EXPERIMENTS
ON THE
URINE DISCHARGED IN DIABETES MELLITUS,
WITH
REMARKS ON THAT DISEASE,
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IN the analysis of the urine voided in diabetes, a few circumstances appear not to have been determined with the degree of precision, which the subject admits, and which it is desirable to attain; though calculated perhaps, rather to have an influence on the pathology of the disease, than on its medical treatment. In consequence of the recent occurrence of two cases of diabetes mellitus under my own care, and of other opportunities for which I am indebted to my colleagues* in the Manchester Infirmary, I have lately been enabled to examine several specimens of this variety of morbid urine. The results, I am well aware, do not present any facts of great novelty or importance. Yet they may perhaps not be unworthy

* Drs. Ferriar, Bardsley, Holme, and Mitchell.

of being laid before the Society; since they contribute to furnish tests of the existence of the disease, and of the degree in which it is affected by diet or remedies, which are more easily applicable than those hitherto employed. Without entering, therefore, at large into the chemical history of diabetic urine, I shall limit myself to the description of a few of its properties, to which I have particularly directed my attention.

I. Of the Specific Gravity of Diabetic Urine, and the Proportion of its solid Contents.

The specific gravity of the urine, discharged in diabetes mellitus, has been left unnoticed by some of the best writers on its chemical history, as Cruickshank, Nicolas and Gueudeville, and Thenard. In about ten cases where I have had an opportunity of determining this property, it has never fallen short of 1028 nor exceeded 1040; 1000 parts of water at 60° Fah°. being taken as the standard. This appears to agree very nearly with the experience of the few writers, who have noticed its relative weight, and especially of Dr. Bostock*, Mr. Dalton†, and Dr. Watt‡. The circumstance of specific gravity I consider as a most useful test of the existence of diabetes in doubtful cases; and, when the disease is unequivocal, taken along with the actual quantity discharged, it furnishes a good criterion of the degree of morbid action. Healthy

* Med. Memoirs VI. 241. † Dr. Bardsley's Med. Reports, p. 161.
‡ Cases of Diabetes, &c. p. 79.

urine I have never found, even in its most concocted state (*viz.* when voided on first rising in the morning), and when an average has been taken of that of several different persons, to have a higher specific gravity than 1020*. In the course of the day, also, it falls greatly below that number; while the specific gravity of diabetic urine, though subject to a little variation, never changes during the same day, to any thing near the same amount. It may be objected, perhaps, to the employment of this test, that it requires more familiarity with the method of taking specific gravities, than falls to the lot of the greater part of medical practitioners. By means, however, of an hydrometer, which is well known to practical chemists, and which may readily be procured at a small expense, the specific gravity of the urine may be taken, in a few moments and with the greatest accuracy, by a person wholly unaccustomed to experiments of this kind†.

* *Note to the 3d Edition.* In a letter to Dr. Marcet, dated April 21, 1817, Dr. Henry states, for the purpose of being inserted here, that "from subsequent experiments he is disposed to believe this number too low, and that a fair average, for the specific gravity of the urine, first voided in a morning, is 1030."

† The hydrometer best adapted to this purpose is made by Mr. W. Twaddell, of Glasgow. To avoid the inconvenient length of the stem, it is divided into four parts; but it is No. I. only of the series, that is required for determining the specific gravity of urine. To reduce the degrees of this instrument to the common standard, the rule is to multiply by 5 and then to add 1000. Thus 6° of the hydrometer denote a specific gravity of 1030; for $6 \times 5 + 1000 = 1030$.

Respecting the proportion of solid contents, obtainable from diabetic urine, little agreement, as might be expected, is to be found among authors; for, besides that the amount actually varies, it must necessarily depend greatly on the degree to which the evaporation is carried. In Captain Meredith's case, described by Mr. Cruickshank*, it appears, at the maximum, to have constituted rather more than $\frac{1}{12}$ of the urine; Dr. Bostock, in a case which he has related in the *Memoirs of the Medical Society of London*†, obtained $\frac{1}{9}$ of a thick syrup; Nicolas and Gueudeville $\frac{1}{14}$ of a mass resembling coarse sugar‡; and Thenard from $\frac{1}{17}$ to $\frac{1}{30}$ ||. By this process, it will always be found difficult to obtain an exact comparison between the urine of different persons, or of the same patient at different stages of the disease. It appeared to me, therefore, desirable to connect, by a set of careful experiments, the quantity of extractive matter with the more certain character of specific gravity. From such a series of experiments, I have constructed the following TABLE, which exhibits at one view, the quantity of solid matter in diabetic urine of different specific gravities between 1050 and 1020. It will be easy, however, to extend the scale, by the rule of proportion, to any case, in which the urine may be found to have a specific gravity above the former, or below the latter, of those two numbers. In the experiments, which furnished the

* In *Rollo on Diabetes*, 2d edition, p. 19. † Vol. VI. page 240.

‡ *Ann. de Chim.* XLIV. 59. || *Ann. de Chim.* LIX. 47.

data of the Table, the urine was evaporated by a steam heat, till it ceased to lose weight, and till it left an extract, which became quite solid on cooling.

TABLE,

Shewing the quantity of solid extract in diabetic urine of different specific gravities.

Specific gravity of the Urine,		Quantity of solid extract in a wine pint, in grains & tenths.	Quantity of solid extract in a wine pint in			
In degrees and tenths of Twaddell's Hydrometer.	Compared with 1000 parts of water at 60° F.		oz.	dr.	scr.	grs.
4.	1020.....	382.4...	6	1	2	
4.2.....	1021.....	401.6...	6	2	1	
4.4.....	1022.....	420.8...	7	0	0	
4.6.....	1023.....	440.	7	1	0	
4.8.....	1024.....	459.2...	7	1	19	
5.	1025.....	478.4...	7	2	18	
5.2.....	1026.....	497.6...	1	0	0	17
5.4.....	1027.....	516.8...	1	0	1	16
5.6.....	1028.....	536.	1	0	2	16
5.8.....	1029.....	555.2...	1	1	0	15
6.	1030.....	574.4...	1	1	1	14
6.2.....	1031.....	593.6...	1	1	2	13
6.4.....	1032.....	612.8...	1	2	0	12
6.6.....	1033.....	632.	1	2	1	12
6.8.....	1034.....	651.2...	1	2	2	11
7.	1035.....	670.4...	1	3	0	10
7.2.....	1036.....	689.6...	1	3	1	9
7.4.....	1037.....	708.8...	1	3	2	8
7.6.....	1038.....	728.	1	4	0	8
7.8.....	1039.....	747.2...	1	4	1	7
8.	1040.....	766.4...	1	4	2	6
8.4.....	1042.....	804.8...	1	5	1	4
8.8.....	1044.....	843.2...	1	6	0	3
9.2.....	1046.....	881.6...	1	6	2	1
9.6.....	1048.....	920.	1	7	1	0
10.	1050.....	958.4...	1	7	2	18

II. *On the quantity of Urea contained in diabetic urine, with some inferences respecting the pathology of the disease.*

Another circumstance respecting diabetic urine, which has not hitherto been sufficiently determined, is the presence or absence of that substance, the secretion of which is the peculiar office of the kidney; and which gives to healthy urine its characteristic properties. Cruickshank*, Dalton†, Fourcroy‡, Nicolas and Gueudeville||, and Thenard§, have been led to conclude that urea is not contained, in any proportion whatsoever, in diabetic urine. Dr. Bostock, in the paper already quoted¶, expresses a different opinion; but that able philosopher was afterwards induced, by further experiments, to adopt the general belief of the complete absence of urea**.

The test, which has hitherto been employed to decide this point, is the addition of nitric acid to the extract of urine dissolved in a small quantity of water. When urea is present, a copious precipitation is immediately produced of bright pearly scales, resembling very nearly in their appearance the acid of borax. And though this test appears to have been considered as somewhat equivocal,

* Rollo on Diabetes *passim*. † Bardsley's Med. Reports, p. 161. ‡ *Système des Connaiss. Chim.* 4to v. 480. || *Ann. de Chim.* XLIV. 69. § *Ann. de Chim.* LIX. 48. ¶ p. 260.

** Bardsley's Reports, p. 174.

from its affording a crystallized substance by its action on sugar, as well as on urea*, yet a little attention will obviate all uncertainty from this source. The change effected by nitric acid on urea, takes place at common temperatures; and, when it does not happen immediately, is entirely prevented by heating the mixture, in consequence of the decomposition of a part of the acid by the urea, and the formation of volatile alkali, which unites with the undecomposed acid, and forms nitrate of ammonia. On the other hand, crystals of oxalic acid are never produced, until after the application of a high temperature. The shape of these crystals also is strikingly different from that of the crystals of nitrate of urea; the latter being readily discriminated, by their flat scaly form and pearly lustre, from the crystals of oxalic acid, even when the figure of the latter is modified, as sometimes happens, by the presence of other substances. In some cases, where doubts appear to have existed as to the nature of the product resulting from the action of nitric acid on the extract of urine, I suspect that it has been a mixture of oxalic acid and nitrate of ammonia, both of which have probably been generated, in consequence of the urine having contained urea as well as sugar; a combination not unusual in the less perfect forms of the disease.

In decided cases of diabetes mellitus, it has in-

* Bostock in Med. Mem. VI. 251.

variably happened, within my own experience as well as that of other persons, that the nitric acid, applied to the extract of the urine, has failed to give any indications of the presence of urea. There appeared to me, however, reason to suspect that the action of that acid on the urea might possibly be prevented, by its agency on the greater proportional mass of sugar. To determine this point, nitric acid was added to artificial mixtures of the extract from diabetic and natural urine*, with the following results.

Extract from 1 measure dia-
betic with 1 of natural urine.	}	The whole presently rendered so-
lid by the abundant precipitation of
nitrate of urea.
Do. from 2 measures dia-
betic to 1 natural urine.	}	In the course of a few minutes a co-
pious precipitation of scales.
Do. from 4 measures dia-
betic to 1 natural urine.	}	No immediate precipitation; but it
commenced in half an hour and gra-
dually increased.
Do. from 6 diabetic to 1 na-
tural urine.	}	A very sparing precipitate of pearly
scales, but not till after 24 hours.
Do. from 8 diabetic to 1 na-
tural urine.	}	No scales in forty-eight hours.

From these experiments, it may be inferred that urea can no longer be made apparent by nitric

* The diabetic urine was that of S. Brookes, whose case is described by Dr. Ferriar, in his *Medical Histories and Reflections*, 2d edit. I. 135. It had the specific gravity 1033. The natural urine was the portion first voided in the morning by a man in strong health, and had the specific gravity 1019.

acid, in the extract from any mixture of diabetic and natural urine, when the former exceeds the latter in a greater proportion than that of six to one: or, as nearly as I can estimate from other experiments, when the solid urea is less than $\frac{1}{20}$ th of the weight of the mixed extract. There is one property however of this substance, originally pointed out by Fourcroy and Vauquelin, which enables us to detect urea, even when present in such minute quantities, as to escape discovery by the nitric acid. Amidst the great variety of animal products, this appears to be the only one which is decomposed, when in a state of solution, by the temperature of boiling water. At this low degree of heat, its elements, held together by a balance of affinities which is easily disturbed, arrange themselves in a new order; ammonia and carbonic acid are generated; and carbonate of ammonia is composed, equivalent in weight to about two thirds that of the urea *. It is in the

* Healthy urine, it is well known, is acid when first voided, and reddens vegetable blue colours, owing, as Thenard asserts, (*Ann. de Chim.* LIX. 270) to its containing acetic acid. After being heated, however, for a short time, the liquor becomes alkaline, in consequence of the production of ammonia. When fresh made urine is distilled, carbonate of ammonia comes over, though in small proportions, till almost the whole of the fluid is evaporated. It is then produced in great quantity, and lines the neck of the retort and the receiver with a solid incrustation. The quantity of carbonate of ammonia, which I have thus obtained from a wine gallon of fresh and concocted urine, has varied from two to three ounces. Its production may chiefly be referred to the urea, which

fluid, therefore, condensed during the evaporation of diabetic urine, that we are to look for traces of the existence of urea; and in this fluid I have invariably found a sufficient quantity of carbonate of ammonia to restore the colour of reddened litmus paper, and to precipitate muriate of lime. When the distillation is carried so far, as to reduce the residuum to charcoal, the last products are strongly acid, in consequence of the production of the pyromucous acid from the decomposed sugar. Even in these latter products, however, a portion of ammonia exists, and may be obtained in a separate form, by first saturating the liquid with pure potash, and then submitting it to a second distillation. The condensed fluid will invariably be found to contain volatile alkali, though often, it must be acknowledged, in very minute quantity. It is on the ammonia, which comes over *early* in the distillation of diabetic urine, that I am disposed chiefly to insist, as establishing the presence of urea; because we are unacquainted with any other animal substance, which can give origin to the volatile alkali under such circumstances.

Another proof of the existence of some portion of urea in diabetic urine, may, in many instances, be obtained by a careful observation of the phenomena attending its spontaneous decomposition. At

is equally decomposed by heat and by putrefaction. I have been informed indeed by persons who distil urine for manufacturing purposes, that little if any increase of volatile alkali is gained by previously allowing the urine to become putrid.

a temperature exceeding 60° Fah°. diabetic urine passes rapidly to the acetous state. But if the succession of changes be carefully watched, it will be found that there is a point at which, before it becomes acid, it exhibits to sufficiently delicate tests, distinctly alkaline properties.

In the account of these experiments, I have not thought it necessary to state the proportion of urea in the fluid submitted to them, because the ingredients of the urine, whether in a healthy or a morbid condition, will scarcely ever be found to have the same proportion to each other. The deficiency of urea in diabetes, however, may be stated as being very considerable. In those cases where I have attempted to estimate it, from the quantity of ammonia evolved by the destructive distillation of the urine, the urea has not appeared to exceed from $\frac{1}{40}$ to $\frac{1}{60}$ the quantity contained in an equal measure of concocted healthy urine. One specimen of diabetic extract, with which I was favoured by Dr. Bardsley, approached so nearly to perfect whiteness, that there appeared to me little reason to expect any evidence of its containing urea. Yet even in the product of the distillation of this extract, after being rectified with the addition of potash, ammonia was found. On distilling, also, a portion of the urine itself, the condensed liquor gave manifest traces of carbonate of ammonia. This urine, however, contained a far less proportion of urea than I had ever before

ascertained; not exceeding, as nearly as I could estimate, $\frac{1}{80}$ of the natural quantity. Making every allowance, then, on account of the increased flow of urine, it will appear that the quantity of urea discharged by persons labouring under diabetes, in any diurnal interval, falls considerably short of the quantity voided in a state of health.

In the examination of diabetic urine, when the disease has not been completely formed, it has occurred to me to find, along with saccharine matter, sufficient urea to give a distinct precipitation on adding nitric acid to the dissolved extract. This is a state of the urine, also, which is often produced by the exclusive use of animal diet. In such cases, I have endeavoured to determine the proportions of the urea and saccharine matter to each other, by the following process: A portion of the extract was first decomposed by destructive distillation; and the product then redistilled with the addition of carbonate of potash. The condensed liquid was next saturated by diluted sulphuric acid of known specific gravity; and from the quantity of this acid, which was required, I inferred that of the solid ammoniacal carbonate, every two parts of which were assumed to indicate three of urea. This process I believe to be much more accurate than the treatment of such a mixed extract with nitric acid; because nitrate of ammonia will be formed, and will be mixed with the crystals of oxalic acid, thus rendering their apparent greater

than their real quantity. The precision, however, which is attainable in this way, can only be required in experiments of research. For all practical purposes, the use of the hydrometer, and the application of the test of nitric acid to the extract, will afford a sufficient measure of the degree, in which the urine deviates from the healthy standard.

Two hypotheses have been framed to account for the principal phænomena of diabetes. According to the one, the seat of the disease is solely in the organs of assimilation. But it has been satisfactorily proved that saccharine matter does not exist ready formed in the serum of diabetic blood*. Until, therefore, it can be shewn that there is a direct communication between the digestive organs and the kidneys or bladder, capable of conveying sugar from the former to the latter without its passing through the general circulation, the theory must be modified by assuming that the blood, which reaches the kidneys, contains *the elements* of sugar, and is deficient in those of urea. To this theory, however, which takes for granted the healthy state of the kidneys, it may be urged as an objection, that it supposes those glands to have a natural tendency to secrete sugar, whenever its elements are

* Nicolas and Gueudeville, Ann. de Ch. XLIV. 69. Dr. Wollaston Phil. Mag. XXXVII. 79; and my own experiments, the result of which is stated in Dr. Ferriar's Medical Histories, 2d edit. i. 146 The same conclusion is established, also, by experiments, which have very lately made.

presented to them. But this is a point which can scarcely be conceded; for besides that the secretion of urea is known to go on under the exclusive use of vegetable food, such a function in the kidneys would be inconsistent with that wise adaptation of parts, which devotes every organ to some specific purpose essential to the healthy state of the animal economy. It appears therefore to be necessary to a just pathology of the disease, that some morbid condition of the kidneys should be admitted, though of a kind which has not yet been explained by anatomical investigation.

At the same time, it is probable that the assimilatory organs are, also, disordered; for the kidneys, though their function is perverted*, so as to render them instruments for forming sugar, still retain, in part, their power of producing urea, when they are furnished with fit materials. This may be deduced from the known influence of animal diet, in diminishing the quantity of urine in diabetes, and in restoring to it that peculiar substance which

* Dr. Rollo, in his valuable work on Diabetes, (p. 418. 427.) expresses an opinion that the kidneys are merely *separating but not secreting* organs, adapted to remove excrementitious or unassimilated matter from the system. They appear to me, however, to partake of the office of secretion equally with every other gland in the body; for there is as marked a difference between urea and any of the proximate principles of the blood, as between the latter fluid and the bile, or any other secreted substance.

characterizes healthy urine. In the cases, which have fallen under my own treatment, as well as in those which have been shewn to me by my medical friends, these have been almost invariable consequences*. But it has not always followed, with equal certainty, as might have been expected from the testimony of some writers, that the disease, in such instances, has been cured. In the first case, which I had an opportunity of treating, the urine, in eight days, was reduced from 14 or 16 pints in the 24 hours to 6 pints. Its specific gravity, at the close of that interval, remained the same; but the extract afforded an abundant scaly precipitate with nitric acid. Notwithstanding this change, the strength of the patient, already reduced to an extreme degree by the duration of the disease, sunk so rapidly, that I acquiesced in his wish to return home to a distant part of the country, and to die in the midst of his own family. In this case (and similar ones, I believe, are not uncommon†) the kidneys must have regained much of their healthy action, while the general disease remained unsubdued. It should appear, therefore, that neither derangement of the organs of assimilation, nor morbid action of the kidneys, is of itself suffi-

* One exception only has occurred to me, which I have stated in Dr. Ferriar's Med. Hist. i. 144.

† See, in particular, Dr. Lubbock's valuable essay in the 5th vol of the London Medical and Physical Journal.

cient to account for the disease: and that both causes are probably concerned in its production*.

III. *Of the remaining ingredients of diabetic urine.*

With regard to the action of chemical tests on diabetic urine, and to the nature and proportion of the *saline substances* which it contains, I have nothing to add to the accurate reports, which have already been given by Nicolas and Gueudeville, and by Dr. Bostock. With their experiments my own for the most part coincide, and tend to establish the conclusion, that the different salts exist

* An opportunity has lately occurred to me of trying the plan of treatment in diabetes, which has been recommended, with so strong a body of evidence in its favour, by Dr. Watt of Glasgow. The patient (a female aged 34) had laboured under the disease more than twelve months, and was then voiding from 12 to 18 pints of urine daily, which had the specific gravity 1037, and gave no traces of urea, except by distillation. Though she was much emaciated, yet her muscular strength did not appear to me to be so far diminished, as to forbid the practice of bloodletting. Between the 28th of December and the 14th of January, she was bled four times, to the extent of twelve or fourteen ounces each time. She was put, also, on a gentle course of mercury, which after some time slightly affected the mouth; and she was laid under no particular restriction as to diet. I did not find, however, that the smallest impression was made either upon the state of the symptoms, the quantity of urine, or its chemical composition; and I, therefore, discontinued the practice. From a solitary case of so hopeless a disease as diabetes, it would be unfair to deduce a condemnation of this or any other plan of treatment.

in diabetic urine, almost in the same proportion to each other as in the healthy state, but that they fall considerably short of the same absolute quantity.

The nature and amount of the *primary animal fluids* (as they have been termed by Dr. Bostock) which are contained in diabetic urine, can scarcely, I apprehend, be determined, till we are in possession of tests, which while they act as precipitants of those fluids, shall have no agency on saline substances. In the present state of this branch of animal chemistry, it unfortunately happens, that all the tests, with which we are acquainted, afford nothing more than equivocal appearances, when applied to the urine. Acetate of lead, for example, is not only precipitated by animal mucus, but by the muriatic and phosphoric salts, which abound in that fluid.

It has been disputed whether the *saccharine matter*, existing in diabetic urine, be identical or not with vegetable sugar. According to Cruickshank*, both substances, if due allowance be made for the saline ingredients of diabetic extract, yield, by the action of nitric acid, very nearly the same proportion of crystals of oxalic acid. Nicolas and Gueudeville and Thenard have obtained, also, by the fermentation of diabetic extract, very nearly

* Rollo on Diabetes, 2d edit. p. 429.

the same weight of alcohol, as would result from an equal weight of vegetable sugar*. These circumstances appear to me to be decisive, with respect to the close similarity between the two substances. On the other hand, it has been asserted that the saccharine matter of diabetic urine cannot, like vegetable sugar, be brought to assume a crystallized form. The absence of this property, however, is not invariable; for I have had an opportunity of observing distinct crystals of sugar, in a portion of diabetic syrup long exposed to the atmosphere. A mouldy scum formed on its surface, which was repeatedly removed and reproduced. In this way much of the animalized matter was doubtless separated; and the residuary syrup afforded regular crystals by spontaneous evaporation. Some slight difference may possibly exist between animal and vegetable sugar, but one depending on those minute differences in the proportion of elements, or in their mode of combination, which cannot be appreciated, till the analysis of the products of organized bodies has attained far greater refinement and accuracy, than belong to it in its present state.

Manchester, Feb. 1811.

* Ann. de Chim. XLIV. & LIX.