the benefit arising therefrom. Travelling about from place to place is to be avoided. Many will be well at warm and sheltered seaside resorts, and to others — especially young and middle-aged patients — a sojourn in some sunny Alpine resort, will be of very great service.

Great benefit can be derived from a course of waters and baths — both at home and at the foreign spas. Adjuvants to the treatment at these resorts are the pleasant surroundings, the freedom from domestic and business cares, and the amount of time spent in the open air. The very young, the
aged, and those suffering from a very severe form of diabetes should not be sent to such places; also may be here included those in whom there is a complicating nephritis.

The cases which benefit are the obese, the gouty, and those suffering from a mild form of glycosuria.

In summer such patients can be treated at our own health resorts, Harrogate, Buxton, Llandrindod, etc.; but they may be sent to some foreign spa—such as Vichy, Neuenahr, Carlsbad, Marienbad, Homburg, Kissingen, and Contrexéville.

The results of a course of waters is to increase the tolerance of carbohydrates; and this is especially noticeable in obese and gouty subjects suffering from a mild form of glycosuria.

The saline and sulphur waters are undoubtedly beneficial in overcoming any tendency to constipation, in cases where there is gastric catarrh, and, in addition, they increase the alkalinity of the blood—a fact which should be borne in mind, seeing that a diminution in the alkalinity of the blood is now known to be the chief cause of diabetic coma.

During the treatment, the body-weight increases, the thirst and dryness of the mouth diminish, the patient sleeps better, and he gains in strength. Following three or four weeks' course of such waters, a further 2 or 3 weeks may be beneficially employed in drinking iron waters—such as the chloride of iron and Kissingen waters—at Harrogate; and this is especially useful where there are any signs of anemia.

It is advisable for such persons to have a course of such treatment once, and it may be twice, every year.

During the winter months, if it is desirable to send the patient from home for a change of scene and to a warmer climate, the Riviera, the Canary Islands, Egypt, and Algiers offer every advantage.

**DRUG TREATMENT**

The number of drugs which have been employed in the treatment of diabetes is enormous, but in spite of the plethora of medicaments vaunted, the drug treatment of the disease, at the present time is anything but satisfactory.

No course of drugs should be prescribed, except in those cases in which the sugar remains in the urine after the removal of carbohydrates from the diet: in such cases, when the sugar finally disappears, the dose should be diminished,
and finally withheld. Furthermore, it is unjustifiable to prescribe any of these drugs unless the patient can be kept under the constant observation of the physician.

Drugs may be required in diabetes to control the glycosuria, to avert or remove coma, or to relieve symptoms and complications.

In determining the value of any drug in diabetes, no alteration should be made in the patient's diet - for obvious reasons; nor should there be any change in his mode of life, since such change often has at first an effect on the excretion of sugar.

Before commencing the treatment of any case of diabetes with drugs, it is important to determine the form of the disease, and also to look for complications.

**OPIUM AND ITS ALKALOIDS.**

The most reliable drug in the treatment of diabetes is undoubtedly OPIUM; it has been in use for over a century, but unfortunately the improvement noticed during its exhibition disappears soon after it is withheld.

Its action is best seen in those cases in which dieting has reduced the sugar excretion to, say, 500 or less grains per diem; diabetics bear opium well.

It temporarily controls the polyuria, the thirst, and the excessive hunger; and its action is most noticeable in those cases in which a rigid diet has failed to arrest the glycosuria. In very severe cases, however, it may be of little or no benefit; it frequently causes obstinate constipation, and consequently increases the tendency to coma; in such cases, of course, it should not be administered.

The action of opium and its alkaloids is obscure; van Noorden holds that such action is indirect - the nervous irritability being first improved, the decrease in the intensity of the glycosuria being secondary. Frerichs believes they have a direct action on the glycogenic function of the liver. Frerichs and Schull object to the use of opium as being likely to cause sleepiness and constipation, whilst there is the danger of an opium-habit becoming established.

In 1869, Pavy investigated the action of CODINE, and, referring to his results with opium, morphia and codeine, states: "Of the three I was led to consider that codeina, in view of the circumstances, constituted the most advantageous for remedial employment in the disease. This opinion, I may say, my subsequent experience has confirmed."
Saundby differs from this opinion, and considers that codeine is a weak substitute for opium or morphia, having little utility except as a placebo; whilst Osler believes that not much effect is noticed with codeine unless the patient is on a rigid diet.

**BROMIDE OF POTASSIUM** is, in the opinion of Osler, a useful adjuvant; and van Noorden recommends it in highly neurotic diabetic individuals.

**SALICYLIC ACID and ASPIRIN.**

Williamson has employed both drugs in large numbers of cases, and he has frequently found them more satisfactory than opium and its alkaloids.

Hausman, in his article entitled "Uber die Einwirkung von Medicamenten auf die Glykosurie der Diabetiker," tells of the use of these drugs in 29 cases; aspirin was used mainly, being found less liable to produce toxic symptoms: the dose of aspirin varied from 45 to 60 grains per diem, and did not give rise to unpleasant effects. It reduced the amount of sugar, and had the advantage of relieving neuralgia and pruritus. He found the only contraindication to its use to be coincident nephritis; but some affirm that the salicylates and aspirin are injurious where cardiac failure is threatened or present.

**Eismuth salicylate** is liable to produce constipation, but is useful in cases complicated with diarrhoea.

The salicylates and aspirin are useful in mild, or in cases of moderate severity.

**G a l o l l** was tried with the idea of combining the good effects of phenol and salicylic acid.

**ANTIPYRIN,** according to Whitle, ranks next in point of merit to the opium series of medicaments; it is eliminated by the kidneys, and gives a tinctorial reaction with ferric chloride.

According to Kaufmann, it is liable to produce albuminuria, and should not be used more than twelve successive days.

**SYNGIUM JANGULANUM** - the bark and seeds of the Java plum - has a great repute in the East Indies and Malayan Archipelago; but it has not justified its reputation in Europe.

Von Noorden and Kaufmann use the fluid extract, well diluted to avoid eliminatory disturbances.

**URANIUM NITRATE** has been used by Hest, and he reports...
a great diminution in the excretion of sugar following its administration.
Saundby says it has no constant or specific action; and von Noorden regards it of no practical value.

Arsenide of glovminine, in doses of from 3 to 5 minims after meals, has been recommended; but it appears to be an uncertain preparation.

Arsenic may be tried, and is certainly a valuable tonic; it is said to inhibit the formation of sugar in animals.

The pancreas, in its raw state, and various preparations derived from the gland, have been tried and found wanting, though they may improve the digestion of fats.

Pilocarpine has been used with a view to stimulating the pancreatic secretion, but with little success.

The acid extract of duodenal mucous membrane has been tried by Moore, Edie, and Abram in three cases, two of which reacted favourably.

The alkalies, though they have no antiglycosuric properties, may prove of temporary service, by improving the general condition and postponing the onset of coma; this will be referred to later on.

Other remedies recommended are: Martineau's specific, which contains arsenic and lithium; calcium sulphide, creosote, phenacetine, exalgin, camphor, iodoform, salicin, sulphocarbonate of soda, cocaine, pepsin, phosphorus, lactic acid, peroxide of hydrogen, ergot, benzosol, potassium iodide, strychnine, quinine, piperaizin.

Diasias was recommended by Russman; but the treatment is costly, and its effect soon passes off.

Ammonia has been used in the form of the citrate and the chloride.

Santonin has also found advocates.

Certain vegetable preparations, of doubtful value, have been employed - such as linseed-tea, beanshell-tea, and whortleberry-tea; and in 1902 von Noorden introduced his oatmeal cure in severe cases; he gave 200 g. of meal per day, cutting off all other carbohydrates.

Coc-liver oil is to be recommended when the patient is wasted.

Amongst the newer recommendations in the treatment of diabetes is Diabetin - a pure crystallised fructose free from glucose; it is recommended as a carbohydrate, as well as for
sweetening the food and drink.

CASE 1. - The patient was a man, aged 35, married, and the father of three children — all living. He was a highly nervous individual, and appears to have had a hard struggle to make ends meet. He could not account for his condition, except by assuming that it was due to several attacks of severe cold from which he had suffered — the colds following on a wetting on each occasion.

When seen, he was much wasted, and had lost flesh rapidly during the past few months. The tongue was dry and furred, and he complained of thirst, loss of weight and strength, and the passage of increasing quantities of urine. There were no complications.

The urine contained 26 grains to the ounce; the specific gravity was 1028; and the amount passed in the twenty-four hours was 140 ounces. Gerhardt’s reaction was absent. There was a trace of albumin, but no tube casts in the liquid examined.

He was dieted — a limited amount of carbohydrate food being allowed for the first week.

This having no appreciable effect, a rigid diet was ordered, when the sugar fell to about 15 grains to the ounce. At the end of the third week, no further improvement having taken place, opium — in half-grain doses — was given thrice daily, when the sugar fell to 11 grains, and the urine to about 90 ounces in the twenty-four hours.

During the fifth week no change was noted. The opium was increased to 2 grains, and then to 1 grain, three times a day with but little result.

Codeine was now tried, in 1 grain doses three times a day, and then 2 grains thrice daily with no better results.

Aspirin was given a trial, and then sodium salicylate in increasing doses, but the patient sank and died in coma.
CASE 2. - A woman, aged 56 years. She was stout, and had suffered from glycosuria for some years. Prior to the time that sugar was demonstrated in her urine, she had lived a life of luxury, and had taken very little exercise; but since then she has dieted now and then, and during the intervals of dieting appears to have indulged herself pretty freely. After one of these periods of indulgence she came under the care of the writer.

She had lost in weight, was sleeping badly, and suffered a good deal from thirst; the tongue was dry, and there was slight constipation.

The urine contained 11 grains of sugar to the ounce; the specific gravity was 1022, and the quantity passed in the twenty-four hours was 86 ounces.

She was dieted and given 10 ounces of saline water three times daily. The sugar fell to 300 grains in the twenty-four hours, and the urine passed amounted to 60 ounces.

No further reduction taking place, sodium salicylate was given — 10 grains every four hours. At the end of seven days no trace of sugar could be found in the urine, and she had gained 3 lbs. in weight.

This treatment was continued with the addition of a hot-air bath, once a week, during her stay in Harrogate.

She gained 1½ lbs. during the third, and 2 lbs. during the fourth and last, week of her residence.

The further history of this case is not known.

SODIUM SALICYLATE
10 grains 4 hourly

Sugar excretion in grains.

SUMMARY

There is no specific treatment for diabetes. In the majority of cases dietetic treatment is all that is necessary.

If, on a moderately restricted diet, the sugar excretion ceases, no drug treatment is required; but when the glycosuria
cannot be arrested by diet, or can only be stopped by a most rigid diet, which the patient finds it difficult to tolerate for any length of time, drug treatment is desirable.

Further, medicinal means may be required to prevent or remove coma, or to relieve symptoms and complications.

Opium is the best antiglycosuric drug at present available; but aspirin and sodium salicylate are useful and valuable - more especially in the milder forms of the disease.

* * *

DIETETIC TREATMENT

The value of dietetic treatment in diabetes mellitus was first pointed out by John Rollo, Surgeon-General of the Royal Artillery, in 1797; and the method is considered by many physicians the only satisfactory form of treatment at the present time. It is equally important in the mild, as it is in the severe, forms of the disease; and by means of it, in some cases, it is possible to cause a complete disappearance, and in others a marked diminution in, the excretion of sugar, as well as other symptoms of diabetes.

Although it is possible that sugar may be derived from nitrogenous sources, it is known that carbohydrate food is its chief source of supply: in consequence of this, the removal, or restriction, of such articles of food from the dietary constitutes the cardinal principle in the treatment of the affection.

Before a dietary can be drawn up, it is necessary in all cases to make a thorough general examination of the patient: the general condition of nutrition should be noted, and it is also important to determine whether any complications are present or not. The body weight must be recorded, as it is an excellent index to the progress of the patient: if he is getting sufficient nourishment and the disease is not progressing, he will either gain in weight or the weight will remain stationary.

The amount of sugar is to be estimated, and the total quantity of urine passed in the twenty-four hours determined. The urine should be tested for Gerhardt's reaction.

To determine whether the case is a mild or a severe one, Seegen and Traube test the urine while the patient is taking a diet free from carbohydrates: if the urine is found free
from sugar, it is a mild case,—if the sugar persists, it is a sign that the patient is converting proteids into sugar, and that the case is a severe one.

Von Noorden employs the following carbohydrate-free diet as a standard:

**Breakfast.**—5 grm. of tea steeped in 200 c.c. of water; 150 grm. of ham; one egg.

**Lunch.**—200 grm. cold roast beef; 60 grm. fresh cucumber, with 5 grm. vinegar; 10 grm. olive oil and salt and pepper to taste; 20 c.c. brandy, with 400 c.c. Apollinaris-water; 60 c.c. coffee without milk or sugar.

**Dinner.**—200 c.c. clear bouillon; 250 grm. beef (weighed raw) basted with 10 grm. butter; 80 grm. green salad, with 10 grm. vinegar and 20 grm. olive oil or 3 tablespoonfuls of some well-cooked green vegetable; 3 sardines à l'huile; 20 c.c. cognac, with 400 c.c. Apollinaris-water.

**Supper.**—2 eggs (raw or cooked); 400 c.c. seltzer-water.

Before the patient is finally put upon this diet, a gradual reduction of the carbohydrates is prescribed. Von Noorden's method of procedure is as follows:

(a) For a few days gradual withdrawal of carbohydrates from the food.

(b) For five days the standard diet.

(c) If the urine now becomes sugar-free, a progressively increasing quantity of starch is added to the standard diet until glycosuria returns. The tolerance is expressed by the formula:

\[ \text{Tolerance} = \text{standard diet} + X \text{ grm. starch}. \]

(d) If, while the patient is on the standard diet, the sugar disappears from the urine, but returns immediately upon the addition of a small amount of carbohydrate, then 100 grm. of meat may be added. The formula therefore reads:

\[ \text{Tolerance} = \text{standard diet} + 0 \text{ grm. starch} \]
\[ = \text{standard diet} + 100 \text{ grm. meat}. \]

(e) If the glycosuria continues after the patient has been put on the standard diet, the case is severe; the amount of sugar is to be determined—its average from the third to the fifth day of the standard diet being estimated, when the condition is indicated by the formula:

\[ \text{Tolerance} < \text{standard diet; sugar} = X \text{ grm.} \]

By such test diets it is therefore possible to determine whether the case is a mild one, one of moderate severity, or
of a severe type.

In mild cases the sugar excretion ceases when the carbohydrate food is simply diminished in quantity.

In moderately severe cases the glycosuria only ceases when the carbohydrates are excluded from the diet, whilst in the severe forms of the disease the most rigid diet fails to remove sugar from the urine.

Having now determined the type of the disease and how much, if any, carbohydrate food the patient can tolerate, the dietetic treatment can be prescribed.

It is well to know the value of the food as estimated in calories—one calorie being the amount of heat required to raise the temperature of one kilogramme of water 1°C.

By oxidation 1 grm. of proteid and 1 grm. of carbohydrate yield about 4 calories each, whilst 1 grm. of fat yields 9 calories. From this total the value in calories of the sugar lost in the urine is subtracted, and the remainder ought to be not less than 2,500 calories daily—the value of the diet required by a healthy man; if it is less than 2,500, more fat should be given—the aim being to provide nourishment to the value of 2,500 calories with the least possible ingestion of carbohydrates.

Generally speaking, the diet should consist chiefly of albumin and fat, whilst sugar, and articles of diet containing much sugar, should be forbidden for the rest of the patient's life; it has been urged that a fat and meat diet predisposes to coma, but this theory is probably unfounded.

The diet should be so ordered that the strength of the patient is maintained and, if possible, increased; a record of the weight and sugar excretion should be kept—the former being probably the more important.

As the tolerance usually remains stationary for an indefinite period, barring complications, it is sufficient to keep the patient upon a diet slightly lower than his tolerance, in order to prevent the return of the glycosuria. Under such treatment the patient's general condition is usually much improved, and in mild cases he is, after a few weeks, able to take an increased amount of carbohydrate food without a return of the glycosuria, whilst in the moderately severe type he is able to tolerate a little carbohydrate.

The different varieties of carbohydrate food vary in their sugar-producing power. Grape-sugar causes the largest percentage of sugar to appear in the urine in the shortest
time, and starch and maltose and dextrin closely resemble grape-sugar; fruit-sugar, when given in like amount, increases the glycosuria only to one-half the extent; whilst milk-sugar stands about midway between the two extremes.

As soon as the patient comes for advice, observation should begin; without altering the diet, he is directed to weigh each article of food, and to collect the urine passed in the twenty-four hours. The difference between the total amount of carbohydrate food ingested and that of the sugar excreted gives the apparent tolerance.

The actual tolerance is determined as follows: As soon as the urine becomes sugar-free, by means of a carbohydrate-free diet, the amount of carbohydrates is gradually increased till sugar again appears in the urine; then the amount is once more reduced until the glycosuria disappears; the actual degree of tolerance lies between the last two amounts tried.

If the urine becomes free from sugar in a few days, and the sugar does not return on the addition of a small amount of carbohydrate food, the case is a mild one.

Such mild cases usually occur in elderly persons who are either obese or gouty, or both. This form of glycosuria is benign, and if such individuals will carry out the medicinal and dietetic treatment prescribed for them from time to time, the disease can usually be kept in check for many years, if not for the rest of their lives. In all cases, both mild and severe, the risks run by failing to comply with the instructions should be carefully pointed out. It is not necessary in such mild cases to lay down any strict or fast lines of treatment: it will be sufficient to forbid articles of food which consist entirely, or in great part, of carbohydrates, and to reduce the ingestion of certain other articles.

Sugar, sweetmeats, pastry, dishes made of flour, preserves, gruels, sweet jellies, and sweet wines should be forbidden, whilst beer and light wines may be allowed in reduced quantity.

If the patient be thin, he should be encouraged to take more fat food—such as bacon, fat meat, plenty of butter and eggs, cheese, with cod-liver oil as a useful adjuvant.

Apollinaris, or other weak alkaline waters, should be taken freely.

A three or four weeks' course of waters at a suitable spa, once or twice every year, will prove of undoubted
advantage.

If the patient is gouty, it is better to withdraw alcohol, except in the case of habitués.

In the case of the obese, it is advisable not to order any severe reduction-cure, as diabetics stand such cures badly. It is sufficient to prevent any increase of the weight.

Attention to hygiene is most important.

In young adults, diabetes, even if of a mild type, is difficult to manage. Constant supervision is necessary; and the carbohydrates should always be kept below the limit of tolerance. It is therefore necessary to determine the limit of tolerance several times each year.

Two or three weeks of strict dieting, preferably in a nursing-home, should be insisted upon three or four times every year.

In all cases, whether young or old patients, the carbohydrate-free diet should be gradually led up to. The diet should not be reduced too abruptly; according to Abstein, Nauyn and others, a rigid diet should not be commenced suddenly, especially in severe cases, for fear of causing coma. The diet should be altered gradually by lessening the quantity of carbohydrate consumed each day - potatoes being excluded first, then bread, and afterwards other carbohydrates. Excesses of all kinds are to be avoided; and if there is much excitability or irritability of the nervous system, bromides will prove useful.

In these young people, it is better to forbid the use of all carbohydrate food, with the exception of bread and potatoes. The amount of bread and potatoes allowed must be ascertained by the tolerance from time to time; after weighing the portions once or twice, they soon learn to estimate by the eye the amount allowed.

Milk, provided it causes no increase of the glycosuria, if given in moderate quantity, should be prescribed.

The free administration of alkalis, in the form of sodium carbonate, is advisable; and large doses, - 3SS, Si,- every two hours, should be given if coma threatens.

The chief distinction between the treatment of young diabetics and older ones is that in the case of the child a strictly carbohydrate-free diet can rarely, if ever, be adopted without bringing about an increase in the acetone and aceto-acetic acid reaction, as well as a greater liability
Moderately Severe Forms of Glycosuria.—In these cases only a insignificant amount of carbohydrate food can be borne.

Von Noorden recommends such patients to undergo a three weeks' course of complete abstinence from carbohydrates at least twice, and if possible three times, in the year, while in the intervals a certain amount of carbohydrates may be allowed.

During the period of abstinence the diabetic should rest as much as possible, both mentally and physically, and be out in the open air whenever convenient. Such periods of abstinence strengthen the patient's sugar-consuming function, and enable him to cope more successfully with the limited amount of carbohydrate allowed after the rigid diet has been stopped.

Some patients, however, will not tolerate a rigid carbohydrate-free diet: they lose weight and become thin, and it then becomes necessary to relax the diet—especially as regards the amount of bread.

Einhorn states that while an absolute meat and fat diet is ideal, because of the low sugar-content, it cannot be borne except for a short time; and the experience of most clinicians shows that it is best to allow diabetics a limited amount of carbohydrates.

When the period of abstinence is over, bread is allowed, and the tolerance duly estimated. Usually about four ounces of bread may be given, and in some cases larger amounts are permissible.

Fat must occupy a large place in the diet, and it may be given in the form of butter, cream, cheese, cream-cheese, eggs, bacon, marrow, or olive-oil; alcohol may be ordered as an aid to fat consumption.

Naunyn points out the value of a fast-diet in those cases in which the sugar excretion can be reduced to a few grammes daily, by strict diet, but no further. For twenty-four hours the patient takes no food, except tea and bouillon or tea, coffee, cream and bouillon. In such cases the sugar often disappears after the fast-day.

The severe forms of diabetes are met with usually in early life, and are seldom encountered after the fortieth year of life. Careful dietetic and other treatment may retard the progress of the disease, prevent complications,
and delay the fatal issue for a time.

The dietary must be a mixed one: it must be plentiful to prevent wasting, and satisfy the polyphagia which is usually present in this form of the disease. The albumin in the diet should be diminished, the fat increased, and a small amount of carbohydrates allowed in the form of white bread and milk. A small quantity of those fruits which contain little sugar may be given—such as cranberries, unripe green gooseberries, oranges [not sweet], raspberries, red currant berries. Cranberries, and green gooseberries stewed, and sweetened with saccharin, may be allowed freely—the others in limited quantity.

Large doses of bicarbonate of soda should be given in soda-water or milk.

On account of the large amount of fat, it is necessary for these patients to ingest, it is advisable to prescribe alcohol; and this is also of benefit to the general nervous exhaustion and tendency to heart failure which is present.

Von Noorden recommends for these cases a strict dietetic treatment, at least three times a year, and during this treatment to give up all mental and bodily exertion.

**********

Mention may here be made of certain "Milk Cure." 

A certain number of patients are greatly benefited by means of a milk cure—especially those in a weakened condition, and those suffering from complications. Milk is a useful addition when it is desired to relax a rigid diet; von Noorden varies the milk diet by giving buttermilk, Koumiss, and cream. An artificial milk, prepared according to the directions of Hutchinson and sugar-free, may be allowed.

**Potato Cure.**

Some diabetics can tolerate potatoes better than bread; and a small amount of the latter may be accordingly replaced by the former.

Mossé first recommended the potato cure as a means of treating patients suffering from diabetes; he replaces all the carbohydrate food by potatoes for several weeks, and found a diminution in the glycosuria and polyuria during the cure, as well as a diminution in thirst and an increase of strength.

The potato has several advantages as an article of diet: large quantities of fat can be consumed with the potatoes in
the form of butter, and the potato can be prepared and served up in various ways—e.g., baked, boiled, fried, and mashed.

Von Noorden recommends replacing a portion of the bread by this form of food.

YOLK CURD. 164

Stern recommends the ingestion of from 10 to 40 yolks of eggs a day, together with a small amount of protein and some green vegetables.

165

Jones reports, as indicating a possible danger in the dietetic treatment of this disease, a case of scurvy in a diabetic who had persisted for twenty months in an antidiabetic diet recommended by a friend.

THE FOLLOWING ARTICLES OF FOOD ARE ALLOWABLE:

Butcher's meat, with the exception of liver, of all kinds; poultry and game; fish of all kinds; tongue; ham and bacon; cheese, cream-cheese, and butter; suet; oils and fat; eggs in any form; nuts—e.g., filberts, hazel and walnuts, Brazilnuts and almonds; cucumber; mushrooms; all green vegetables—e.g., spinach, curleys, lettuce, mustard and cress, watercress, green cabbage with the white portions removed, Brussels sprouts and broccoli; lemons; pickled walnuts; onions; all soups; beef-tea, beef-essences, and broths prepared from butcher meat and poultry, if not thickened with farinaceous materials; jellies, custard, and isinglass devoid of sugar; the recognised bread-substitutes made from gluten, almond, bran, aleuronat, and cocoa-nut.

THE FOLLOWING ARE FORBIDDEN:

Sugar and all saccharine substances; bread and biscuits of all kinds, save those already mentioned; all farinaceous substances—e.g., flour, meal, macaroni, vermicelli, arrowroot, rice, sago, tapioca, semolina; all sweet fruits, fresh or dried or preserved, as jams or fruit—jellies; most vegetables that are white—e.g., celery, turnips, potatoes, vegetable-marrow, Spanish onions, and parsnips; also beetroot, carrots, peas, beans, and chestnuts; pastry and puddings, and soups of all kinds made with farinaceous materials; oysters, mussels and cockles, and the soft parts of lobsters and crabs, though
the muscle-meat of these may be eaten; liver of all animals.

OF LIQUIDS, THE FOLLOWING ARE ALLOWABLE:
Water (plain or aerated); tea, cocoa-nibs; coffee, and lemonade made without sugar; acid buttermilk; dry sherry; hock, and all dry wines; claret; burgundy; chablis; brandy and whisky in small quantities.

THE FOLLOWING ARE FORBIDDEN:
Milk, cocoa and chocolate; beer, ale and porter; all sparkling and sweet wines; sweetened gin; rum; liqueurs of all kinds; and aerated sweetened waters.

THE FOLLOWING FOUR TABLES ARE TAKEN FROM VON NOORDEN’S ARTICLE IN THE TWENTIETH CENTURY PRACTICE OF MEDICINE:

TABLE I.

FIRST GROUP: UNCONDITIONALLY ALLOWABLE FOODS

(These are free from carbohydrates, or contain them only in minute quantities.)

Fresh meat: All the muscular parts of the ox, calf, sheep, pig, horse, deer, wild and domestic birds - roast or boiled, warm or cold, in their own gravy or with mayonnaise sauce.

Internal parts of animals: Tongue, heart, brain, sweetbreads, kidneys, marrow-bones - served with non-farinaceous sauces.

Preserved meats: Dried or smoked meat, smoked or salt tongue, ham, smoked breast of goose, American canned meats, Australian corned beef.

Fresh fish: All kinds of fresh fish, boiled or broiled, prepared without bread-crusts or cracker-meal, and served with any kind of non-farinaceous sauce, preferably melted butter.

Preserved fish: Dried fish, salt or smoked fish such as cod, haddock, herring, mackerel, flounders, salmon, sardellen, sprats, eels, lampreys, etc.; tinned fish, such as sardines in oil, anchovies, etc.

Fish derivatives: Caviar, cod-liver oil.

Shell-fish: Oysters, mussels, and other bivalves, lobsters, crayfish, crabs, shrimps, turtle.

Meat extracts: Meat peptones of all kinds.

Eggs: raw or cooked in any way, but without any admixture of flour.

Fats of all kinds, animal or vegetable.

Fresh vegetables: Green lettuce, endives, cress, spinach, cucumbers, onions, leeks, asparagus, cauliflower, red and
white cabbage, sorrel, French beans. The vegetables, as far as they are suited to this mode of preparation, are best cooked with meat broth or a solution of Liebig's extract and salt, and covered plentifully with butter, lard, suet, or goose fat. The addition of flour is not permissible.

Preserved vegetables: Tinned asparagus, French beans, pickled cucumbers, in brine or vinegar, mixed pickles, sauerkraut, olives.

Spices: Salt, white or black pepper, Cayenne pepper, curry, cinnamon, cloves, nutmeg, English mustard, saffron, aniseed, caraway-seed, parsley, dill, borage, pimpernel, laurel, capers, chives, garlic, etc. Many of these spices contain, indeed, a rather large proportion of carbohydrates, but they are added to the food in such small quantities that this may be disregarded.

Soups: Clear soups and broths, with or without eggs, marrow, fresh or dried vegetables (Julienne), clear turtle soup, etc.

Cheese: Staracchino, Neufchâtel, old Camembert, Gorgonzola, and all other fatty and so-called cream cheeses.

Beverages: All kinds of natural and artificial carbonated waters, either clear or with lemon juice and saccharine or glycerin, or with rum, cognac, whisky, arrack, cherry brandy, Nordhäuser, rye whisky, etc. Light Moselle or Rhine wines, claret or Burgundy in amounts prescribed by the physician. Coffee, black or with cream, without sugar but sweetened with saccharin if desired. Tea, clear or with cream or rum.

**TABLE II.**

**SECOND GROUP: FOODS PERMISSIBLE IN MODERATE QUANTITIES.**

These contain carbohydrates, but so little that they need not be considered, and demand no compensation by a reduction in the allowance of bread. Some of the articles contain a rather large percentage of carbohydrates, but the absolute quantity in which they are consumed is small.

The amounts here given have been fixed by practical experience, and it will seldom be found necessary to increase them. Of the dishes here given, when they are allowed at all, only a few (from two to four) are to be selected each day. It is possible in this way to secure a large variety in the patient's dietary.

Internal parts of animals: Calves' liver, giblets, up to 100 grams.
Sausages: Liver sausages, preferably the fatter kinds, liver sausage with truffles, black pudding, 60 grams. Meat sausages, 80 grams. German sausages, Frankfurter sausages, and the like, brawn, head-cheese, sausage-meat balls, 100 grams.

Patties: Paté de foie gras, potted beef, ham, tongue, salmon, lobster, anchovies, etc., one-half to one tablespoonful.

English sauces, such as Worcestershire, Harvey, beef-steak, anchovy, lobster, shrimp, India soy, China soy, one tablespoonful.

Cream, from four to six tablespoonsfuls a day.

Cacao, prepared without sugar, 25 grams.

Cheese: Emmenthal, Romadur, 60 grams; Gervais, Stilton, Brie, Holland, Gruyère, 50 grams; Edam, Cheddar, Gloucester, Roquefort, Parmesan, 30 grams; Cheshire, 25 grams.

Vegetables (prepared without flour or sugar): 5 Teltower turnips; salsify, turnip-rooted celery, turnip cabbage, pumpkin, 2 tablespoonsfuls; green peas, beans, carrots, Brussels sprouts, 1 tablespoonful; ½ artichoke; 1 truffle; 5 medium-sized champignons; 1 tablespoonful of morels or other edible mushrooms.

Raw vegetables: 8 radishes; 2 sticks of celery; 2 medium-sized tomatoes.

Nuts: 2 walnuts; 6 hazelnuts; 3 almonds; a thin slice of coconut; 8 Brazil nuts.

Fresh fruits: One thin slice of lemon; one small apple (tart); one or one and a half peach; one spoonful of raspberries of strawberries; 4 spoonfuls of currants; 6 green gages; 12 cherries; half a medium-sized pear; corresponding amounts of other fresh fruits.

TABLE III.

THIRD GROUP: CONDITIONALLY ALLOWABLE FRUITS.

The condition under which dishes from the following table are permitted is that an equivalent shall be deducted from the allowance of bread. The amounts given below are the equivalents of 50 grams of white bread, containing about 30 grams of starch. Advantage is taken of the fact that larger amounts of certain carbohydrates (cane-sugar, milk-sugar, fruit-sugar, etc.) may be allowed than of starch. Some of the dishes given in the preceding table appear again here because, if they are eaten in larger quantities, an account must be
taken of the carbohydrate which they contain.

1 litre of milk (sweet, sour, or buttermilk).
1½ litres of kumyss (prepared in the Russian way).
1 to 1¼ litre of kephyr (fermented for at least two
days and prepared with the addition of sugar).
1 litre of cream.

60 grams of rye bread, Graham bread, or Hamburg pumpernickel.
65 grams of Westphalian pumpernickel.
100 grams of aleuronat bread, prepared after Ebstein's
formula (containing 27.5 per cent. of carbohydrate and 32 per
cent. of vegetable albumin; the aleuronat breads are very
variably compounded).

35 grams of zwieback and simple coffee-cakes (made
without sugar).
30 grams of English cakes of various sorts.
30 grams of "eichel cacao" (Stollwerck's).
30 grams of chocolate (Stollwerck's).
30 grams of chocolate (French make).
40 grams of chestnuts shelled, or 60 grams unshelled.
35 grams of cane sugar, brown sugar, or rock candy.
35 grams of sweet preserves.
40 grams of fruit sugar.
40 grams of milk sugar.
50 grams of fruit jam.
40 grams of honey.
40 grams of flour, wheat, rye, barley, buckwheat, millet,
or oat, or corn-meal.
45 grams of bean, pea, or lentil flour.
35 grams of starch preparations, potato, wheat, or rice
starch, tapioca, sago, maizene, mondamin, etc.
35 grams of rice.
35 grams of farinaceous preparations, nudel, maccaroni,
oatmeal, grits, barley.
50 grams of lentils, peas, beans, weighed dry.
100 grams of green peas.
180 grams of new potatoes.
140 grams of winter potatoes.
120 grams of apples, pears, green gages, plums, damsons,
mirabelles, apricots, cherries, grapes.
200 grams of strawberries, raspberries, gooseberries,
mulberries, currants, blackberries, whortleberries, blue-
berrries.
3 peaches.
40 grams of raisins or dried dates.
50 grams of figs.
3 bananas.
A handful of walnuts, hazelnuts, almonds, or Brazil nuts.
§ litre of beer of any sort.
1/8 litre of sweet wine.

**TABLE IV**

**FOURTH GROUP: ESPECIALLY VALUABLE FOODS.**

The great value of the following articles, of which, however, there is but a small choice, is due in part to the high percentage of albumin and in part to that of fat. The proportion of albumin and fat given for each 100 grams of the food substance. Some contain carbohydrates also, the percentage of which is given for the sake of completeness, but its nutritive value is not counted.

<table>
<thead>
<tr>
<th>Food</th>
<th>Albumin</th>
<th>Fat</th>
<th>Carbo-</th>
<th>Caloric Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetable oil</td>
<td>100</td>
<td></td>
<td>930</td>
<td></td>
</tr>
<tr>
<td>Buttr</td>
<td>1</td>
<td>85</td>
<td>0.5</td>
<td>830</td>
</tr>
<tr>
<td>Bacon (salt or smoked)</td>
<td>10</td>
<td>76</td>
<td></td>
<td>746</td>
</tr>
<tr>
<td>Devonshire cream</td>
<td>2</td>
<td>57</td>
<td>2</td>
<td>538</td>
</tr>
<tr>
<td>Cream cheese (Gervais, Neufchâtel, etc.)</td>
<td>19</td>
<td>41</td>
<td>445</td>
<td></td>
</tr>
<tr>
<td>German sausage (Cervelatwurst)</td>
<td>18</td>
<td>40</td>
<td></td>
<td>446</td>
</tr>
<tr>
<td>Ham</td>
<td>25</td>
<td>36</td>
<td></td>
<td>437</td>
</tr>
<tr>
<td>Cheddar cheese</td>
<td>28</td>
<td>36</td>
<td>2</td>
<td>442</td>
</tr>
<tr>
<td>Fat pork</td>
<td>14</td>
<td>37</td>
<td>400</td>
<td></td>
</tr>
<tr>
<td>Smoked ox-tongue</td>
<td>24</td>
<td>32</td>
<td></td>
<td>396</td>
</tr>
<tr>
<td>Fatty cheese (average)</td>
<td>25</td>
<td>30</td>
<td>1.5</td>
<td>381</td>
</tr>
<tr>
<td>Yolk of egg</td>
<td>18</td>
<td>31</td>
<td>0.5</td>
<td>354</td>
</tr>
<tr>
<td>Fat goose</td>
<td>16</td>
<td>30</td>
<td></td>
<td>345</td>
</tr>
<tr>
<td>Fat beef and mutton</td>
<td>17</td>
<td>29</td>
<td></td>
<td>337</td>
</tr>
<tr>
<td>Brie cheese</td>
<td>19</td>
<td>26</td>
<td>1</td>
<td>320</td>
</tr>
<tr>
<td>Fresh-water eel</td>
<td>18</td>
<td>28</td>
<td></td>
<td>312</td>
</tr>
<tr>
<td>Smoked mackerel</td>
<td>19</td>
<td>22</td>
<td></td>
<td>382</td>
</tr>
<tr>
<td>Caviar</td>
<td>31</td>
<td>16</td>
<td></td>
<td>276</td>
</tr>
<tr>
<td>Cream</td>
<td>4</td>
<td>23</td>
<td>4</td>
<td>230</td>
</tr>
<tr>
<td>Fat salmon (fresh or smoked)</td>
<td>22</td>
<td>18</td>
<td></td>
<td>210</td>
</tr>
<tr>
<td>Hens' eggs (weighed with the shell)</td>
<td>12</td>
<td>10</td>
<td>0.5</td>
<td>142</td>
</tr>
</tbody>
</table>

***************
BREAD SUBSTITUTES.

One of the greatest difficulties in the management of diabetic cases is to find a satisfactory substitute for bread—it being desirable to prescribe a rigid diet free from sugar and starch.

Before prescribing any diabetic bread, it should be tested for starch with a watery solution of iodine and iodide of potassium; a drop of this solution, if allowed to fall on a piece of ordinary white bread, will produce a deep blue-black colour owing to the presence of starch.

Many of the diabetic bread substitutes are not reliable, and contain little less starch than ordinary bread. Furthermore, most patients find these substitutes objectionable after a month or two of their employment.

GLUTEN BREAD is made from gluten flour from which the starch has been washed out. Other preparations made with gluten flour are:

- Gluten Borridge.
- Gluten Pudding.
- Gluten Pancakes.
- Gluten Biscuits.

BRAN BREAD, made from bran flour, is now seldom used.

SOYA BISCUITS or BREAD may be made from Soya bean, which is a Japanese product.

ALMOND CAKES and COCONUT CAKES are of considerable value.

ALEUROTINAT is a vegetable albuminous substance containing but a small percentage of carbohydrates; BUNS and CAKES may also be made with aleuromat flour.

ROBORAT BREAD.—Roborat is a vegetable albumin obtained from wheat; it contains a small amount of carbohydrate, and has a satisfactory taste.

PLASMON is an albumin prepared from milk, and is free from carbohydrates; BISCUITS and COBS can be made from it.

PROTEIN is an albuminous substance separated from milk; it can be made into COBS and ROLLS, BISCUITS and BREAD.

CASOID BREAD and CASOID MEAL BREAD are practically free from starch and sugar, and are composed chiefly of milk albumin.

KALARI and PROLACIO BISCUITS are composed chiefly of the same albumin, and are often eaten with cheese and butter.

PEANUT FLOUR is used in making various dishes.
INULIN BISCUITS are expensive.
[With the exception of casoid preparations, the bread substitutes referred to can be prepared at home.]
COCOANUT CAKES contain a large amount of fat; they are
cheap and most useful for poor people.
TORRIFIED BREAD consists of thin slices of bread toasted
very dark-brown, or almost black.
COCOANUT PUDDING forms a cheap and excellent substitute
for rice and farinaceous puddings. A quarter of an ounce of
German yeast is mixed with a little lukewarm water, with a
quarter of a pound of desiccated coconut powder. The mixture
is kept in a warm place for fifteen minutes. Then half an
ounce of butter, a pinch of salt, and a little milk are added.
All to be well mixed. The mixture is placed in a pudding-dish,
and baked in a moderate oven, for twenty or thirty minutes,
until the surface is brown.
Unfortunately, many of these bread substitutes vary in
the amount of starch which they contain. Some may contain
as much as, or more than, 40 per cent., and offer little
advantage over ordinary bread.
These antidiabetic breads have one drawback, namely, that
the patients believe that they can consume them without
stint.

SUBSTITUTES FOR SUGAR.

Many of these are sold under trade names such as
CRYSTALLOSE and DIABETIN.
Preparations of INULIN, INOSITOL, MANNITOL, and FRUIT-
SUGAR have been suggested as being less injurious than cane-
sugar.
GLYCERINE is sometimes used, but is condemned by
many.
SACCHARIN (benzol-sulphonic-acid) is largely employed.
It has a very sweet taste, and it may be procured in tablets
which are equal in sweetening power to an ordinary lump of
sugar. If taken in quantities not exceeding 5 grains a day,
it is harmless.
SAXIN, a coal-tar product, is said to be six hundred
times sweeter than sugar; it may be employed in tablet form.
GARANTOSE (sodium-benzol-sulphonic-imid) is more soluble
than saccharin.
DULCIN (paraphenatolcartanid) is commonly used in
Germany. It is harmless, if used in small quantities, but in large amount it may give rise to such symptoms as icterus. More than 8 grains should not be given in one day. It may be had in tablets containing 0.025 grms. each.

Sugar-free marmalades, jellies, and jam are manufactured by Callard & Co., who also prepare preserved fruits, which are said to contain less than 2 per cent. of sugar.

Beverages.

Diabetics are possessed of a chronic thirst, and consume large quantities of water. The drawbacks of polydipsia are the distension of the stomach and the increase in the work of the heart; both these effects are diminished by taking small quantities of water frequently.

Sucking pieces of lemon or ice, or sipping very hot water, may diminish the craving for liquids.

Hypodermic injections of pilocarpine stimulate the flow of saliva, and relieve the dryness of the mouth; and glycerinum acidi carbolicici, in 5 minims doses, is said to have the same effect.

The beverages which are free, or almost free, from carbohydrates may be allowed; they have already been mentioned.

The fluids should be taken mostly before, and not after, a meal.

Milk, if allowed, should not be prescribed in large or unlimited quantities in any case of diabetes; it is of use in all severe cases, and especially if the digestion is feeble.

Hutchinson's sugar-free milk has been referred to already.

Skimmed milk has been recommended by Donkin as an exclusive food in diabetes.

Buttermilk offers to many a pleasant and wholesome drink.

Alcohol.—Alcoholic drinks, which contain a large amount of carbohydrates, may be allowed in moderation.

In the severe forms of the disease alcohol is of some use, as it enables the patient to take large quantities of fatty food, when prescribed, without dyspeptic trouble.

Benedict and Törökö conclude, as the result of their determinations of the urinary acetone, sugar, nitrogen and ammonia, and the respiratory acetone excreted by diabetes on
fixed diets with varying amounts of alcohol, that the use of alcohol is beneficial; they found that it reduced the production of acetone, decreased the sugar elimination, and spared the proteid consumption better than fat does. The amount should be regularly determined, and not left to the patient's desire.

Contraindications are usually albuminuria, neuritis, arterio-sclerosis, and diabetes in childhood.

TREATMENT OF THE COMPLICATIONS.

MOUTH.

The mouth must be carefully looked after; and dental caries and inflammation of the gums should be guarded against by strict cleanliness. The teeth should be brushed, and the mouth rinsed, after each meal; before retiring to bed for the night, a 3 per cent. solution of borax is a suitable mouth-wash.

Stiff toothbrushes are not suitable, being likely to produce slight wounds of the gums.

STOMACH AND INTESTINES.

GASTRO-INTESTINAL CATARRH is always a disquieting complication; and in combating it, the special diet of the diabetic must often be neglected for the time.

Opium is of service in not a few cases; and calomel, on account of its disinfecting properties, may be prescribed.

CONSTIPATION may be overcome by any laxative which does not contain sugar. The saline aperient waters are probably the most suitable. If the tendency to constipation is not great, a free use of vegetables in the diet may overcome it.

DIARRHOEA, if it tends to become chronic, will weaken the patient, and it may tend to bring on coma.

Von Noorden recommends calcium carbonate for the relief of this condition.

Salicylate of bismuth and opium may be employed. Tea and red wine, which contain tannin, are the most suitable drinks.

The diet will probably have to be altered.

SKIN.

PRURITUS is one of the most troublesome complications of diabetes; it must be guarded against by the most absolute cleanliness.

The patient should be wiped gently with a sponge, or
some soft material, wrung out of a solution of permanganate of potash or sodium borate, after micturition, and then powdered with bismuth or oxide of zinc—the contiguous surfaces being kept apart with muslin bags.

Alkaline baths, such as those of Harrogate, are both soothing and curative; the patient stays in the bath for from forty minutes to one hour. The baths are taken daily.

If the surface of the skin is excoriated, boracic, zinc or iodoform ointment may be applied instead of the powder.

Irritation and eczema of the prepuce and surrounding parts are to be treated in like manner.

In all skin diseases associated with diabetes, it is essential to treat the underlying constitutional state.

Daily alkaline baths are most serviceable. The wearing of fine, and not coarse, clothing next the skin is important.

Gangrene.—Palliative treatment consists in rest in bed and keeping the patient dry. The quantity of starch is to be limited, and opium, or one of its alkaloids, given to reduce the sugar in the urine and relieve pain.

If the gangrene has spread to the foot, amputation in the upper part of the limb is to be performed.

Respiratory System.

Pulmonary Phthisis.—The ordinary treatment for diabetes will still have to be followed. These patients are not able to follow out sanatorium treatment in cold or bleak situations; a fairly warm and sheltered place should be chosen.

Fat should be taken in as large amounts as possible, with the addition of alcohol.

Creosote and guaiacol are useful drugs; but the prognosis, even under the most favourable conditions, is unfavourable.

Diabetic Coma.

The indications for the treatment of coma are to prevent the further formation of fatty acids, and to combat acid intoxication by neutralising the acids already formed.

In the severe forms of diabetes, when the urine gives a marked reaction with perchloride of iron, there is imminent danger of coma developing. Such persons should avoid over-
fatigue, over-exertion, sudden changes of diet, and constipation. If constipation be present, purgatives are indicated, and a free action of the bowels becomes imperative. The failure to metabolise carbohydrate food is seldom absolute, and some such carbohydrate food as bread should be allowed.

Von Noorden says that oatmeal gruel is tolerated when other forms of carbohydrates are not.

In order to neutralise the acids, sodium bicarbonate should be prescribed freely until the urine becomes alkaline. It may be given in doses of from 20 to 50 grains, and from 400 to 500 grains may be taken in the twenty-four hours. It may be administered in milk, or as an effervescent draught with citric acid and saccharin (Yeo).

Reynolds recommends citrate of potash in doses of half a drachm, dissolved in copious draughts of water, and given freely.

Forthwith on the supervention, intravenous or subcutaneous injections of warm alkaline or saline solutions are to be employed; the intravenous injection acts quicker, and it is more satisfactory than the subcutaneous. The solutions commonly employed are:

A 3 to 5 per cent. solution of sodium bicarbonate in 0.6 to 0.7 per cent. sodium chloride solution;
A 5 per cent. watery solution of sodium bicarbonate;
A solution of 10 grammes of sodium bicarbonate and 7 grammes of sodium chloride in a litre of sterilised water;
A 0.6 per cent. solution of sodium chloride.

A large quantity of fluid is necessary - from 2 to 5 or 6 pints at a temperature of about 100°F.

Other methods of treatment are rectal injections of sodium bicarbonate and lactulose; inhalations of oxygen, on the grounds of the association of the condition with defective oxidation; hypodermic injections of ether, strychnine, and camphor.

Notwithstanding every care and attention, when coma supervenes the life of the patient is to be measured by hours, rather than by days.

F Y E.

The treatment of the ocular complications of diabetes will consist chiefly of attention to the general health and condition. The eyes should be rested as much as possible - by avoiding reading, bright lights, and by wearing
coloured glasses.

**NEURALGIA and NEURITIS.**

Of the nervous complications of diabetes, one of the commonest is NEURALGIA. The pain thereof may be relieved by such drugs as antipyrin, aspirin, phenacetin, and by local anodyne applications.

The treatment of NEURITIS is similar.

**SPINAL CORD AFFECTIONS.**

Symptoms of spinal cord disease may be present with glycosuria; such affections are best treated by rest, massage, electricity, and exercises calculated to improve the co-ordination.

**PSYCHICAL TROUBLES.**

Psychical phenomena, such as DEPRESSION and MELANCHOLIA, are common and difficult to influence favourably. Proper sleep, change of air and surroundings, travel, and, above all, the knowledge that consequent upon suitable treatment satisfactory progress is being made, will help to dispel the gloom.

**DIABETICS AND OPERATIONS.**

The superstition against operating upon diabetics no longer prevails.

Operations on such patients should, if possible, be preceded by a course of preparatory treatment. In mild cases, carbohydrates should be withheld gradually from the diet, and until the glycosuria disappears. In severe cases, the acidosis is most to be feared, and a moderate amount of carbohydrate food may be allowed.

The general health should be improved by tonics, such as iron and arsenic, by easily digested food, and massage.

Operations should, of course, be avoided as far as possible: for wounds tend to heal badly, and gangrene is easily excited.

Asepsis is to be preferred to antisepsis, and the thermocautery to the knife in the event of there being any choice between the two.

General anaesthesia may be looked upon as contraindicated,
unless the operation is strictly necessary.

The prognosis is better for a patient in good condition with a high percentage of sugar, than for one in poor condition with a low percentage.

Karewski says in abdominal cases the usual cleaning-out of the intestines, and the preliminary starvation, should be avoided; and that the patient should have, before and after the operation, large quantities of water containing alkalies.

Coma may be an indication for immediate operation, especially in the cases of carbuncles and gangrene.

The general anaesthesia should be as short as possible, and no more anaesthetic than is absolutely essential to success should be given.

Furuncles, if treated at all, should be excised; and carbuncles should never be temporised with, but removed at once.
A  0  0
/ / 1 0 A L CASES.
C A S E  I.

David W., aged 42, a merchant.

Family History. - Father died, when 64, from apoplexy; the mother died from bronchitis, aged 59. There are two brothers living and well; one died from heart failure at the age of 33. Three sisters living and well; one died from pneumonia when 36 years of age.

Personal History. - The patient received a severe blow on the occiput when a child of 9; three years ago he was troubled with polyuria, but this passed off after a duration of three weeks; two years ago he suffered from boils on his back and legs.

History of Present Illness. - In the winter of 1906, he began to be troubled with marked thirst, and the passage of large quantities of urine. Shortly after this, his sight began to grow dim, and his weight was falling. He suspected diabetes, and put himself upon a special diet. At the beginning of 1907, he suffered from severe headaches, felt himself growing weaker, and was loosing weight more rapidly than hitherto.

Present Condition. - On presenting himself for examination, he was found to be thin; his cheeks were rather flushed. Alimentary System. - Tongue coated and dirty; teeth bad, many having fallen out. The appetite was good. Bowels constipated.

Respiratory System. - Apparently normal.

Circulatory System. - Pulse 64, soft and of low tension; walls of the vessels atheromatous. Heart: Nothing abnormal found.

Nervous System. - Knee-jerks absent; also plantar reflex and ankle clonus. No pain or tenderness anywhere. Sensation to heat and cold good.

Muscular System. - The muscles generally were soft and flabby.

Ocular System. - Diabetic cataract was present, and in both eyes.

Urinary System. - The urine was straw-coloured, acid, had a specific gravity of 1042, but contained neither albumin,
casts, pus, nor blood; sugar was present to the extent of 12 grains to the ounce; Gerhardt's reaction absent.

TREATMENT. - The carbohydrates in his diet were gradually cut off; potatoes, and all articles of diet containing much sugar were forbidden - e.g., sweets, sugar, pastry, and puddings. He was allowed meat, beef-tea, tea, toast, fish, game, poultry, green vegetables in moderate quantity, cream, cheese, butter and eggs.

At the end of seven days, his condition had improved: the sugar had fallen considerably, to 4 grains per ounce, and the amount of urine passed, from being 86 ounces in the twenty-four hours, fell to 63 ounces. His weight was the same - 8 st. 6 lbs. 2 oz.

The same diet was prescribed for the second seven days: at the end of that time the weight had increased by 1 lb., but sugar was present to the same extent.

Opium was now given, in half-grain doses, night and morning: a week later no sugar was present in the urine.

The bowels were kept open daily by sulphur-water, 16 ounces, before breakfast every morning.

At the end of four weeks he had greatly improved, was putting on weight, sleeping better, and able to take more exercise.

CASE II.

Thomas M., aged 61, a retired merchant.

Family History. - Mother died of cancer of the uterus at the age of 63. Father died, aged 60, of paralysis - cause unknown. No brothers or sisters.

Personal History. - He had had gonorrhoea in youth, and rheumatism one and a half years ago. He is a moderate drinker and smoker.

Three months before seeing him, he suffered from constant and severe pain in the epigastrium, which was worse at night; this pain, in the course of time, spread to the umbilical and right lumbar regions. He complained of great hunger, and constant thirst - having to rise several times each night
to satisfy both. He passed water, on an average, eighteen times during the day, and oftener at night. Insomnia was one of his most distressing symptoms. He complained of frequent attacks of severe headache, also of attacks of dyspnoea—especially at night. His eyesight is gradually becoming dimmer.

Four weeks ago he noticed his feet and ankles swollen; pain was felt in both ankles and legs, and a feeling of cold and numbness was present in these parts. He is losing weight.

**Present Condition**—On presenting himself, he was found to be thin, and he appeared to walk with some difficulty.

His appetite was ravenous, the tongue was furred, the teeth were bad, and the bowels were constipated.

The heart was enlarged, the apex beat being in the sixth interspace and just outside the nipple line. A systolic murmur was present over the mitral area. The pulse was regular, and the walls of the blood-vessels felt normal.

The lungs were normal.

There was tenderness on deep palpation in the right epigastric and right hypochondriac regions; but nothing abnormal could be felt.

The feet were slightly swollen.

The knee-jerks were present. No ankle clonus. Sensibility to heat and cold dull.

The urine was straw-coloured, alkaline in reaction, of 1022 specific gravity, but incapable of response to Gerhardt's test. Sugar 2.5 per cent. There was a deposit of mucus and phosphates.

**Treatment**—The carbohydrates were gradually left off, as in Case No. I., and half-grain doses of codeine were given thrice daily after meals.

At the end of two weeks, there was very marked improvement: he had gained one and a half pounds in weight, was sleeping better, the thirst diminished, and the swelling of the feet and ankles had disappeared. The urine was sugar-free, and the amount passed in the twenty-four hours had fallen to about half.

The opium was stopped; and, no return of the sugar being observed, he was allowed a small amount of carbohydrate, in the form of bread, at each meal. A potato was then added, and the amounts gradually increased.
CASE III.

Agnes D..., aged 49, a single woman.

Family History.— Father died, aged 56, cause unknown.
Mother died, aged 40, from pneumonia. One sister living and well.

History of Present Illness.— She had had no illness up to 1907. She was very fond of sweets and sugar, and took large quantities of each. She had suffered from bilious attacks for the past year, and had been losing weight gradually. Had not menstruated for four years.

About sixteen months ago, she began to be troubled with excessive thirst and the passage of large quantities of water: she had to rise four or five times at night to micturate. She complained of feeling drowsy at times.

Present Condition.— Although she has lost weight, she is still stout.

The teeth are good. The tongue is dry, red and painful. The appetite is good, and the bowels are constipated.

On examination, the respiratory, circulatory and nervous systems showed nothing abnormal. The abdomen gave negative results.

The urine was pale, slightly acid, and showed a specific gravity of 1038; no albumin, pus or blood could be discovered. Sugar was present to the extent of 660 grains in the twenty-four hours. No acetone reaction.

Treatment.— Carbohydrates were gradually eliminated from the diet as before; and by the end of the first week she was practically taking a carbohydrate-free diet.

The sugar disappeared on the fifth day.
No drugs were given.
She was kept on the above-mentioned diet for another seven days, when one potato a day was allowed; no sugar appearing, bread was added, in small amount at first, and gradually increased.
Her bowels were regulated by salines.

CASE IV.

Thomas N., aged 51, married, no children.

Family History: Father living and well. Mother died of asthma at the age of 47 years.

History of Present Illness: He had been occasionally troubled with indigestion, and had had an attack of lumbago six years ago. Piles used to trouble him about eighteen years ago.

Three weeks before seeing him, he complained of having constantly a dirty tongue, a sour taste in the mouth, with marked dryness. He was drinking between three and four quarts of water daily, and passing urine about twelve times per diem, as well as six times during the night.

Present Condition: He is well-nourished and appears healthy. The teeth are beginning to go; the tongue is cohered with a brown fur, and the mouth seems to be dry.

With the exception of a high-tension pulse, the organs of the body are healthy.

The urine is pale, has an acid reaction, and gives a specific gravity of 1038; albumin, pus and blood absent. The amount of urine passed in the twenty-four hours is 75 ounces, and the sugar amounts to 2730 grains. Gerhardt's reaction is absent.
Treatment. — He was dieted similarly to the preceding three cases. He being a great believer in the efficacy of drugs, sodium salicylate was prescribed in 5 grain doses every four hours.

He made excellent progress — the sugar disappearing on the eleventh day.
REFERENCES.

1. Fletcher Morley.- Practitioner, July, 1907, p. 95.
4. Saunby.- Allbutt's System of Medicine, Vol. iii., p. 188.
5. Furdy.- Diabetes Mellitus and Glycosuria [Klein], p. 20.
9. Von Noorden.- Twentieth Century Practice of Medicine, Vol. ii., p. 64.
10. Osler.- Principles and Practice of Medicine, p. 410.
11. Favy.- Physiology of the Carbohydrates, p. 263.
22. Von Noorden.- Ibid., p. 66.
32. Von Noorden.- Syst.of Med.[Allbutt], Vol. iii., pp. 203, 204.
33. Opie.- Practitioner, July, 1907, p. 15.
34. Schafer.- Principles and Practice of Medicine[Osler], p. 418.
35. Osler.- Ibid., p. 413.
38. Recklinghausen.- Diabetes Mellitus and Glycosuria [Klein], p. 35.
42. Halliburton.- Practitioner, July, 1907, p. 5.
44. Von Wering.- Ibid., p. 49.
46. Underhill and Closson.- Ibid., p. 9.
48. Lustig and Peifer.- Diabetes Mellitus and Glycosuria [Kle£n], p. 34.
53. Naunyn.- Diabetes Mellitus and Glycosuria [Kle£n], p. 111.
57. Guincke.- Ibid., p. 208.
64. Frerichs.- Diabetes Mellitus and Glycosuria [Klein], p. 99.
68. Cavazzani.- Ibid., p. 207.
69. Saundby.- Ibid., p. 207.
70. See£en.- Practitioner, July, 1907, p. 69.
71. See£en.- Ibid., p. 42.
75. Mayer.- Ibid., p. 110.
77. Straynowski. - Diabetes Mellitus and Glycosuria [Kleen], p. 118.
84. Bernard. - Diabetes Mellitus and Glycosuria [Kleen], p. 189.
91. Naunyn. - Ibid., p. 102.
94. Seegen. - Ibid., p. 493.
95. Trousseau. - Principles and Practice of Medicine [Osler], p. 415.
98. Lusk. - Ibid., p. 89.
100. Von Noorden. - Ibid., p. 98.
102. Stadlemann. - Ibid., p. 92.
106. Von Noorden. - Ibid., p. 110.
112. Schmitz. - Ibid., p. 106.
113. Hirschfeld. - Ibid., pp. 8r, 85.
121. Latham. - Ibid., p. 221.
122. Senator. - Ibid., p. 222.
129. Williamson. - Ibid., p. 490.
132. Rosenschen. - Ibid., p. 119.
133. Seegen. - Practitioner, July, 1907, p. 69.
134. Von Noorden. - Ibid., p. 74.
136. Kleen. - Diabetes Mellitus and Glycosuria [Kleen], p. 139.
139. Frerichs. - Practitioner, July, 1907, p. 149.
140. Frerichs and Schull. - Ibid., p. 149.
141. Pavy. - Carbohydrate Metabolism and Diabetes, 1908, p. 131.
144. Osler. - Ibid., p. 423.
145. Von Noorden. - Practitioner, July, 1907, p. 150.
148. Whitla. - Dictionary of Treatment, 1902, p. 204.
149. Kaufmann. - Practitioner, July, 1907, p. 151.
156. Seegen and Traube. - Diet in Health and Disease [Friedenwald and Ruhrhahn], p. 470.
159. Von Noorden. - Diet in Health and Disease [Friedenwald and Ruhräh], p. 477.
160. Einhorn. - Progressive Medicine, April, 1906, p. 490.
163. Mossé. - Diet in Health and Disease [Friedenwald and Ruhräh], p. 483.
164. Sterm. - Ibid., p. 484.
166. Donkin. - Diabetes Mellitus and Glycosuria [Kleen], p. 277.
168. Von Noorden. - Diet in Health and Disease [Friedenwald and Ruhräh], p. 481.
170. Ólafsson. - Medical Chronicle, 1891, p. 338.
INDEX.

Course, duration and termination of diabetes, 67

Diabetes in association with other affections;
enteric fever, 66
Dupuytren's contraction, 67
rheumatic pains, 66
tumours, 67

Diagnosis of,
Acetone in,
Le Nobel's test for, 72
Rubner's " " , 73
Trommer's " " , 72
quantitative estimation of, 73
E-oxibutyric acid in, 74
circumpolarisation test in, 73
diacetic acid in, 73
fermentation test in, 74
Fischer's test in, 70
Moore's " " , 70
Nylander's " " , 69
Rubner's " " , 71
Trommer's " " , 69

Etiology of,
age in, 6
alcoholism in, gout, 8
chronic affections in, 14
contagion in, 12
geographical distribution in, 15
heredity in, 6
injuries in, 30
liver, diseases of, in, 28
miscellaneous factors in, 21
nervous system, diseases of, in, 29
obesity in, 18
occupation in, 11
pancreas, diseases of, in, 22
psychical affections in, 10
race in, 9
Etiology of, [Continued.]
season in,
sex in,
social circumstances in,
specific fevers in,

General clinical course,
acute form,
chronic form,
mild form,

History of,
Operations in,

Pathology of,
liver in,
nervous diseases in,
nervous injuries in,
pancreas in,
poisons in,

Pathological anatomy of,
alimentary tract in,
appearance of cadaver in,
blood in,
blood-vessels in,
heart in,
tegument in,
kidneys in,
liver in,
lungs in,
nervous system in,
pancreas in,
reproductive organs in,
spleen in,

Prognosis of
Symptoms, analysis of,
circulation,
heart,
pulse,
intestines,
liver,
lymphatic system,
mouth and throat,
gums in,
saliva in,
Symptoms, analysis of, [Continued.]

- taste in,
- teeth in,
- thirst in,
- tongue in,
- nails,
- nervous system,
  - coma,
  - ocular manifestations,
  - psychical disturbances,
- pancreas,
- reproductive organs,
- respiratory system,
  - gangrene,
  - pneumonia,
  - tuberculosis,
- skin,
- stomach,
- urine,
  - acetone in,
  - albumin in,
  - ammonia in,
  - B-oxybutyric acid in,
  - colour of,
  - creatinin in,
  - diacetic acid in,
  - hippuric acid in,
  - mineral constituents in,
  - odour of,
  - oxalic acid in,
  - pneumaturia in,
  - quantity of,
  - reaction of,
  - specific gravity of,
  - sugar in,
  - sugar, quantitative estimation of,
    - by aerometry and fermentation,
    - by Fehling's solution,
    - by polarisation,
  - urea in,
  - uric acid in,
Theories of,  36

Treatment of,  76

Complications,  101
    coma,  102
    gangrene,  102
    gastro-intestinal catarrh,  101
    mouth,  101
    neuralgia,  104
    neuritis,  104
    ocular complications,  103
    phthisis,  102
    pruritus,  101

    diet in,  85
        beverages,  100
        bread substitutes,  98
        carbohydrate-free diet,  86
        milk cure,  91
        potato cure,  91
        sugar substitutes,  99
        tolerance factor,  88
        yolk cure,  92

    drugs in,  78
        acid extract of duodenal mucous membrane,  81
        alkalies,  81
        antipyrin,  80
        arsenic,  81
        aspirin,  80
        Jambul,  80
        opium and its alkaloids,  79
        pancreas,  81
        pilocarpine,  81
        salicylates,  80
        uranium nitrate,  80

    drug treatment, safety remedies,  81