

IV. *A singular Case of Diabetes, consisting entirely in the Quality of the Urine; with an Inquiry into the different Theories of that Disease.*
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ALLEN HOLFORD, Esq., aged thirty-four years, strong, healthy, and corpulent, accustomed to free living and strong corporeal exertions in the pursuit of country amusements, in December, 1787, was seized with diabetes; but the cause of the great degree of emaciation and debility which gradually came on was not discovered until March 20th, 1788, at which time his urine was found to be sweet, fermentable with yeast, and two pounds, on evaporation, yielded about five or six ounces of sweet black extract, exactly resembling that preparation of melasses made by confectioners for children, and vulgarly called *coverlid*.

Within the above-mentioned period the quantity of urine evacuated was never observed to exceed what is usual in health, or to be disproportioned to the ingesta, though the state of it had been frequently inquired into, and even the quantity of liquids drank and voided measured. For these reasons the quality of it was not suspected

pected until it became inconceivable, considering the quantity of aliment taken in, how such a degree of exhaustion could ensue, unless the body was drained by the quality of what was rejected as apparently excrementitious.

Variety of medicines, the usual consequence of inefficacy and despair, were successively administered. Decoction of bark with vitriolic acid and alum, with astringents and aromatics, with chalybeates, with *sacc. saturni* and opium, and with cantharides, together with cold bathing in salt water, were the principal means used, and at first had a very good effect; but soon afterwards every medicine disagreed with the stomach, and the patient gradually sunk and died on the 18th of June.

The disease was at first attended with severe pain in the rectum, caused by piles, and all the while a considerable degree of costiveness, the usual cause of hæmorrhoidal affections, prevailed. For some time before his death slight hectic symptoms appeared: his thirst became intolerable; his mouth and fauces very clammy; his tongue deeply chapped; his skin dry and scaly; and his appetite, which at first was tolerable, gradually diminished, and latterly was changed into an aversion even of a sight of solid food.

food. His only support, therefore, in this stage of the disease, was derived from a plentiful supply of nutritious liquids.

About this time, when he voided urine, he usually applied his hands to the hypochondria, and expressed a sensation of sinking, as if the urine came from those parts.

Within the last three days of his existence the quantity of urine was considerably increased, the power of retention much diminished, and his right arm was frequently agitated with convulsive motions for a few minutes, and then became steady. Delirium and convulsions closed the scene.

Notwithstanding this progressive increase of fatal symptoms, the only apparent cause, the saccharine matter in the urine, daily decreased in proportion, and latterly two pounds yielded only an ounce and a half, whilst the quantity of urine evacuated seldom exceeded four or five pounds in twenty-four hours, and had changed from a very light straw colour to one deeper and more natural.

Appearances on Dissection.

The kidneys were of the usual size, but appeared to me to be rather paler and softer than
what

what is natural; when opened longitudinally through the pelvis, nothing preternatural was discovered.

The liver was much wasted. It was externally of an ash colour, or nearly like pipe clay, and its consistence was very plastic, or like an oedematous tumour, which might be moulded, like dough, into any shape. It was perfectly free from any scirrhus or steatomatous tumours taken notice of by Dr. Mead, and, when cut into, exhibited its usual colour.

The gall bladder contained its accustomed quantity of bile, and adhered to the mesocolon.

The pancreas was full of calculi, which were firmly impacted in its substance. They were of various sizes, not exceeding that of a pea, white, and made up of a number of lesser ones, which made their surface rough, like mulberry stones; and in all respects they appeared analogous to the calculi which we sometimes meet with in the salivary ducts. The right extremity of the pancreas was very hard, and appeared to be scirrhus.

No other marks of disease could be discovered in the abdomen, and the contents of the thorax were perfectly sound.

Obfer-

*Observations and Experiments on the Urine and
Extract.*

There was no oiliness on the surface of the urine; when fresh, it had a very faint sweet odour; and when kept two or three hours in a close warm place, it began to smell sour. During evaporation a slight urinous odour was diffused; but this was scarcely perceptible in the extract, and in some parcels of it not discernible.

EXPERIMENT I. A small quantity of urine, set by in a phial, spontaneously entered into the vinous, and then into the acetous fermentation, discharging a great quantity of mephitic gas. A white cloud formed in the center, which gradually fell to the bottom in the form of a white precipitate. In short, the whole of this experiment corresponded with Dr. Dobson's*.

EXPERIMENT II. Vitriolic acid poured into the urine caused no change; neither did fixed alkali, when added to it, excite any pungent odour. This proves that the urine contained very little or no ammoniacal salt, as the fixed alkali, by decomposing it, and setting the vo-

* Medical Observations and Inquiries, Vol. V. p. 303.

latile alkali at liberty, would have excited a pungent smell.

EXPERIMENT III. A small quantity of the extract put into water dissolved very rapidly.

EXPERIMENT IV. A small quantity of the extract put into spirit of wine neither dissolved nor communicated any colour to it, but immediately became very hard and brittle.

It appears, by the last experiments, that the extract consists of sugar united with gummous or coagulable matter, all which ought to remain in the body for its support, and that little of what is excrementitious passed through the kidneys but superabundant water, the vehicle of this nutritious matter.

Healthy urine yields, on evaporation, more or less of coarse black or brown extract; but this extract has a strong urinous smell, deliquesces when exposed to the atmosphere, and is soluble in spirit of wine, being in its nature saline and saponaceous, and entirely excrementitious*.

As the analysis of urine does not seem to have been properly attended to by writers on the diabetes, I think it necessary here to enter more fully into it than has hitherto been done. This

* Vide Journal de Medecine, Nov. 1773 & Avril 1777.

I shall do in the words of a late celebrated writer*.

“ A mesure que l’urine s’évapore, elle prend
 “ une couleur de plus en plus brune & foncée,
 “ par le rapprochement de la partie favonneuse
 “ extractive qu’elle contient. Les premiers
 “ cristaux qu’on obtient, sont l’espece particu-
 “ liere de sel connu par les chimistes sous les
 “ noms de *sel natif ou essentiel de l’urine, sel fu-*
 “ *sible de l’urine, sel phosporique, sel microcos-*
 “ *mique.* C’est celui qui contient l’acide pro-
 “ pre a faire le phosphore. Il y a une partie de
 “ ce sel qui est a base d’alkali volatil, & qui est
 “ par consequent de nature ammoniacale; l’au-
 “ tre partie est a base d’alkali fixe mineral.

“ En continuant l’évaporation & le refroi-
 “ dissement alternatifs, on retire successivement
 “ de l’urine les autres sels moins cristallifables
 “ qu’elle peut contenir, mais principalement le
 “ *sel commun,* ou le sel febrifuge de *Sylvius,* dont
 “ elle est toujours abondamment chargée. On
 “ retrouve aussi tous les sels neutres qu’ils ont
 “ pris, soit par la voie des alimens, soit autre-
 “ ment.”

* Macquer. Dictionnaire de Chimie. 4to, Tom. II.
 p. 645.

From this analysis it appears that healthy urine contains a variety of saline matter, the principal of which are the following: — Phosphoric salt, or salt composed of phosphoric acid and vegetable, mineral, or volatile alkali; common salt; and the febrifuge salt of Sylvius, or salt composed of marine acid and vegetable alkali. — As phosphoric acid and volatile alkali are generated in the body, we may easily suppose the following chemical decompositions and attractions to take place: — The common salt taken in with the aliment is decomposed by the phosphoric acid, which unites with its alkaline basis, and forms one species of the fusible salt of urine: the marine acid, now at liberty, unites with the vegetable alkali taken in with our aliment, and forms the salt of Sylvius; and the superabundant phosphoric acid, uniting with the volatile alkali, forms the ammoniacal phosphoric salt. The quantity of these salts must be variously proportioned, according to the quantity of aliment taken in, the quality of it, and the intervals of repletion.

Hence it appears probable that the want of saline matter, or ammoniacal salt, so much talked of, in diabetic urine, proceeds from a deficiency of phosphoric acid and volatile alkali,

without which the saline particles taken in with our aliment cannot be decomposed, or form any new combinations, but must be ejected by the excretive powers as they entered.

The *acidum perlatum*, which has been discovered in microcosmic salt, is too little known to require any attention at present *.

Inquiry into the different Theories of this Disease.

The consideration of the above case naturally leads to an inquiry into the different theories of this disease. Is it a defect of assimilation, a disease of the liver, or an affection of the kidneys?

As to assimilation, the antecedents of the disease point out no defect in digestion. It has frequently attacked persons in the vigour of life, and has usually been attended in all its stages with a voracious appetite; from which it may be inferred that digestion has not only been properly performed, and the chyle conveyed into the circulation in a state fit for nutrition, but experiment confirms it. The serum of blood

* Vide Bergman on Elective Attractions.

taken from the arm had no preternatural sweetness*.

If want of assimilation, and its supposed consequence, are the effects of a weakened state of the animal functions, why is not diabetes the usual concomitant of that state?

That the cause of diabetes and quality of the urine have long been subjects of speculation, and that the idea of defect in the assimilatory powers is not new, will appear from the following quotations:

“ Ad renes pertinere is affectus videtur, quem
 “ alii hydropem matellæ, alii urinæ profluvium,
 “ alii diabetem, alii Διψακον appellant. Equi-
 “ dem cum hætenus bis duntaxat videre potui,
 “ supra modum sitientibus infirmis, atque su-
 “ binde bibentibus. Quare exuberanter quo-
 “ que reddunt, id quod biberunt, eo a sua qua-
 “ litate non mutato.”—Galen, l. 5. de loc. affect.
 cap. 3.

“ Causam vero hujus affectionis reddere dif-
 “ ficillimum, & pauci autores inveniuntur, qui
 “ in ea reddenda inter se conveniunt. Nos in
 “ re obscura, salvo cujusque judicio, statuimus,
 “ proximam hujus mali causam esse facultatem

* Home's Clinical Experiments, page 308.

“renum retentricem læsam, & quidem ab urinæ
 “vel copia, vel *qualitate*.”—*Sennert. op. Folio.*
 Lugdun. 1650. Tom. II. p. 1094.

In the same chapter from which the preceding quotation is taken is the following question:—
 “An potus immutatus planè per urinam in diabe-
 “bete reddatur?”—Galen, Alex. Trallian, Aetius, Amatus Lusitanus, and Trincavellius, say it is not changed; and the latter observes, that in one case he found it “servans eundem
 “calorem, consistentiam, saporem atque odo-
 “rem.”—*Ibid. p. 1095.*

Dodonæus, J. Baptista Sylvaticus, and others, having taught a contrary doctrine, Sennertus, in giving his own opinion, attempts to reconcile both.—“Ideoque in diabete non solum ad po-
 “tum, sed etiam alia respiciendum. Sunt
 “enim primò diabetæ quidem gradus. In
 “principio enim, cum vires nondum dejectæ
 “sunt, & vis alteratrix, nondum extremè labo-
 “rat, non mirum est, si potus aliquomodo mute-
 “tur; temporis vero progressu, ubi vis altera-
 “trix magis labefactatur, potus plane immuta-
 “tus excernitur. Deinde potus etiam alius mu-
 “tatur facilius, alius difficiliter. Aquam, cum
 “parum mutari possit, non mirum est, eodem
 “colore & reliquis accidentibus non mutatis,
 “excerni:

“ excerni : alii vero potus, qui magis compositi
 “ sunt, non ita facile transeunt, quin aliquam
 “ mutationem accipiant. Præterea id, quod in
 “ diabete excernitur, non saltem potus est, sed
 “ sæpe etiam accedit corporis colliquatio, unde
 “ plus urinæ emittitur, quam potus assumptum
 “ est.” — *Ibid.* p. 1095.

Then comes the following question: “ Quæ-
 “ nam diabætæ causa sit?” — Answer. “ Vulgata
 “ quidem, & quam plerique sequuntur, sen-
 “ tentia est, proximam hujus mali causam esse
 “ renum intemperiem calidam, ob quam illi
 “ serum copiosius e venis attrahant, quodcum
 “ ob imbecillitatem & copiam retinere non pos-
 “ sint, venas rursus a jecore, hoc ex intestinis
 “ & ventriculo trahere, unde orificium ventri-
 “ culi vellicetur, ac fitis excitetur, ob quam
 “ assumtus potus mox a venis & renibus attra-
 “ tur, atque iterum ad vesicam mittatur.” — *Ibid.*

J. Baptista Sylvaticus, after Galen, Aretæus,
 and Actuarius, having delivered the following
 doctrine — “ Insignem calidam intemperiem in
 “ hepate & toto venoso genere succensam, san-
 “ guinem fundere, ejusque portionem aliquam
 “ in serum mutare.” — Sennertus farther observes,
 “ His autoribus posterioribus assentimur in eo,
 “ quod

“ quod non tam in renibus quam aliis partibus
 “ causa diabetis quærenda sit. Sit enim, de
 “ quo tamen, ut ex superioribus patet, non im-
 “ merito dubitatur, quod renes fortiter attrahant :
 “ tamen nisi serum adsit, id attrahere non pos-
 “ sunt ; & renum fortis attractio, feri seu urinæ
 “ copiam jam præsupponit.”—*Ibid.*

“ Quapropter diabetem sanguinis potius &
 “ immediatius quam renum affectionem esse, &
 “ originem suam inde sumere credimus, qua-
 “ tenus cruoris massa velut deliquescit, & in
 “ serositatem copiosè nimis funditur : quod e-
 “ quidem ex urinæ quantitate ita in immensum
 “ aucta, quæ non nisi a sanguinis deliquio, &
 “ consumptione procedat, facile constat
 “ Itaque opinari ducor sanguinis crasin five
 “ miffionem ita laxari, & quadantenus dissolvi,
 “ ut particulæ aquosæ a crassioribus contineri
 “ nequeant, quin illæ harum amplexionibus
 “ cito elapsæ, & salinis imbutæ, per vias re-
 “ num maxime patentes excurrant.”—*Willis,*
Pharm. Ration. p. 105.

“ I believe the chief and most frequent cause
 “ of diabetes consists in the too-much dissolved
 “ and lax mixture of the blood.”—*Bonetus's*
Guide. Folio translation. Book iv.

“ For

“ For their blood being by this means so im-
 “ poverished as to be utterly unable to assimilate
 “ the juices received into the mass, they pass off
 “ crude and undigested by the urinary passages.”
 —*Swan's Translation of Sydenham*, p. 313.

The discovery of the circulation of the blood naturally destroyed the theory of attraction by a supposed *calida intemperies*; and the discovery of the quality of diabetic urine by Willis, settled all disputes on that head: but the cause of the disease, notwithstanding those great discoveries, seems still to remain as unsettled as ever.

A late very celebrated writer* has pitched upon the liver for the seat of diabetes. He says he always found a steatomatous collection in it; to which he attributes a vitiated secretion of bile, deficient of saline matter to properly mix and assimilate the fluids.

This theory, as it is nearly allied to the circumstances of Mr. Holford's case, appears plausible; but it must be observed that the state of the liver, described by Dr. Mead, differs essentially from that of the case before us: this, however, is not a sufficient objection, as different states of the liver may be supposed to produce a mor-

* Mead. *Essay on Poisons*, page 28.

bid state of bile, similar, or equally unfit for the purposes of assimilation. It is necessary, therefore, to oppose authority to authority; and here another very eminent author assures us, that though the liver has sometimes been found diseased, yet this concurrence does not often take place.—“ In twenty instances,” says he, “ which I have seen, there was not, in any one of them, any evident affection of the liver*.”

To this authority, exclusive of the negative proofs contained in the following dissections, may be added the testimony of Dr. Home, who says, “ the liver was natural †.” May we not, therefore, consider the disease of the liver as a complication in the case of Mr. Holford? and may not the same be said of the calculous state of the pancreas?

Unfortunately we have few dissections of this disease to refer to; nevertheless what we have, excepting Dr. Mead’s general assertion, expressly describe such an affection of the kidneys as we might, *a priori*, expect to find.

“ Anno 1590, Filia Præsidis Hollandiæ 18 annorum aliquot ante obitum annos diabete

* Cullen. First Lines, Vol. IV. page 89.

† Clinical Experiments, page 311.

“ laborabat Renes huic non absumpti, ve-
 “ rum flaccidiores solito, figura cineritia non
 “ impense rubra.” — *Petrus Parvius* *, Ob. An. 2.
 “ Aperto cadavere ren sinister inventus est
 “ lapide obsessus exiguo : ren in magnam mo-
 “ lem undique increverat, adæquabat renem
 “ bubulum magnitudine : paulum saniei in eo
 “ erat : dexter adeo parvus erat ut fere reperiri
 “ non potuerit ; macruerat multum.” — *Ballo-*
nus †, eph. & epid. l. 2. p. 152.

“ In Nob. N. a febre ardente extincto, pulmo
 “ niger & admodum tumidus repertus est ; in
 “ utroque rene duo magni calculi : hic copio-
 “ siores justo fundebat urinas, aquæ simillimas,
 “ sitimque intolerabilem patiebatur, ut quæ nul-
 “ lo potu sedari poterat ‡.”

“ Ren sinister lapide angulos obtufos habente
 “ obsessus est, in ureteris principium implanta-
 “ tus. Ren alter lapide non obsessus, justo
 “ minor erat, & pene collapsus. Nullum com-
 “ memorabile vitium quod sub obtutum cade-
 “ ret.” — *Ballonius* §, eph. & epid. l. 2. p. 183.

* Vide Sepulchretum Boneti, Lib. iii, sect. xxvi. ob. 1.

† Ibid. ob. 2.

‡ Ibid. ob. 3.

§ Ibid. ob. 5.

“ Hic enim intra decem horarum decursum
 “ ultra duodecim urinæ mensuras, incredibile
 “ dictu, excreverat: & post aliquod tempus,
 “ accedente aliq. graviori morbo defunctus, at-
 “ que secatus, ureterem dextrum, insigniter &
 “ farcininis instar expansum, quin ejusdem la-
 “ teris renem in molem sinistro duplo majorem
 “ elevatum ostendit *.”

“ Remotis intestinis, &c. in oculos mihi in-
 “ currit ureter dexter mirum in modum distor-
 “ tus, atque hic illic multum expansus, ut in-
 “ testinum ratione crassitie representaret. Pel-
 “ vis quoque adeo erat distenta ut malum au-
 “ rantium mediocre facillime, & citra difficul-
 “ tatem admitteret. Parenchymate omnimodo
 “ consumto, nil præter membranosas partes,
 “ perquam induratas superstes videbatur †.”

“ Vir quidam in ætatis flore, diu atrocibus
 “ nephriticis doloribus vexatus, renisque ab-
 “ scessum passus in diabetem incidit. Singulis
 “ septimanis dolium dimidium cerevisiæ ingur-
 “ gitare difficile illi non fuit. Post mortem. . .
 “ viscera satis bene constituta, exceptis renibus
 “ & ureteribus, conspexi; uterque enim ren ex

* Hoffmanni Consult. & Resp. Med. Casus 85.

† Ruyschii Dilucid. Valv. obs. 13.

“ parte confumtus erat, præfertim dexter; cu-
 “ jus substantiâ planè confumtâ, ejus membra-
 “ nas summopere incrassatas & contractas, pel-
 “ visque capacitatem adæquantes vidi *.”

“ On examining the kidneys, the left was
 “ larger than natural, and its substance softer.
 “ There was no uncommon appearance in the
 “ right kidney, except a greater degree of
 “ softness. The substance of both kidneys had
 “ a sour odour †.” —Dr. Monro observes on the
 above case, that “ both kidneys seemed to be of
 “ a large size, were of a remarkably pale co-
 “ lour, and felt rather softer than common †.”

Morgagni has been quoted on this subject;
 but the case ep. 41. art. 13. confirms nothing,
 the kidneys not having been examined; and ep.
 42. art. 43. he says, “ Nec Valsalva, nec ego
 “ quenquam ex diabete mortuum dissectui-
 “ mus.”

From the proofs above adduced, extracted
 from the most respectable writers, it appears
 that the kidneys have invariably been found con-
 siderably diseased; but as it has been fashiona-
 ble, in consequence of a revival of the crude

* Ruysschii Obs. Anat. Med. Centuria, ob. 13.

† Home. Clinical Experiments, page 310.

‡ Ibid.

system of the last century, to call this the effect, and not the cause, it is necessary to inquire more particularly into the circumstances of the disease; the remote or occasional causes of it; and the method of cure which has now and then succeeded.

An increased discharge of urine, excepting in the case of Mr. Holford, has always been the first symptom of diabetes; the other symptoms have been consequential and in proportion. Can an imperfect digestion or assimilation be supposed capable of stimulating the kidneys to *excrete* five or six times the usual quantity?

Chyle is at all times mixed with the blood, the blood vessels being the vehicles of it, or the organs of its distribution. If diabetes be not a disease of the kidneys, why do they not permit the nutritive, chylous, or saccharine matter to pass at all times? For it cannot be denied that such saccharine matter is perpetually conveyed, mixed with the blood, by the emulgent arteries, and presented, along with the excrementitious matter, to the excretory vessels of the kidneys.

The principal argument against diabetes being an affection of the kidneys is this — “ Sugar is
 “ found in diabetic urine. Sweet chyle is the
 “ first product of the stomachic and intestinal
 “ digestion;

“ digestion ; as chyle in the thoracic duct, and
 “ milk, which is a speedy secretion of it, con-
 “ tain much saccharine matter. This is changed
 “ in some hours, by the animal process, into
 “ an ammoniacal salt, which is that found in
 “ all the secretions. But the saccharine salt still
 “ remaining in the urine, which is the most
 “ perfectly animalised fluid, shews that there is
 “ great defect in the animal process *.”

It must be allowed that sugar is found — that
 sweet chyle is the first product—and that urine is
 the most perfectly animalised fluid, &c. but it
 does not follow that the chyle is of no other use
 than to be converted into ammoniacal salt, or
 that any original defect in the animal process is
 the cause of that want of conversion : this defect
 of ammoniacal salt, or rather saline matter, for
 the quantity of ammoniacal salt has been much
 over-rated, appearing, as I have attempted to
 explain above, to be owing to a want of phos-
 phoric acid, (which I take to be a modification
 of the saccharine) and the saccharine matter like-
 wise appearing to be the cause rather than the
 effect of the disease.

* Home. Clinical Experiments, page 319.

I shall now farther observe, that the saline matter discharged by the kidneys in health ought to be considered as the product of nutrition, or rather the refuse of that process; for when the nutritive part of the blood has been applied to its various uses, and secerned, are not the particles unfit for those purposes retained, and brought back into the circulation to be discharged through the kidneys as excrementitious in various saline forms, which have been thus generated and rejected by the powers of nutrition?

May we not, in this manner, easily account for the small quantity of excrementitious matter in the urine, without supposing any defect of assimilation? For where nutrition is very sparingly performed, the quantity of excrementitious matter, the result of it, must be small in proportion.

The remote or occasional causes, noticed by authors, are, mineral and animal poisons—intemperance in drinking and exercise—large doses of antimonials—opiates and diuretics—large draughts, too frequently repeated, of Harrogate and Epsom waters: to which may be added debility succeeding intermittents, and nephritic affections.

The

The method of cure likewise coincides with the idea of diabetes being a disease of the kidneys. Tonics, astringents, aromatics, agglutinants, absorbents, and opiates, are the only medicines which have succeeded. Many cures performed by these, together with variety of formulæ, sufficiently complicated and farraginous, may be found in the following works: — Vide Riolani op. p. 336. — Sennerti op. Tom. II. p. 1095. — Bonetus, lib. 4. — Pitcairn, p. 272. — Riverii op. p. 361. — Zacuti Lusitani op. p. 423. — Baglivi op. ep. 4. — R. Morton op. p. 15. — Martini Lister Exercit. Med. p. 27. — Willis Ph. Rat. p. 105. — Etmulleri op. Tom. II. p. 714. — Hoffmanni Consult. & Respons. Medic. Casus 85.

Upon the whole, considering the office of the kidneys to be merely that of percolation, I take the proximate cause of diabetes to consist in a morbid dilatation of the uriniferous tubes of those organs, whereby they become pervious to the nutritious matter, whose globuli, in a state of health, are too large to be admitted through them; and that this morbid state does exist either with or without a diarrhœa thereof.

When we consider that the quantity of urine

voided by Mr. Holford was singularly small, and that it did not contain latterly a greater proportion of saccharine matter than has been met with in other cases, where the patients have discharged four, five, or six times the quantity, and nevertheless withstood the ravages of the disease for years, the quantity of aliment demanded by the constitution and taken in having been adequate to the loss, is it not probable that a cure would have been effected, provided the stomach and organs subservient to digestion had retained their digestive power to supply the demands of the system?

Chester,

July 30, 1788.

V. Obser-