a thesis
on
Diabetes Mellitus.

Reginald Broadbent.

1893.
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Diabetes Mellitus.

I have termed this a Thesis on Diabetes Mellitus, but its scope is limited to remarks on a case which occurred in a child after Influenza, with a brief review of the subject generally.

Few things have been so remarkable about the recent Influenza epidemics, as the different forms it has assumed, simulating other inflammatory diseases, and also leaving behind its complaints which appear totally different. A short time since the physicians of Marseilles were puzzled with an epidemic there of a choleraic character, which was believed by many to have been Influenza, although subsequently it was proved to have been Cholera. During the epidemic of 1891, I had a young woman as a patient, who had all the symptoms of Meningitis, with
a temperature of 104° F. and at a consultation the diagnosis of meningitis was confirmed. But the subsequent history of the case, left no doubt but that it must have been Influenza.

The epidemics have left all manner of complaints as sequelæ, but perhaps the most extraordinary is Diabetes or Glycosuria. Mr. Hoysted published the first case in the Lancet of April 2nd 1892. The case was that of an adult male in whom the disease appeared suddenly and with a good deal of severity. But the disease at first proved specially amenable to treatment, and it was believed that a recovery had taken place. This led Mr. Hoysted to suggest at the time the diabetes as a sequel to Influenza may be marked by a tendency to disappear with appropriate treatment, whereas the disease
in its usual form has no such tendency. But this hope appeared too sanguine, for in a later communication to the Lancet (Feb. 11th 1893), it was reported that after three months, the disease appeared as violent as ever, and that the case did not ultimately recover.

A second case of Diabetes following Influenza however, was reported in the Lancet of Jan. 21st 1893 by Mr. Atherington and Dr. Brown which appeared to confirm the first impression of Mr. Hoysted that the disease appearing in connection with Influenza, has a special tendency to recover with treatment. The case was that of a boy 15 years of age, in whom the glycosuria ceased with anti-diabetic food and medicine. Now Diabetes in children is noted for its malignity, for its rapidly fatal character, and a cure is of such
an unusual occurrence, that this fact amply justified the publica-
tion of the case. And as yet no relapse seems to have taken place.

Having searched the literature on the subject of Diabetes
in children, one is struck with
its paucity, and with the small
number of cases that have been
reported. This is no doubt due to
the fact that the complaint in
children is rare. The two facts
then that distinguish diabetes in
children from that in adults, are
its rarity, and its rapidly fatal
character.

With regard to statistics,
the most complete list we have
was published by Ravy in the
Out of 1360 cases, 8 only occurred
under 10 years of age, that is to
say 0.58 percent of the total.
Dr. Story in his Croonian Lectures
on page 22, reports Dr. W. R. Hinsey
of Ceylon, to the effect that there the disease is "very rare in children". In the Report of the Registrar General for 1886, two deaths occurred in children under one year of age. At a recent meeting of the Leicester Medical Society, the senior member present remarked that he had been for forty years in general practice, but had never met with a case of diabetes in a child.

All these facts tend in the same direction, but in order to obtain more definite information on the subject, I made enquiries at many of our principal hospitals with that end in view. The result has not been so satisfactory as could be wished, as in several instances the information was "not available for statistical purposes". However, the Secretary of the Metropolitan Hospital informs me that during the last five years,
there has occurred in that institution only one case of diabetes in a child, a female three and a half years of age. At St. Thomas Hospital, London, during the last ten years there have been ninety-two cases of diabetes, but only one of this number was under six years of age.

At Westminster Hospital during the last ten years, there have been thirty-three cases admitted as in-patients, the youngest was twelve years of age.

During the last ten years at King’s College Hospital, there have been thirty-five cases of diabetes, one of which occurred in a child four years of age, one at the age of twelve, three at sixteen, one at eighteen, the others were all over twenty.

According to the Annual Reports of the General Hospital at Birmingham, there have been one hundred and eight cases during the last eleven years.
of those that died none were under five years, one was under ten, two under twenty.
At the Leicester Infirmary, as far as can be ascertained, there has been only one case in a child for the last five years.

**Tabular Statement**

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<th>Name of Institution</th>
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<td>11</td>
<td>1</td>
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So that out of a total of 268, 5 cases occurred in children, which gives a percentage somewhat higher than that given by Dr. Pavy.

These facts go in support of the general idea that diabetes in children is very uncommon. Two other facts which may be
of minor importance, are also worth mentioning, as distinguishing the disease in children from that of adults, i.e. 1) the majority of cases are females, 2) the onset in children is abrupt. In support of the first, the eight cases that came under Dr. Pavy's notice, out of the 1360, five were female, three were male. The only case in a child mentioned by Saunby, p. 92, is that of a female. In the statistics mentioned above, in each case where the sex has been quoted, it has been that of a female. The one that I am about to record is of the same sex. On the other hand, in advanced life the majority of cases occur in males—Pavy.

Then again the onset in children is sudden; I cannot find any case mentioned where it has been otherwise. In elderly persons the disease occasionally appears insidiously.
Cases have been recorded in which recovery from diabetes has taken place in children, and also cases of a chronic character; but these are few and far between. Diabetes is generally rapidly fatal in children. Thus D. Saunby states in his Croonian Lectures p. 92. that it is generally rapidly fatal under forty years of age, but it is acute and rapidly fatal in children and young persons, running a longer course in direct proportion to the age. Pye-Smith makes a similar statement in the Clinical Journal for Feb. 1st 1893. But it is more than possible that mild cases in children may be overlooked, as one does not expect to find such cases, this may make such cases appear more rare than they really are.

Then comes the question, Can we give any explanation for this phenomenon? It is well known
that children cannot go without food for any length of time, in fact they require feeding very frequently. It is also known that if they lose their body heat, they quickly succumb. But the body heat depends upon the metabolism of the body, and the metabolism depends upon the supply of food. But the same loss of heat from diminished production will take place, in spite of a proper supply of food, unless that food undergoes the proper chemical changes, by which the heat is generated.

Now in diabetes these two factors, which are so important in the life of a child, are at a low ebb. That is to say, the temperature in diabetes is usually subnormal, because a part of the food taken escapes by the kidneys without undergoing the chemical changes whereby heat is produced as in health. That is the subnormal
Temperature, in part at least, depends upon the loss of what may be called this raw material. But from whatever cause, these two factors which are so important in the life of a child, are below their normal standard, and this seems to me to be one feasible explanation of the very fatal nature of diabetes in children.

But why is it sometimes chronic, and sometimes acute? For a definite answer to this question, we must wait till the pathology of the subject is more complete. But it seems probable that if the disease depends upon some glandular derangement, such as that of the liver or pancreas, the course of the complaint is likely to be short. If on the other hand it be due to nervous disease, implicating the brain, its course would vary with the nature of the cerebral mischief.
being slow if it did not implicate vital centres, but implicating those centres of course it would be acute.

The case I am about to report, and to refer to at some length, is a case of diabetes mellitus occurring in a young child after influenza. There may be difference of opinion as to the connection between the diabetes and the influenza, as to whether it is post-hoc or propter hoc. But the association is a matter of clinical interest, and I venture to think that the influenza is responsible for the diabetes.

Case. Clara S. 6t. 4 years and 4 months, was brought to my consulting room by her mother on Sept. 26. 1890. The mother complained that the child was passing water very frequently during the day,
wetting the bed every night, and had great thirst. These symptoms had come on quite suddenly during the last four days, but appeared to be getting worse rather than better. The mother also noticed that the child was listless and languid, and would not play as usual.

The child had been brought up on the breast, had had no previous illness, with the exception of influenza a few days earlier. The attack of influenza had been moderately severe, there had been no complications, and the child had been confined to her bed for three days only. All the other members of the family also suffered from the same about the same time.

Family History. This is exceptionally good. No member of the family, and no relative
had ever suffered from symptoms of diabetes.

The mother, whose temperament is of the bilious variety, is healthy and strong, and has always been so. But whilst carrying this child, the mother had an attack of bronchitis. She has had eight children, two stillborn. The father, of a nervous temperament, is healthy, and is always well.

The patient has three sisters, whose ages are 10, 19 and 21. All are in good health, with the exception of the eldest who has developed severe hysterical manifestations occurring at each menstruation. This hysteria commenced two years after the onset of the diabetes in the youngest child.

The brothers, four in number, whose ages are 8, 18, 23 and 25, are all in good health.
Clara S. aged 6 yrs. April 1893.
Diabetes commenced Sept. 1890.
None of the uncles or aunts has any serious illness.

Grandparents:—The grandmother died at the ages 64 and 69. Of the grandfathers, one lived to be 83, and one was killed by an accident at the age of 48.

State on examination two years after onset of symptoms.

Weight 39 pounds. Height 42 inches. A well developed child, not so fleshy as she was two years ago, but still she is not markedly thin, her face especially is round and plump, the muscles of the limbs are rather flabby. In facial expression the child is languid and pale, with sometimes a look of exhaustion and depression; at other times she looks quite well as if nothing is the matter. The skin of the lips is dry. There is no cyanosis. Fair skinned, and fair or yellow hair, in this respect agreeing with the expressed
opinions of Drout and Eajge who state that diabetes is more common in the fair. The hair is not rough, and has not lost its glossy appearance. No sweet smell noticed in the breath to indicate the presence of acetone. The knee jerks are diminished. Vision is good, and all the other organs of special sense are normal.

Appetite is greatly increased, so that after having an ordinary breakfast, the child usually sits down to a second, eating as much as two or three other children to the amazement of the parents. Digestion is perfect. Condition of the tongue—clean, moist and red. Bowels—constipation is the rule. Ten grains of compound jalap powder is usually necessary twice a week. At the outset of the complaint the teeth
were sound and good, well shaped, but decay set in soon after, until at the present time four sound teeth are all that remain. Neuralgia will be mentioned under complications. The gums are sound, and the teeth have not dropped out, nor are they loose, their decay appears to be due to the development of bacteria.

Abdomen. On examining the abdominal viscera, particular attention was given to the pancreas, but neither induration nor enlargement, nor any abnormality of this part could be detected. Bacon, and especially bacon fat is taken with great relish, as also cod-liver oil and milk, so that one hardly could expect derangement of this gland, which has for its function the emulsification of fat. Stools are normal, and although hard
are not oily. The liver, which in the typical form of diabetes is usually enlarged, in this case is not so, the dulness in the nipple line does not extend below the margin of the ribs.

Thorax. There is no dyspnoea. The heart is normal in size. Cardiac sounds are also normal. No feebleness is noted in its impulse. The lungs appear to be healthy.

The pulse shows nothing unusual, it is always regular and fairly strong. The peculiar odour of the breath which has been described as that of a drawer in which apples have been kept, and which is ascribed to the presence of acetone and ethyllic ether, is not, and never has been noticed.

The body weight frequently varied by a few pounds, but the variations were never great.
and the body weight did not increase in proportion to the height of the child.

**Weight of the child.**

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These variations are doubtless due to the difference in the daily amount of sugar and urine voided, and in the amount and quality of food taken.

The specific gravity of the
urine varies as much as the body weight, or the amount of urine passed, or the amount of sugar, but in spite of these three factors varying, there appears to be no direct relationship in their variations. For instance on Feb. 21, 1893, the specific gravity of the urine was 1.042, of which the amount of sugar passed was 100 parts per thousand, the amount of urine 91 ounces; on August 25, 1892 the specific gravity was the same, but the sugar passed was 58 parts per thousand, whilst the amount of urine was 98 oz. The specific gravity varies from 1.030 to 1.043, but generally stands at 1.040. A high specific gravity is no proof of the presence of sugar, and it is just in these cases of high specific gravity due to excess of urates, that a reduction of Fehling's solution
is liable to take place owing to the presence of urates in excess. On the other hand a low specific gravity is no proof of the absence of sugar, when the two go together it is (according to Saunby) generally in elderly diabetics, and two such cases have lately been reported in the medical press.

The colour of the urine is typical, being of a pale straw colour.

Reaction is always acid. There has never been any sediment. Albumen has never been detected. Sugar is invariably present, in amount it varies from 33.32 to 100 parts per thousand. The amount of urea varies from 0.25 to 0.65 per cent.

The details of the case, as to the amount of urine and sugar passed will be seen in the following tables, likewise specific gravity and % of urea.
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In reference to the preceding figures, it should be noted that the quantity of urine passed at first and until the end of June was measured by a half pint jar, but subsequently a vessel containing 200 ounces was used, in which the urine was collected. So that it is probable that the difference in the quantity passed before and after August 1892 is more apparent than real.
Also until August the proportion of sugar present was estimated by means of Kiebiq's Saccharometer, subsequently Pavi's method was invariably used.

The treatment, as far as medicine was concerned, has been indicated, but its discussion is postponed, suffice it to say now, that it was twice interrupted by slight attacks of bronchitis.

* An asterisk has been placed opposite the figures denoting the proportion of sugar when it was found that the child had been eating sweets.

Complications. It is rare for a case of diabetes to continue for two and a half years without complications, and there have been complications, but these have not been of any great moment. It would have been a matter of surprise if
Constipation had not been present, indeed so marked a feature of the disease is constipation and so constant is it, that it seems very doubtful whether it should be mentioned under the heading of complications. The constant drain on the system, due to the large amount of water that is passed by the kidneys, leaves the tissues with a lowered percentage of water, in fact it has been estimated in certain cases that the water passed has been in excess of that which has been inbibed, which leads one to infer that the tissues have absorbed moisture from the atmosphere. The constipation is therefore primarily due to insufficiency in the watery secretions of the intestine, which gives rise to hardened faces difficult to expel. Muscular activity is also lowered in
diabetes, and a diminution in the vermiform movements of the intestine may therefore play a secondary part. The rational treatment for this form of constipation is therefore to give diluents freely, and as a medicine there is probably nothing better than Cascara Sagrada, for the action of this drug is to stimulate the muscular movements of the intestine. Purgatives which act on the intestinal secretions are contra-indicated, as they would augment the cause of the constipation, and leave matters worse than they were before. When the action of the kidneys are defective as in Albuminuria, then purgatives which increase the intestinal secretions are eminently satisfactory, as their action in ridding the system
of superabundant watery elements is a compensatory one. For the same reason in diabetes their action is very temporary, and should not be given as they increase the cause of the constipation.

Decay of teeth is another complication which is most intractable, and intractable because it depends upon the disease, and will always tend to take place as long as the diabetes lasts. This child had at the outset of the disease a good set of sound teeth, she now has only four, all the others being extensively affected with caries, with the exception of two upper incisors, but these also have commenced an active decay. Then the question that arises is, why do diabetics suffer from caries of the teeth more than other people? Evidently
does not depend upon the loss of the watery elements of the body, as this factor is present in diabetes insipidus in not a less marked degree than it is in true diabetes mellitus, and yet caries of the teeth is by no means a constant factor in simple polyuria. The explanation is found in an aggravation of the conditions which usually predispose to caries. And acidity of the contents of the buccal cavity is the chief cause (Dental Anatomy and Surgery, Sewell). And this acidity depends upon secretion of the mucous membrane and decomposition of particles of food. The normal acidity of the secretion of the mucous membrane is neutralised by the alkalinity of the salivary secretions, in diabetes this acidity is increased, and therefore may not be so thoroughly neutralised. Again
The acidity depends upon decomposition of particles of food, decomposition depends upon the presence of bacteria, and the bacteria thrive in a weak saccharine solution. It is a matter of common observation, noted by the laity, that children who indulge excessively in saccharine food, are those who most frequently suffer from caries. And that sugar is present in the secretions of the oral cavity of diabetics is proved by the analysis of those secretions, as also by the fact that diabetics complain of the sweet taste in the mouth. These then appear to be the reasons why diabetics suffer so markedly from caries. And the rational mode of meeting this complication is in the free use of alkaline mouth washes. **Neuralgia**. This appears to depend upon the preceding
fact, that of caries. In the case reported, neuralgia was intense, lasting for several weeks, and although it was not particularly worse at night, it was so bad as to account for many a sleepless night. Neuralgia was combined with headache, which seems to have been in great part due to the opium which the child was being given for the diabetes. For the last three months the child has been free from neuralgia. For this painful affection, I gave exalgine, in doses of one grain which gave relief, and which appeared to have no influence on the diabetes. I have frequently found exalgine most beneficial in neuralgia, which fact I have noted in an article on the "Toxicity of Exalgine" in the Lancet for July 30th 1892.
One complication which is interesting from the light it may give to the essential cause of the diabetes, is that a few days after the onset of the diabetes, the child became markedly jaundiced. This was treated by calomel, and slowly passed off after being present for seven or eight days.

A complication which caused some anxiety was that of bronchitis, which has appeared three times during the progress of the case. But in each instance, the attack was cut short by confining the child to bed and giving expectorants. The bronchitis seemed to have no direct connection with the diabetes, but the anxiety was due to the fact that in this wasting disease, incipient phthisis is so liable to intervene; and
diabetics are much more liable than other persons to succumb to such affections as bronchitis and pneumonia.

With regard to the integumentary system, which is so commonly the seat of inflammatory affections in diabetes, eczema genitale was at the commencement of the diabetes very troublesome, but the eczema never became general, it confined itself to a few inches round the vulvae. The skin generally was dry, but there was no tendency to desquamation of the epidermis.

On Oct. 1st 1847 urticaria appeared over the body and limbs, but it did not last for more than an hour, and came on subsequently to eating some hake fish. There never has been any cyanosis.
It will be thus seen that the complications which have occurred during the two and a half years that this case has been in existence, have been by no means numerous, and those that have occurred have been for the most part of a trivial character, and have not materially altered the course of the disease, nor the treatment adopted.

**Diagnosis.** The symptoms of the case that has now been reported at some length, at the outset pointed so markedly to diabetes that a qualitative examination of the urine was made, with the result that it was found to be loaded with sugar. Now diabetes mellitus or glycosuria is almost the only disease in which an absolute diagnosis
of the disease may be made without one ever seeing the patient. This is done by making a chemical examination of the urine, for the cardinal fact in diabetes mellitus is the presence of grape sugar in the urine. But then the question "Can sugar be present in healthy urine" is one about which there is some dubiety at the present time, and authorities differ in their reply to this question. Some writers maintain that it can exist in considerable quantities, and that traces of sugar may exist in health has been admitted by several writers for several years. But if it be admitted that it is possible to be present, there is still the question to be considered, as to whether its presence is
evanescent or permanent, and whether the latter is compatible with health.
At the present time I propose merely to review the general position of the profession on the question.
I may mention Dr. Saunby, of Birmingham, as an authority who takes up the first position, and maintains that sugar may be present in health in considerable quantities, and permanently present. And this idea he bases on a case which he mentions (Croonian Lectures p. 83). A man, æt. 32, came to be examined for life insurance, was found to be healthy in every respect, but his urine had a specific gravity of 1029, and was "loaded" with sugar. This man's condition remained in status quo, presenting the same
phenomena one year later. The same author mentions, but fails to confirm, HINT as an authority, who has stated that sugar is present in 1 out of every 377 healthy persons in obvious degrees.

Thirty years ago Dr. Bence Jones asserted that all normal urines contained a trace of sugar. Dr. George Harley, at the meeting of the Royal Medical and Chirurgical Society held on the 14th Feb. last, stated that normal urines were not always free from traces of sugar; and this view was supported by Dr. W. Hunter. Others, amongst whom I may mention the names of Pavy, Schwartz, and Mc G. Shillingfleet Johnson, hold that normal urine contains no sugar, but the fact that other ingredients contained
in urine cause a reduction of cupric salts build in alkaline solutions, and that insufficient familiarity with this fact not infrequently led to the conclusion that sugar was present in a sample of urine simply because a certain amount of oxide had been reduced thereby.

The principal substances which may bring this reduction about are: 1) in normal urine: - Uric acid, according to Pavy, one fourth of the reducing action of normal urine is due to this; creatinin this may account for the other three fourths, but this does not generally act as a reducing agent. 2) Substances abnormally present: - Chloroform; certain carbo-hydrate substances; same effect is produced in the urine of patients who are taking
chloreal hydrate; glycuronic acid; due to the assimilation of Borneo camphor; aldehyde; lactic acid; lactates and lactose; lacticin; salicyluric acid, due to taking salicyl compounds.

With regard to the reducing action of uric acid, this as a rule does not take place to any appreciable extent, unless it be present in excess, and as it is in these cases that the specific gravity is high, the fallacy is apt to be confirmed by the latter test. But it is after sugar has been detected that excess of uric acid is liable to take place, and this owing to the adoption of a diabetic diet. Thus Dr. Haig has recorded a case (British Medical Journal, Feb. 93) in which Fehling's solution continued to be reduced as long as the patient continued to live on a nitrogenous diet.
but disappeared when a mixed diet was resumed. This reduction was evidently not due to the presence of glucose, but no doubt to uric acid.

And sugar may be present in urine apart from diabetes, unless the latter term is taken to include all cases where sugar is present in urine; at least sugar may be present as a physiological fact, without disease being present. In such cases it has passed out of the organism because more sugar has been taken than the organism can manage. On the other hand it may appear on the least provocation, without undue indulgence. The following case illustrates the latter point. A gentleman in this Town had been treated for some time for a complaint the diagnosis
of which was not clear. Then he consulted a London physician, who diagnosed diabetes, on several previous occasions his urine had been examined with negative results; at a later consultation sugar was again detected; these facts were then cleared up by discovering that each time the patient had gone to London he had freely indulged in honey for breakfast. Fowler had noticed similar instances. Again sugar may be present pathologically, and yet the case may not be one of true diabetes. Thus Goodhart has published several cases of glycosuria in association with neurasthenia, McTigue has also stated, at the New York Academy of Medicine, that he had found sugar present in urine in connection
with several chest complaints, such as incipient phthisis, emphysema, chronic bronchitis, chronic pleurisy, heart disease; as well as in certain liver troubles.

As regards the latter it is highly probable that the cases were cases of true diabetes, for diabetes is eminently associated with disordered functions of the liver, and it is highly probable that such disorders are the essential factor in diabetes.

So that before we can definitely state a case to be one of diabetes, it is not only necessary to detect sugar in the urine, but it is also necessary to take certain other facts into consideration.

But it is not safe to rely upon Fehlings test alone, as we have seen there are other substances which may bring about a reduction of cupric salts. Hence it is necessary
to do one of two things, before finally deciding on the presence of sugar, after using Fehling's method, the first is to confirm this test by other tests; or secondly, we may eliminate the other substances on which the reduction of the cupric salt may depend. To eliminate kreatinin, which is supposed to account for three fourths of the reducing action of normal urine, Dr. G. S. Johnson at the recent meeting of the Royal Medical and Chirurgical Society, described a new method, which he maintains completely removes this substance. The test depends upon the fractional precipitation of kreatinin by mercuric chloride. This test cannot remove sugar, but it effectually removes kreatinin from the un Concentrated solution.
If uric acid be in excess it is easily neutralised. The presence of any carbo-hydrate substance may be detected in the following way:—a sample of urine is rendered alkaline by the addition of some caustic soda solution, to this add a small quantity of benzoyl-chloride, shake; if any carbo-hydrate be present it will come down in the form of a precipitate. Another test is by adding a solution of a naphthol and a little sulphuric acid, when a violet colour is produced if any carbo-hydrate be present. Some say that sugar may be present in urine in quantities that are not appreciated by the ordinary tests. But we have two very delicate tests for sugar. Dr Curznow has stated that a tenth of a grain of
of sugar to the ounce of urine, could be detected by means of the following test, supposed to have been introduced by Fischer and Schwartz independently, but Dr. Cagney points out (Lancet, March 4, 1893) that this test was fully described by Prof. von Falko in his book "Klinische Diagnostik" several years ago. The test is as follows:—

1. Add to urine lead acetate, and filter after the precipitate has formed, render this alkaline by caustic potash, add a solution of phenylhydrazine, shake and boil. An orange colour is produced, and an orange precipitate when excess of the acetic acid is added.

M.C.S. Johnson never detected sugar in normal urine by this method, which confirms him in his view that sugar is not present in normal urine. But on the other hand T.W. Hunter
does not consider the test conclusive.

Another test which is considered delicate in detecting the presence of sugar is the fermentation test. Two test tubes are taken, the one is filled with water and inverted over a saucer containing water, the other tube is used in a similar manner only using urine in place of water, a piece of yeast the size of a split pea is put into each tube. The two are allowed to stand at a temperature of 60°F for 24 hours. At the end of that time, if sugar be present in either case, fermentation will have taken place, carbonic acid gas being given off, and collected at the closed end of the tube. If sugar or air is introduced with the yeast, the gas will be in both tubes, and hence such a
fallacy is detected. Dr. Saunby considers that the fermentation test is the 'most certain and the most delicate.' But Roberts in his book ('Urinary and Renal Diseases,' p. 181) considers that the test is useless unless the urine contains 2½ grains of sugar. It seems to be that fermentation would take place if a fraction of a grain of sugar be present, but the carbonic acid gas being so small in amount it would be very readily absorbed. I have proved that this absorption takes place over and over again by Gan's instrument for the quantitative estimation of sugar, when it has been allowed to stand for a few days.

And all the other well-known tests were employed for the detection of sugar in this case of diabetes in a child.
and all of them with positive results; among others Moore's test with caustic potash gave the dark brown colour on heating; Frommer's test with sulphate of copper and liquor potassa, which on boiling gave the yellow colour, indicative of the presence of sugar, and which ultimately passed into the reddish-yellow granular precipitate of the suboxide of copper; and also the usual standard test with Fehling's solution; also Pavy's modification of Fehling's process, the precipitated oxide being kept in solution by the presence of Ammonia; and the picric acid test introduced by Dr. G. Johnson.

These then are the tests which were relied upon in detecting the presence of sugar in diabetic urine, but not many
of them are in common use.

But once having established the cardinal factor of diabetes, that is the presence of sugar in the urine, we pass on to see what other features of the disease are present, before considering the quantitative analysis of the urine which is not used in estimating the diagnosis but rather the prognosis of the disease.

Wasting. In the acute form of the disease this is excessive, but varies when the disease is chronic, and no doubt depends in part on its cause, which is not always clear, and as our present knowledge of the disease is so limited, cannot always be defined. For instance if a malignant tumour of the brain is the cause of the
diabetes, the tumour will per se cause rapid wasting; if on the other hand the disease depends upon some other cerebral lesion, which in itself causes no wasting, such as a lesion in the grey matter in that part of the floor of the IV ventricle which controls the blood supply to the abdominal viscera (such a condition may be produced by the lancet artificially as was first pointed out by Claude Bernard in book, "Sur le Diabète. Leçons de Pathologie Experimentale," Tome I, Paris 1855.), then the wasting will depend on the amount of sugar passed, always supposing the amount of food taken remains the same, and all other physiological processes continue in their normal state. But the amount of food taken does
not remain the same; in the large majority of cases the appetite is greatly increased. This increase of appetite is not the disease, but its result, and so constant is it that it may be classified as another symptom of the malady. This being the case, the amount of wasting in the earlier stages of the disease is scarcely ever so great as it otherwise would be.

Few facts are so well marked in pathology as the compensatory effect produced in certain organs of the body by disease in other organs by which they are in part or in whole destroyed, whereby structural changes are produced in the compensating organs. Taking the kidneys as an example, if one is destroyed the amount
urine voided is not diminished in proportion. Why? Because the other kidney, so to speak, has come to the rescue, and in order that diuresis may continue in some proportion to the amount of fluid absorbed, the second kidney has increased in physiological activity, as more work has been laid on it, and has hence taken on in part or in whole the double function. And in the case of the kidney this increase in function has been accompanied by certain changes in its macroscopical and microscopical structure. But instances may be recorded in which organs that are neither analogous nor homologous may take on physiological compensation, in which cases the increase in function is not always
accompanied by an appreciable change in structure. For instance, in persons who are blind, after a time their other organs of special sense become more acute; their hearing becomes more distinct, and may indeed become so sensitive that in another individual who was not blind might be termed hypersensitive, but in this instance it may be regarded as a case of physiological compensation, in organs that are not physiologically analogous nor anatomically homologous, in that they differ both in function and structure. And yet their functions are in part similar, for though the eyes are adapted to receive impressions of light, and the ears to receive impressions of sound,
yet they are analogous in that they are both adapted to receive impressions, either agreeable or disagreeable, so that it will be seen to be a relative term when the term analogous is used in describing the functions of an organ. So too, when we come to chemical considerations, and speak of the metabolism of the body, the two functions on which nutrition depends, the import and export of chemical compounds, it is necessary that the appetite should have a certain relation to the waste that is going on. Waste may depend on the increase of metabolism, as in fever, or on the exportation of chemical compounds without undergoing their normal chemical changes in the body, whereby their potential energy is not
transformed into their kinetic equivalent. Then when the waste is increased, by whichever method it may be, in order that nutrition may remain the same, it is necessary that the importation of suitable chemical compounds should be increased. In order that nutrition may not suffer these functions must bear certain relations to one another.

To apply the argument, in diabetes the waste depends upon exportation of raw material which has not undergone the normal chemical changes within the body, to compensate for this loss the vitality of the body demands a greater supply, hence the appetite is increased. When wasting depends upon the other factor, that of increase in metabolism, as soon as the vitality
is restored the appetite is increased, as is so commonly seen in practice, in convalescents after acute fevers. It is the effort of nature in the struggle for existence to maintain the status quo; and the increase of appetite is the physiological compensation for the increase in waste; physiological compensation in functions that are not analogous, and that does not result in appreciable change of structure.

So in diabetes mellitus, wasting takes place, not because metabolism is increased, for the temperature in diabetics is usually subnormal, but because a part of the nourishment that is taken is allowed to pass through the body as if it were waste material, its potential energy remains potential as far as the body is concerned.
This symptom of wasting in advanced life is, as a rule, not so great, and often not remarked as the sufferers are frequently stout to start with, as diabetes seems to have a preference for such persons rather than thin ones. The case that has been recorded in the previous pages of this thesis is an instance of the wasting in a child simulating that of an aged diabetic. It is hardly sufficient to be appreciated, true—the child does not gain flesh and weight as one her age with fairly rapid growth should; absolutely she has gained weight, relatively to her height she has lost. The disease has now lasted two and a half years, and the patient weighs over forty pounds, whereas at the outset her weight was thirty—
six pounds. This will lead one to infer that the wasting in diabetes is in direct proportion to the chronicity of the disease, and it has probably nothing to do with the patient's age; but as the disease in the great majority of cases runs an acute course in children, this symptom is also acute as a rule; but the rapidity of the disease has not so much to do with the age of the patient, but is in more direct relation to the rapidity of the wasting; and this idea is supported by reference to these facts as they occur in the aged. In this respect I am quite in accordance with Dr. Saunby's remark which he makes on page 92 of his lectures. But the same writer makes the remark that the weight of diabetics
commonly varies by a few pounds every few days. I can only say that the evidence of my case does not support this statement, for as a rule the weight did not vary by more than a pound at intervals of several weeks, this is however in part due to the fact that the absolute weight of a child being so much less than that of an adult, the amount of variation would likewise be very much less. Again the evidence from this case does not support the view that the degree of acuteness in a case is proportionate to the amount of sugar passed, for 100 per 1000 parts would be a large amount for an adult but for a child five years of age it is enormous, and yet the case is running a very chronic course, the child
appearing no worse now than at the outset of the complaint, indeed a stranger would not suppose that the child was ill from looking at it.

To sum up the evidence with regard to wasting, I have to say it should form a prime factor in forming an opinion as to the prognosis, it is to be put in fact as far as prognosis is concerned, far above the percentage of sugar or age of the patient in importance; and that it very materially depends upon the digestive powers of the individual. So long as the digestive powers remain intact, and so long as this is accompanied with polyuria, the fatal issue may be averted for an indefinite time.

Polyuria. The arguments with regard to wasting and
increase of appetite, are equally applicable to polyuria and increased thirst. The latter depends upon and is a sequel of the former. Both are so constantly present as to form prime factors in the disease. The fact that so large an amount of the fluids of the body are passed through the kidneys leads to an increase of thirst of the individual. The increased thirst is an effort of nature to maintain the status quo, it is an effort of nature and does not depend upon any mental argument as to the advisability of drinking freely. It is another instance of compensation, a large amount of fluid is passed, this would leave the tissues
of the body with a lowered percentage of water and effete material would tend to accumulate as they would not be so soluble in water containing a high percentage of solids. Then thirst is increased and this leads to a process of balancing. In this case the compensation is accompanied with more evident histological changes, for the increased work thrown on the bladder frequently causes an increase in the muscular elements of the walls of this viscus.

A similar increase may take place in the muscular coats of the intestine, as is found in cases of stricture, in order to overcome the obstruction resulting in constipation; but this effect is not so evident in the intestine as it is in the case of the bladder.
The amount of urine passed was measured by a graduated chamber containing 200 ounces, which was emptied once in 24 hours, and into which the urine was voided. For an adult 50 ounces per day passed is considered a normal quantity. In a child six years of age, we should expect 30 or 40 ounces, but the average amount passed by my patient is 100 ounces approx. The tissues of the body become so drained by this constant loss, that the other usual emunctories are so to speak dried up, the sweat glands are deprived of their use, and hence the loss of their function leads to a dry and harsh state of the skin, which readily becomes inflamed, and is especially subject to such
diseases as eczema. The activity of the kidneys is so great in secreting fluids, that if the quantity imbibed is restricted, it seems that the tissues absorb moisture from the atmosphere (Sir Thomas Watson, reported by Jaggie, p.562, Vol. 2.). In simple polyuria, that is when it is accompanied with glycosuria, thirst is also increased. Therefore it is evident that the latter symptom is dependent upon the polyuria and not upon the glycosuria. Many cases of polyuria have been reported, and as it is so nearly allied to True diabetes, I will add another, which came under my observation a few weeks after the case of glycosuria. In saying that polyuria is nearly allied to glycosuria, the saving clause should be added that
clinically it is only in this symptom that there appears to be a close relation; but pathologically they are more nearly allied, for the two conditions are readily induced by lesions in the floor of the IV ventricle, as Bernard has demonstrated, the glycosuric centre being situated immediately below that of diabetes insipidus. And the case is of interest as it supports this view of the origin of diabetes insipidus, being caused by a blow on the back of the head. Miss K., Oct. 26, unmarried, came to me complaining of frequent micturition, and passing large quantities of urine. A few days previously, in helping to remove furniture whilst changing houses, she fell back, knocking her head
against the stone steps. She also had valvular disease of the heart, and was very anaemic, and menstruation was absent. She was treated with Valerianate of锌 for ij ter die. In the course of about eight weeks the polyuria gradually ceased.

So much for the cardinal factor in diabetes vera, i.e., glycosuria. And the other prime factors in the symptomatology of the disease have also been considered, i.e., wasting with boulimia, and polyuria with thirst.

Prognosis. Saunby puts the age of the patient as of the first importance in considering prognosis; it does, he says, as a rule depend upon the age of the patient, under forty it being generally rapidly fatal. With the light that this
case throws on the subject, the age appears of minor importance. It seems to be that the cause of the disease is of prime importance. But as the cause is frequently so obscure, we must fall back upon other facts more obvious, such as the age, and it being a clinical fact that diabetes in children is as a rule rapidly fatal, when we only have this fact to guide us, the prognosis is necessarily very unfavourable. When diabetes comes on as a sequel to influenza, it would appear to be not of such grave import. At least such an inference is certainly supported by the evidence of this case. For in children diabetes is notoriously deadly, and yet it has now existed in Clara S. for two and a half years without apparently having done her very
great harm. Influenza must henceforth be set down as one of the causes of diabetes, and as such it must be admitted that it lends a more favourable prognosis to the complaint.

Then diabetes may appear from eating too much sugar. In these cases the remedy is obvious and effective. A family tendency to diabetes is of grave import. The prognosis is less favourable when there is a family tendency to nervous affections. In the case of which I have been writing there is no evidence of a family tendency to diabetes. The only member of the family who suffers from a nervous weakness, is the eldest sister who for the last year has suffered from severe hysterical attacks at each menstruation, but as such affections are so common in persons of her
age, it can hardly be said to throw much light on the case, as to affect the prognosis. There is no history of gout or rheumatism in the family; but generally speaking when diabetes is related to gout the outlook is more favourable.

The degree of wasting should be put among the foremost factors in forming an opinion as to prognosis. If this is allowed to guide us in the case of Clara S. we may consider the prospect fairly good. I believe that the degree of wasting is of more importance than the age of the patient, and as to prognosis I would put it second only to the cause of the disease.

Influence of treatment, it is evident that those cases which are easily controlled by attention
to diet, are more favourable than those which are not so influenced.

Generally speaking, the greater the severity in the prime symptoms, the less favourable must the outlook be; thus, the greater the amount of polyuria the graver the case.

The total amount of sugar passed. Other things being equal, the gravity of the case will bear a direct relation to the amount of sugar passed. The amount of sugar passed in this case has varied considerably; other factors, such as the specific gravity and amount of urine have also varied, but there does not appear to be any direct relation between their variations. The average amount of sugar passed between August 1892 and Jan. 1893 was 58.16 parts
per 1000, or 27.53 gms. per ounce; in other words 2769.02 grains per day, as the average amount of urine passed per day was 100.55 ounces, which is considerable for so young a child. The lowest amount was passed on Sept. 1st 1892, which was estimated at 33.32 per 1000, multiplying this figure by .15735 we get 15770.2 grains per fluid ounce of urine, and as the amount of urine passed on that day was 102 ounces, the total amount of sugar passed on Sept. 1st 1892 was 1609.25 grains. I recognise the fact that the percentage of sugar varies according to the meal previously taken, and also seems to vary with the time of day, although the latter variation probably depends upon the former.
But as all the urine was passed into a common utensil, and as the sample was invariably taken from this mixture, the mean amount of sugar passed was obtained and estimated by analysing the sample of this mixture. On March 13th, 1893 the amount of sugar passed was 100 parts per 1000, which gives us 47.35 grs. to the fluid ounce, and as on that day 87 ounces of urine were passed, we have a total for that day of 4119.45 grains of sugar. 4,000 grains a day is a very large amount considering the age of the patient, and as the course of the illness has been comparatively so favourable, this would lead one to give a secondary place to the amount of sugar passed when estimating the prognosis of diabetes.
So much then for the prognosis, and to sum up, I would in this reference give the place of first importance to the cause of diabetes when it can be discovered, secondly for a prognosis consider the amount of wasting, and lastly regard the severity of the general symptoms— and of these giving the place of first importance to the amount of sugar passed. As to age, I consider this to be of minor importance when the cause is detected, when this is obscure, then in the case of a child, this fact must always must be of the gravest import. And again when we say influenza is the cause of the diabetes, this is vague, as we do not know the exact way in which it acts as the cause, and in different cases it may act...
differently, and if so its relation to prognosis will vary. But the modus operandi in which influenza causes diabetes is a question in pathology.

Quantitative Analysis. This seems to be the place in which I should mention the methods I have adopted in estimating the quantity of sugar passed. The method relied upon has been that introduced by Dr. Pavy to the Royal Society in 1870, and a description of its application was published by him in the Lancet of March 1884. A solution of cupric oxide is blue, if this solution be boiled in the presence of glucose it is reduced, as a result of this reduction the suboxide of copper is precipitated. If ammonia be present
the reduction will still take place, but as the suboxide is soluble in the presence of ammonia, no orange coloured precipitate takes place; the liquid is merely deprived of its blue colour and becomes colourless when all the cupric salt has been reduced. Ten cubic centimetres of the standard ammoniated cupric test solution is taken, and for convenience of working in facilitating accuracy, is diluted with twenty c.c. of water. The 10 c.c. of cupric test solution are discoloured by, and therefore stand equivalent to 0.005 grammes of glucose. On account of the delicacy of the test the urine to be tested has to be greatly diluted, and in proportion to the amount of sugar it contains. In my examinations
I invariably used it at a strength of 1 in 40. So that 2½ c.c. of urine were mixed with 100 c.c. of water. The test solution is heated to boiling, and the solution of glucose is slowly and carefully allowed to drop into the cupric solution whilst it is boiling, as the colour of the cupric solution fades the solution of glucose is added more slowly until the blue colour of the cupric solution has entirely disappeared. When this stage in the operation has been reached five milligrammes of glucose have been used. The quantity of saccharine solution required to decolourise the cupric solution is then estimated, this amount of diluted urine contained five milligrammes of glucose. On the continent the expression
used is as parts per 1000, and this is recommended by Pavy. This is arrived at by a simple rule of proportion. The amount of glucose required to decolourise the cupric solution, 0.05 gramme, is multiplied by 1000, and divided by the number of c.c. of diluted urine used; as the urine used had been diluted forty times, the result obtained must now be multiplied by forty to get the amount of sugar in the original urine expressed as parts per 1000.

This is Pavy's method and the usual one adopted.

An older method is by using Fehling's solution, in which there is no ammonia, and the application of the test is similar to that already described, but it is better to use an opaque porcelain dish in which to detect the stage at
which all the blue colour of the cupric solution has disappeared, than the transparent glass vessel used in Pavy's method. This is used in the latter examination as being enclosed the ammonia does not so readily escape. In Schling's method when all the blue colour has disappeared and given place to the orange coloured precipitate of the suboxide, the test is complete; the amount of diluted urine used is read off as in Pavy's method, and the proportion of glucose present is similarly estimated by the rule of three.

The picric acid method.

Circular polarisation. Grape sugar has the property of rotating a beam of polarised light to the right, and the degree of rotation depends upon the amount of sugar present,
hence it is easy to calculate the amount. The best known instruments are those of Soleil-Ventzke, and Laurent.

But a new saccharometer, which is not so well known, and about which therefore I wish to speak at greater length, has been introduced by Dr Edgar Gans of Carlsbad, and manufactured by R. Freibig, Alexandrinen-Strasse 27, Berlin S. W. which I have used frequently. It was first brought before the medical profession in England by Dr Scott in the Lancet Jan. 1892. The instrument is made of glass and is exceedingly neat. Dr Gans claims for his instrument that in its application and accuracy it is as exact as that by polarisation, but unlike the polarimeter it is equally efficient when albumen is present.
The instrument consists of two arms, the one long and graduated terminating in a narrowed neck but which is open to atmospheric pressure, the other arm is spherical in shape with an elongation at its further extremity which is fitted with a hollow glass stopper.

The lower portions of the two arms are connected by a hollow glass tube, and this is fixed to a glass stand. In connection with the short arm, the glass stopper and the neck to which it fits are bored by a hole, and by a turn of the stopper when it is in position, these two holes may be so placed
that air can freely enter the hollowed spherical chamber.
To complete the apparatus, it is required to have a glass vessel
graduated to contain 100 c.c.
and a tube to contain 10 c.c.
Method of application. The test
depends upon fermentation,
under the influence of yeast,
grape sugar breaks up into
carbonic acid gas and alcohol.
A piece of bakers' yeast, about the
size of a split pea, is placed in
the vessel containing 90 c.c.
of water, to which is added 10 c.c.
of the urine, and the whole
is well shaken, until the
yeast is intimately mixed up
with the mixture. Then 10 c.c.
of this mixture is measured
out and poured into the
spherical chamber of D'ans
instrument. The glass stopper
is then replaced and turned
until the hole in it is opposite
that in the neck, by which the air in the spherical chamber is in direct communication with that outside. The instrument is then tilted till the surface in the liquid in the long arm is at the level of the figure 0. By a turn of the stopper, the hole in it is no longer opposite that in the neck, hence when the instrument is placed erect on its stand, the spherical chamber being air tight, the surface of the liquid in the long arm remains at the figure 0, although the surface of the liquid in the chamber is much higher. As fermentation takes place, carbonic acid gas collects in the spherical chamber as it is air tight, the result of the pressure of this gas on the surface of the liquid here forces it down, and hence it rises in the longer and
graduated tube. And as the amount of carbonic acid gas formed depends on the amount of sugar present, and as the surface of the liquid depends upon the amount of carbonic acid gas, the surface of the liquid in the longer tube will be high in proportion to the amount of sugar in the mixture.

The principle of the test is as good as can be, but in its practical application there are certain drawbacks which will debar it from being generally utilised.

The first and foremost objection is the temperature, fermentation does not take place freely and rapidly except at a temperature from 60° to 70° F. and as we can only depend upon such a temperature in this country for a very few months out of
each year, this appears to me
to be an effectual hindrance
to its general application here.
This drawback renders the instru-
ment almost useless, it is easy
to heat a room artificially
to the required temperature,
but it is not easy to keep it at
that temperature for twenty-four
hours. So we must consider
the test at a lower temperature,
and find out if the results can
be depended upon. After several
testings at a temperature of
55° F. and thereabouts and
checking the result by use of
Pavy's quantitative method,
I found that a fairly correct
result is obtained if the
operation be continued for
at least 48 hours. For instance,
take the examination I made
on March 21st last, which by
Pavy's method gave 64.48 per
1000, as the proportion of sugar
in the urine, the thermometer stood at 55° F. by Gans instrument after 24 hours, the instrument only registered 3.0 percent, after the lapse of another 24 hours it registered 6.0 percent which limit it did not exceed after another 24 hours at the same temperature. On another occasion Feb. 17th Pavy's method gave 90.88 parts per 1000, the temperature was lower than on March 21st by about two degrees, after 24 hours Gans instrument registered 7.6%, and for the next two days it made no progress, then the thermometer rose to 59° F. and after 84 hours from the commencement of the operation the instrument registered 8.0%, on that occasion the operation was discontinued at this stage. Hence it may be said that when the temperature is below
60° F. Gans's instrument is useless, unless one is willing to wait several days before learning the result of the operation. Hence the length of time required to perform the operation efficiently at the usual temperature debar the instrument from being extensively used in this country, for a busy practitioner often has more than one examination to make in several days, and he would therefore require several instruments of this kind. One other fact in connection with the application of the test is worth noting; absorption of the gas takes place, whereby a fallacy will occur unless the test be rapidly applied (that is to say applied at a temperature of 60° F.), or unless the register is frequently taken so as not to pass the maximum, on
one occasion after the instrument had registered 7.2% of sugar, 18 hours later it had fallen to 5.5%, and a similar fall always occurs when the instrument is allowed to stand for a long time. Another drawback, but one which can be remedied in the future manufacture of the instrument, is that the long graduated arm is not long enough, at present it does not register a solution containing over 98% of glucose. The instrument would not so correctly register a larger percentage, unless it was taken into account that the pressure of the column of fluid would be in proportion to its length, and would therefore cause a compression of the gas, so that the graduations on the glass should be at slightly shorter intervals.
But in my analyses I found the graduations to be 0.1 not always sufficient, for sometimes the urine I had to examine contained a 10%. The first analyses that were made were made by means of this instrument, and found useless, on account of the long arm of the instrument not being long enough, for looking at the instrument I frequently found that the column of liquid had reached the top of the graduated arm and was overflowing. This enforces the fact that at the commencement of the illness the amount of sugar contained in the urine was considerable.

Pathology. Few subjects promise so much in the way of elucidation to original research as the pathology of diabetes. So much is
known of diabetes, so many causes have been discovered, yet its essential factor as it appears in disease is still obscure. Probably in disease, as when induced experimentally, there are various causes to this condition. The pathology of diabetes may be considered the domain of the experimental researcher, and one who has not such opportunities is not likely to add much of value to the subject. And, not having had the opportunity of making a post-mortem examination, I do not propose to enter into the subject of the pathology of diabetes, nor to go through the various theories as to its nature; but enter at once into the question of treatment which I have had an opportunity of testing for myself.
Treatment.

The first indication in diabetes with regard to treatment is to regulate the diet. And our first and only object in this direction is to diminish the amount of carbo-hydrates as far as possible, that is to say, no saccharine and no starchy matters should be given. With this end in view when the case reported first came under observation, a diet consisting principally of nitrogenous material was ordered, i.e. meat. Green vegetables were allowed. And gluten bread ordered. Unfortunately it was found impossible to keep the child on this alone, toasted brown bread was given next, but this did not suffice, and a little white bread has been given by the mother daily ever since.
Bacon, milk, cream, eggs, rice, tapioca were also allowed. It may be repeated that the symptoms at the first onset were as severe, if not more so, than at any succeeding period, and that during this time, lasting from two to three months, only gluten bread was given; but in spite of this, there was no material improvement in the general health of the child, although the treatment seemed to check the virulence of the disease. Subsequent observations on the amount of sugar passed would be valueless if the diet was changed from day to day, if white bread had been allowed for a few days and then discontinued; but when a little was allowed every day (although it was still restricted in quantity as far as the mother's feelings would let her),
changes in the amount of sugar passed must bear a direct relation to the medicinal treatment adopted, and it is on this ground that some claim may be made as to the value of the observations. A solution of Saccharine was always used in place of sugar. It was unfortunate for the child that the parents commenced to sell sweets, but fallacies from this cause were diminished to a minimum by constant vigilance on the part of the mother, who I may say is a very sensible working woman, and by severe admonition from myself. I believe my rules in this respect were only broken on three or four occasions altogether, and then were discovered by an unusual increase in the amount of sugar passed, which in each
case is noted in the clinical record.

In some other respects this case was peculiarly adapted for observing the effect of medicinal treatment. In some diseases there is a natural tendency to a spontaneous cure, with regard to diabetes this is not the case, except as it occasionally occurs in old people on restricted diet. In diabetes of children the invariable tendency is downward, and when any benefit is experienced it may pretty accurately be attributed to the treatment adopted. Also here we had a chronic case to deal with. And lastly all observations hitherto as to value of medicines in this disease have been made on adults, and it was hoped that if the same observations were made on a
child, where the liver is relatively larger than in the adult, some new clinical fact might be brought to light. There is at least one fact brought out here, and that is, that the true index as to the state of the child's health, has been rather its general appearance, its activity, and condition of nutrition, rather than the exact amount of sugar in the urine. And one fact noted as to opium, and that is, whilst it appeared to check the amount of sugar, it never had any soporific effect.

Drastic diseases require drastic remedies, and when the child first came for treatment, it being only four years of age, a quarter of a grain was ordered four times a day in the form of a pill which the child took well, the opium
was subsequently pushed and in Nov. 1892, six grains of
opium were being taken per
day, but the case did not
illustrate the usual narcotic
symptoms of opium which
commonly appear when that
drug is being taken, the
child was not at all sleepy
during the day, and the
pupils were not contracted, but
the mother remarked that the
child appeared 'queer' at times,
and headache was constant
and severe, and for this reason
when the opium reached six
grains per day it was dis-
continued. In the case of
codein grs. viij were adminis-
tered daily without any specific
effect being observed.

This tolerance of opium ap-
peared so remarkable, that at
a later date I determined
to test the accuracy of the
observation, as it is well known that children generally are so susceptible to the influence of opium. For this purpose I obtained the drug from a different source, and commenced on March 19th last with gr. f per day, until at the time of writing the patient is again taking opii grs. vj per day. The result has been to confirm the first observations in every particular, there is no soporific effect, the pupils are not unduly contracted, but the child at times is said to be 'queer', and there is pain in the head, and there appears a slight swelling about the features of the face.

Dr. Pavy has recommended codeia as being more efficient in checking diabetes than opium which up to that time was
generally employed for that purpose, since that time codeia had been in great demand. But Dr Bruce in the Practitioner for 1888 published certain cases which seemed to make it doubtful whether codeia was superior to opium. And finally in the British Medical Journal for Jan. 19th 1889, Professor Fraser published the result of lengthy observations on the subject which went to prove that morphine and opium were more effectual in checking the disease than codein.

I had hoped by estimating carefully the quantity of sugar and urine passed in this case (in spite of the fact that the patient was fed on a mixed diet), to be able to add something to the literature on this important subject.
Observations have been made on the case for two and a half years, but for nine months they have been of a detailed character, in which the amount of sugar passed has been at short intervals carefully estimated and recorded. But I cannot say that the result has been of such a definite character as one could wish, neither opium nor codeia reduced the amount of sugar, although these substances were pushed to an enormous extent, so far in fact as this case is concerned it goes to prove that in some cases neither substance is of material value.

I will not repeat all the details of the observations made on the case, and which will be seen in the tables of the clinical record, but will be content with a brief summary.
In order that the value of codein might appear apart from any effect due to previous treatment, during the month of July 1892 and first ten days of August, no treatment whatsoever was given, with the exception of the moderate restriction in diet, which restriction so far as it went (white bread being used in moderation) was continued in the same degree the whole time the observations were being made. Then on Aug. 11th codein gr. 1/4 was given four times a day, until Aug. 27th when it was increased to grs. 1/2 per day, this was continued till Sept. 5th when grs. 2/3 was given during the day, on Sept. 11th this was increased to grs. 1/4 per day, on 21st this was increased to grs. 1/2 per day, Sept. 28th to grs. 1/3 per day, till on Oct. 6th grs. 1/3 were given.
daily, and on Oct. 13th till 20th
grs. viij per day. When the
codein had reached this
amount, it was considered
unwise to increase it, especially
as no material benefit had
been experienced, although on
the other hand no bad effect
had been produced by such a
large dose considering the age,
the greatest inconvenience
being severe headache. The
average amount of sugar
being passed whilst gr. j was
given was 45.99 parts per 1000,
by the time grs. iv were given
daily this average had been
reduced to an average of 35.91
parts per 1000; when this amount
of codein was increased no
Corresponding diminution in
the amount of sugar passed
was experienced, but no weight
can be put on this as it was
discovered that the child had
eaten some sweets. But the average amount of sugar passed during the time the child was taking grs. viij of codein a day, with this indiscrption in regard to sweets, was 65.14 parts per 1000. So that during the time the child was taking codein when no fallacy was introduced, the amount of sugar passed was diminished by 10.08 parts per 1000.

Table to show influence of Codein.

<table>
<thead>
<tr>
<th>Date</th>
<th>August</th>
<th>September</th>
<th>October</th>
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<tbody>
<tr>
<td></td>
<td>11.13</td>
<td>11.16</td>
<td>11.18</td>
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<tr>
<td>Dose grs.</td>
<td>1</td>
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Graph showing the relationship between sugar in urine (gr. per 1000 cubic inches) and specific gravity (Sp.Gr.).
The preceding table illustrates the influence that the codein had on the amount of sugar and urine passed, and its specific gravity. It will be seen that the amount of sugar at first decreased, but later it rose considerably, but this doubtless due to the child eating a few sweets. The amount of urine steadily decreased. There was no permanent alteration in the specific gravity. In the child's general appearance there was no marked improvement.

After the treatment by codein, an interval of seven days was allowed, during which no medicinal treatment was pursued, and during which time the ill effect of the sweetmeats or huge doses of codein, whichever might have caused the increase in the sugar, passed off so far that the quantity of
sugar passed was 50.00 parts per 1000. On Oct. 27th opium gr. f was ordered twice a day, and increased on Nov. 3rd to gr. f thrice daily, on Nov. 9th four times daily, on Nov. 16th to five times daily, and on Nov. 23rd it was increased to six times a day.

The result of the opium treatment was that the child appeared better in itself, being more cheerful, but the child was not sleepy in the daytime, as one would naturally expect the child to do when taking six grains of opium, on the other hand the headache became severe; and the amount of sugar gradually increased. Once and once only was it discovered that the child had taken sweets, that was on Nov. 18th when the child passed urine containing 83.32 parts sugar per 1000.
Table to show influence of Opium.

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<tbody>
<tr>
<td>Dose in grs.</td>
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<td>85</td>
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<tr>
<td>Sugar in urine</td>
<td>30</td>
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The preceding table well illustrates the great increase which takes place in the amount of sugar passed in the urine. The sugary matter was taken on the 18th Nov. No opium was taken after Nov. Whilst the opium was being given, it did not seem to cause
any diminution in the amount of sugar passed. But the amount of urine passed and its specific gravity remained lower than when codein was given.

In order to verify or refute this partial tolerance of opium in this case, especially in its having no narcotic effect, on March 19th last I recommenced the administration of opium, and pushed it until it again reached grosfj per day, but the drug had no narcotic effect. I obtained the opium on this occasion from a different source than on the first occasion. Its administration however had to be dropped for a few days, on account of a slight attack of bronchitis, and it is interesting to see how the amount of sugar increased at this time, apparently without any indiscretion in diet.
It will be seen by this diagram also that the opium failed to bring about any marked benefit, so far as any diminution in the amount of sugar passed is concerned. Let us now compare the effect of codein and opium on this the cardinal factor of diabetes.
The observations on codein extended over a considerable period longer than they did in the case of opium in either instance, but as best we can we will diagramatically compare the effect of the two drugs on the sugar secreted. Taking the last instance in which the action on opium was observed.

**Codein versus opium.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Codein</th>
<th>Date</th>
<th>Opium</th>
</tr>
</thead>
<tbody>
<tr>
<td>August</td>
<td></td>
<td>September</td>
<td></td>
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<tr>
<td>11</td>
<td>1</td>
<td>7</td>
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<td>13</td>
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<tr>
<td>28</td>
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<td>8</td>
<td>8</td>
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<tr>
<td>20</td>
<td>4</td>
<td>11</td>
<td>15</td>
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<tr>
<td>10</td>
<td>5</td>
<td>18</td>
<td>18</td>
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</tbody>
</table>

**Sugar passed with Codein**

**Sugar passed with Opium**

Sugar Parts per 1000.
This comparison will tend to favour the old view with regard to the action of these drugs in diabetes. But, when we remember that the observations were made whilst the patient had home treatment instead of hospital management, this result will hardly be taken as conclusive evidence with regard to the comparative merits of opium and codein in diabetes. But the case must be taken for what it is worth, and it is hoped that it will help to elucidate this question, for the labour and care involved has been considerable. The comparative merits of morphine have not been investigated.

**Pancreatic Treatment.**

Since Sir William Gull first described Myxœdema in 1873 (Trans. Clin. Soc. Vol. VII) the same condition has been produced in monkeys by Prof. Victor Horsley (Brit. Med. Journal Jan. 1885) by extirpation of the Thyroid
gland, which condition has been called artificial cretinism, a condition first observed by Dr. Reverdin and Kocner of Geneva and Berne respectively. This association of cretinism with artificial extermination of the thyroid, led physicians to treat the disease by means of the thyroid gland of the sheep, with results that have proved themselves to be eminently satisfactory as adduced by Dr. Murray and several others. (Brit. Med. Journal Oct. 29, 1892, p. 940, 941 by Dr. MacKenzie, and Dr. Fox, Jan. 7, 1893, p. 102; Barber, p. 87; Cockhill, Jan. 14, 1893, by Dr. Lundie). The principle of treatment was first suggested by Dr. Brown-Séquard by his experiments with the testicular juice on the aged; indeed M. Constantine Paul goes so far as to treat mental diseases by injections of ‘cerebrin’, and chronic renal disease by ‘nephrine’ (an emulsion of the kidneys), Lancet, Feb. 4, 1893, p. 257.
A similar association exists between pancreatic disease and certain forms of diabetes, as between cretinism and thyroid disease. At first the association was noted as a clinical fact, and more recently in 1890 von Mering and Minuskowski (Arch. f. exp. Path. u. Pharm. Vol. 26, p. 371) have demonstrated the association by producing the disease in dogs by complete removal of the pancreas; since which the fact has been demonstrated by many observers, among others by Dr. Vaughan Harley (Brit. Med. Journal Aug. 27, 1892, p. 482) noting the good effect of treatment by thyroid juice in a disease which could be produced by extirpation of that gland. Dr. Ramsden suggested at the meeting of the British Medical Association held in Nottingham in 1892, that treatment by means of the pancreatic gland might be equally efficient in a disease which could be produced by extirpation of that
gland, i.e. diabetes. And the suggestion was repeated by Dr. Mansell-Jones in the Journal Jan. 7, 1893 p. 50. In the Journal of the following week, four cases of diabetes were reported with the result of treatment by the pancreatic juice, by Dr. Hector Mackenzie and McNeville Wood, both independently, but with results of a somewhat uniform character; in each case the general condition of the patient having improved, in three of the cases there was a diminution in the thirst and diuresis. In both of the cases reported by Dr. Mackenzie, not of the diabetic type, the amount of sugar passed was unaffected; in one of McWoods the sugar increased, but in the other that of a boy at 13, who was suffering from the pancreatic type, the amount of sugar decreased by grs. 1/2; per ounce of urine, which gave promise of treatment of some value.
These reports were not of a conclusive character, and the improvement observed in the general condition in three cases out of the four, seemed to favour a further trial of this treatment. So that when the usual remedies had failed to bring about any marked benefit in my case, I determined to give pancreatic treatment a trial. So from Dec. 31st 1892 till Jan. 25th 1893 no medical treatment was adopted. From Jan 26th to 28th the pancreas of the sheep, after being boiled was given to the child with the water in which it had been boiled was given to the child, in all about six ounces were given per day, but on the 29th it was discontinued because it became so nauseous to the child, even to cause vomiting. So on Feb. 1st Benjers Liquef. Pancreaticus was commenced, 3 ff being given thrice daily after meals, but this also became
So nauseous that the amount was reduced to 3/4 of thrice daily. This was continued till Feb 16. No marked improvement having taken place in the glycosuria, on the 17th a new preparation, which has recently come into the market, consisting of a combination of bile and pancreatic secretion, and known as Liquor Pancrobin (Reed and Carnick), was tried, and this was continued till March 13th. 3/4 being given three times a day.

The result of the pancreatic treatment has been to corroborate the statement of the previous observers; that the patient appeared to improve in general health, being more lively and brighter, and thirst was not so great, and the amount of urine passed was less, but the specific gravity remained much the same, and there was no diminution in the
amount of sugar passed, it did in fact increase from 68.92 to 100 parts per 1000. The patient never passed so much sugar at any time as she did under this treatment, although her general health seemed to be benefited. The general conclusion we must come to, is, that in diabetes, not of the pancreatic type, pancreatic treatment does not have any beneficial influence on the cardinal factor of diabetes mellitus, although it acts beneficially on the other symptoms. The following diagram will illustrate this point. And with this I bring to a close a somewhat lengthy report on observations that have been continued for a considerable time on what will be admitted to be an interesting case of diabetes, running an unusual course.
Influence of Pancreatic Treatment:

**Date**

- January 30
- February 4, 7, 9, 11, 15, 17, 21, 27, 2, 13

**Preparation**

- Sheep's gland
- Benjors Lq. Pancreaticus Lq. Pancreobilin

**Graph**

- Red line: Sugar
- Blue line: Urine
- Green line: Sp.Gr.

- Sugar: 70, 80, 90, 100, 110
- Urine: 80, 85, 90, 100, 105
- Sp.Gr.: 30, 35, 40, 45, 50, 55, 60

- Coordinates: 103.5, 104.5, 104.0, 103.0, 102.5