SUGAR IN THE ECONOMY

IN HEALTH AND DISEASE

A THESIS

BY

JAMES L BRYDEN

1855.

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Introduction.

The Doctrines of Liebig on their first publication, while they charmed the superficial reader with the definite and purely chemical manner in which they dealt with facts which physiological research & chemical investigation had up to that time failed to explain, were at the same time looked on by the more philosophical with suspicion, and were deemed by not a few altogether chimerical. — That the latter class had some grounds for their objections must be admitted, for however plausible the theories seemed when taken as a whole, if the individual steps of the processes by which the ends were accomplished were narrowly scrutinized, links were often found wanting to complete the chain of evidence. — Liebig's generalizations nevertheless stand unquestioned, & have formed a basis on which a vast superstructure of physiological truth has been built, & to which additions are continually being made.

The most important of these, and the one

which has gone furthest to strengthen former theory, while it has added to physiological science facts at once new & indisputable, is Bernard's great discovery of the Sugar-forming function of the Liver.—

My object in this dissertation is, to attempt an exposition of the normal relations of Sugar in the economy, & of the modifications of its Rôle under morbid influences, using as my groundwork the general institutes of Liebig, and the fact as promulgated by Bernard – that we have throughout life within the Body a constant & never-failing source of Sugar for its uses.

My endeavour has been to make use of well grounded Chemical & physiological fact to establish such propositions as I have advanced, and I have tried to turn to account statements corroborative of my purpose brought forward by trustworthy authorities, many of them in defence of theories long since abandoned. The truths which I may have collected, I have arranged, and in this collection & arrangement my aim has been to give Continuity & integrity to the subject of my dissertation.—

(1) On Stomach & urinary diseases. 1840. p. 40.

(2) p. 34

I am not aware that the subject has been treated as a whole – indeed previous to the discovery of Bernard it could not have been dealt with in a satisfactory manner, since at every step the varieties of animal existence, and the variations in their nutritive ingesta, presented a barrier at which even the most sagacious stumbled. The vagueness of the ideas entertained of the Rôle of Sugar in the system may be illustrated by the innumerable and discordant theories of Diabetes which have successively been propounded. The treatment of this disease, I think we may say, has been almost entirely empirical, and the results of such practice most unfortunate. Prout says "perhaps there is no disease in which so much mischief has been done on false principles, & by random experiment as in this." (1) But even in Dr Prouts' hands, (& no man has seen more of this malady, since he says in the last edition of his work, that he has had upwards of 700 cases under his care) the most approved treatment has been found unavailing, & he remarks: (2) "The general

prognosis

must be always unfavorable." It must be then that this disease is incurable, or that the patients have been treated on a wrong theory. Can it be that a disease characterised primarily by no organic lesion is incurable? If the disease be purely of a chemical nature, is Chemistry powerless to provide us with the means of rectifying and obviating the evil which causes the aberration from health, & maintains & perpetuates the abnormal condition? I think not. —

In the pathological Section of this Essay I have proposed a theory of diabetes, and have adduced such facts as I thought likely to strengthen it. Founded on this theory I have sketched out a plan of treatment which is that which I should be inclined to adopt in any case that might come under my care. Similar treatment on different theoretical principles has been tried and has been found not less efficacious certainly, than any other of the many methods which have been employed.

History of Sugar in the Economy.

A short enumeration of the facts connected with Sugar in the economy, which have helped to elucidate the part it plays as a constituent of alimentary material, and as a foreign ingredient in certain of the normal excretions. as these were recognised & successively described up to the period of Bernard's discovery, at which date we propose to take up the subject in detail. may not be out of place as an introduction to the more particular investigation of the subject, which we intend to pursue according to the plan laid down in the conclusion of this chapter. Such a statement in fact is almost essential, since it is not my intention in the sequel, to enter into any minutiæ as to the place & manner in which the amylaceous ingesta are converted into Sugar in the digestive passages - a question which for years past has occupied the attention of the ablest physiologists, & more especially those of the French School, the results of whose researches are recorded for the most part in the Annals of their Academy. —

(1) "Quod autem plerique Authores potum aut parum aut nihil immutatum reddi asserunt, a vero longissime distat; Quoniam urina in omnibus, quos unquam me novisse contigit, et credo eta in universis habere, tum a potu ingesto, tum a Juvis humore in corpore nostro jugiter solito plurimum differens, quasi melle aut saccharo imbuta mire dulcescebat."

Thomae Willis, Opera omnia. Genevae 1680

I. 101.

(2) Anatomy. fifth edition. p. 139.

(3) Vol. IX. 290. 1488.

We have no evidence that the Ancients were acquainted with the existence of Sugar, either as a product of the digestion of Starch, or as a constituent of the urine in Diabetes.

Thomas Willis was the first to indicate that in Diabetes the Urine tasted as if Sugar or Honey had been mixed with it. I translate from him as follows. 1674

"The statement made by most authors to the effect that what is drunk passes out little if at all changed, is very far from being true; since in every case which has fallen under my notice (& I believe the fact to be of universal application) the urine has been of wonderful sweetness, as if in short impregnated with honey or sugar and in this respect differing most essentially, not from the patients drink only, but from every fluid which we know to be generated in our system in ordinary conditions".(1)

Cheselden made the remark that carbuncles 1750
"are attended with sweet urine as in a diabetes."(2)

Thomas Cawley gets the credit of first showing 1788
the sweetness of diabetic urine to be due to sugar.(3)
His observations are contained in the London Medical Journal

(1) Medical observations & Inquiries. 1779. V. 298. et seq.

(a) page. 305.

(b) page. 304.

(c) page. 307.

& there he certainly makes no such claim. He gives in this paper an excellent digest of the theories of the older physicians, & his contemporaries, in reference to the disease, but as regards his experiments on the urine, he merely agrees with Dobson, whose observations had been made many years previously.

Dobson writes thus (1) "The white cake which remained after the evaporation of two quarts of this diabetic urine, weighed ℥iv. ʒij. ʒij. - It smelled sweet like brown sugar, neither could it by the taste be distinguished from Sugar." (a) He adds further. "The Serum of the Blood was sweetish, but I thought not so sweet as the urine." (b) He was thus the first to observe Sugar in the blood. And his deduction was "that this Saccharine matter (of the urine) was not formed in the secreting organ, but existed previously in the blood." (c) He anticipates Liedemann & Gmelin when he asks "Does it not appear that Saccharine matter is a product of the Animal economy?" or that as vinous Spirits are the product of the vinous fermentation, that in like manner a saccharine substance is the product of the digestive fermentation?" In support of his theory he brings forward the circumstance of the

1774

production

(1). Rollo. Traité du diabète sucré. trad. par Alyon avec des notes du cit. Fourcroy. Paris. An. VI. p. 151-2.

(2) De curandis hominum morbis. Manheim. 1794. Vol. V. 44.

(3) Note sur le sucre de diabète. Bulletin de la Soc. Philomatique Paris. 148

(4) Recherches sur la digestion. trad. par Jourdan Pasquier

of Sugar during the "Vegetative fermentation" of Grain, & the maturation of fruits.

Fourcroy does not therefore deserve the merit 1798
ascribed to him by French Authors, of being the first to advance the above hypothesis. There can be no doubt that he was well aware of Dobson's views, since he first published his theory as a note to a french translation of Rollo's well known & admirable treatise on diabetes, who on Dobson's principle showed the great advantage to be obtained by witholding amylaceous substances from the food in this disease. (1)

Frank. (J.P.) showed that there was not 1794
necessarily an increase in the amount of urine in Saccharine diabetes. He gives a case in which he obtained from two pounds of urine, no less than six ounces of Saccharine matter "licet ultra quam Sanus consueverat, non mingeret aegrotus." (2)

Chevreul recognised diabetic Sugar to be 1815
identical with Grape Sugar. (3)

Tiedemann & Gmelin first absolutely demonstrated 1827
the presence of Sugar in the primae viae, during the digestion of Grain &c. in various classes of Animals. (4)

Prout.

(1) London Medical Gazette. 1831. 185.
(2) Journal de Chim. Méd. 1836. II. 130.

(3) Comptes Rendus 1845. XX. 143. 303. 1026.

(4) Comptes Rendus 1845. XX. 1347.

(5) Philosophical Mag. 1845. 323. 418

(6) Comptes Rendus 1846. XXIII. 189.

(7) Nouvelle Fonction du Foie, pancréas.

Prout found Sugar in the Urine in Gout &c.(1) 1831
& Ambrosini extracted Sugar from diabetic blood.(2)

Bouchardat has published numerous papers 1838-52
on diabetes in many parisian journals. I do
not see that he has gone beyond Dobson either
in fact or theory. His opinions are discussed
subsequently as also those of Mialhe. 1844

Bouchardat & Sandras ascribed to the Salivary 1845
& Pancreatic glands the power of determining
the transformation of Starch into Sugar.(3)

Lassaigne allowed not the pancreas possessed
the property attributed to it by these observers
but denied that the Saliva could act on crude
Starch.(4)

Thomson (Glasgow) announced that Sugar
existed as a normal constituent of the blood
in animals fed on Starch.(5)

Magendie Confirmed this statement and 1846
showed that the Blood had the power of causing
the resolution of Starch into Sugar.(6)

Bernard proved that animals as well as 1848
plants & carnivorous animals as well as omnivorous
& herbivorous, Constantly elaborate Sugar within their
economy.(7) & that the Laboratory from which Sugar is

continually thrown into the circulation is the Liver.—

In the prosecution of the investigation of my subject, the following is the course I shall pursue.

I shall separate the whole into two great divisions — the first — Sugar in the economy in health — will embrace the discussion of three questions.

1. How, & in what forms is Sugar furnished to the Economy?

2. What changes does Sugar undergo within the Economy?

3. To what purposes in the Economy is Sugar subservient?

The second division — Sugar in the economy in disease — will be occupied in considering

1. What circumstances tend to prevent the normal Rôle of Sugar in the Economy, and bring about its appearance in the excretions.

2. What constitutes Diabetes Mellitus.

3. How & on what theory ought this disease to be treated.

In this arrangement I think I include all particulars connected with the physiological & pathological relations of Sugar so far as I have been able to gather them from the writings of others, as well as deductions drawn from recorded fact, or from personal observations.

Without further introductory detail I proceed with the first part of this essay

Sugar in the Economy in Health

& begin by inquiring — how & in what forms is Sugar furnished to the Economy? —

The Sugar of the Liver

& The Institutes of Bernard.

The observation of the comparative acts of nutrition in plants & animals — the continual formation of Starchy & Saccharine matters by the first, & their continual destruction by the latter — led all Chemists & physiologists to conclude, that it was to the vegetable kingdom & to it alone, that animals were indebted for the Sugar which under certain abnormal conditions was found in their excretions. Nor indeed was this inference to be wondered at, for Chemists had never yet fabricated except from amylaceous substances a Sugar truly fermentescible, while experimental physiologists had looked for Sugar in the Animal fluids, only after they had first added it to the food of the subjects of their experiments. In certain abnormal states indeed large quantities of a truly fermentescible Sugar had nearly two centuries before been discovered in the urine, from which circumstance the

Observers

added the specific name of mellitus to the generic term Diabetes, which had formerly been assigned to the other accompanying symptoms of the malady. The source whence was derived this saccharine element was naturally at that time concluded to be the saccharine or amylaceous ingesta, & this belief was no doubt countenanced & perpetuated by the fact of the great diminution in the excretion, on the removal of such bodies from the alimentary supply. Certain facts however negatived this assumption, for in some cases it had been shown that during the intensity of the disease, the quantity of Glucose eliminated by the Kidneys, exceeded in amount what could possibly have been procured from these nutritive matters, & that when even all such substances were rigidly withheld, still the excretory process was to a great extent continued as before. — All this tended to show that there existed in such circumstances some independent laboratory for the matters so excreted.

Thus far had we advanced in our knowledge

of these phenomena, when reasoning on the above facts Bernard, in 1843, set himself to inquire - if such a laboratory existed - where or in what organ it was to be found, and under what conditions its agency was called into action.

The results of his investigations have from time to time appeared in the Parisian Journals, & have more recently (1853.) been collated & published in a separate form, under the title of "Nouvelle Fonction du Foie." and in this work he undertakes to prove that in the liver we have a constant fabrication of Glucose taking place, not in man only nor in Mammals, but in every animal vertebrate or invertebrate, which possesses a liver. The experiments by which he supports his assertion have been conducted with the strictest regard to logical accuracy, & leave nothing to be desired by way of further illustration.

Subsequent observation has added nothing of any importance to the details as given by Bernard, we are therefore shut up to the necessity of giving an abstract of his own statements and experiments on the subject.

this however we shall do as briefly as possible, introducing such remarks & suggestions as we have to offer, and taking into consideration certain objections which have very ~~xxx~~ lately been brought forward, calling in question the accuracy of the deductions of Bernard.

The mode in which the discovery was made is not devoid of interest. Bernard had resolved to ascertain in what organ the sugar of the alimentary canal taken into the circulation was destroyed. He fed a dog on food abounding in saccharine matters, and calculating on the sugar being absorbed by the radicles of the portal vein & carried through the liver, & with the object of determining whether or not the liver accomplished the resolution of sugar, he killed the animal soon after its last meal. He examined the blood of the hepatic vein & found sugar abundant, hence he naturally concluded, that the liver did not destroy such sugar as passed through it during digestion. But following out the primary purpose of his experiment. namely the determination of the question whether there

created

in the Body an organ which organized Glucose, it was necessary by way of Counter proof to show, that the sugar so found in the hepatic vein was really the sugar derived from the alimentary material. A dog was therefore fed for seven days on a purely animal diet, but on destroying it as in the former case, he found to his astonishment on examination of the blood of the hepatic vein, just as much sugar as the blood of the dog fed on Saccharine matter only. Here then was a fact altogether new, and the establishment of it was in future the ~~object~~ end of all Bernard's researches. The experiments were at once repeated, & they have been repeated again & again by many Physiologists besides Bernard, on animals which have subsisted for many months on food absolutely devoid of Amylaceous or Saccharine substances, & always with the same result. The possibility that this sugar was not really formed in the liver, but was brought to it by the portal vein from some other source, was forestalled by the invariable examination of the contents

of the Splenic, mesenteric, & portal veins without sugar being detectable by any test. That this was a true grape sugar was demonstrated beyond a doubt, since every test applicable to ordinary glucose or diabetic sugar, applied equally to this. It was found eminently capable of undergoing the alcoholic fermentation, Bernard indeed manufactured alcohol from it. In solution it caused the deviation of polarised light to the right, while the tests of Moore & Trommer at once revealed its presence.

Such were the broad facts on which Bernard came to the conclusion that he had found a new source of a truly fermentescible sugar, independent of the vegetable kingdom, and that the liver possessed a true glucogenic function, possibly the origin of the sugar in diabetes.

In treating the subject in detail Bernard makes the two following propositions the basis of his argument.

1. "The sugar which we meet with in the liver, does not necessarily come from without – it must be formed within the system

for we meet with it in the hepatic tissue independently of saccharine & amylaceous alimentation."

2. "The hepatic sugar produced in the Economy is not accumulated or deposited in the liver after having had its origin in some other part of the Body. it is formed primarily in the Liver, which therefore ought to be regarded as an organ which produces or Secretes saccharine material."

He supports these propositions by such experiments as the following, — a dog was fed for eight months on tripe exclusively & was then killed. No sugar whatever was to be found in the intestine, but the hepatic tissue yielded it abundantly. In dogs fed solely on animal diet there was no trace of saccharine matter in the blood of the portal vein, the blood of the hepatic vein always on the contrary contained from 1 to 2 p. cent of hepatic sugar.

I have said that every experimenter has confirmed the constant existence of sugar in the Liver.

(1) Comptes Rendus 29 Janvier. 230. (1855)

and I should not have stopped to consider an objection which has been raised against the fact of the ~~Sugar~~ Liver being a sugar-producing organ, but that the Editor of the Monthly Journal seems to attach some importance to it, by promising an abstract of M. Figuier's paper (1) in the April number. The sum & substance of the objection is this. Bernard's experiments on dogs submitted to animal diet for months lose their significance, since M. Figuier holds that sugar exists in blood as procured from the shambles. Vessels, he says, exist in the muscle on which these dogs are fed, these vessels contain blood, & blood contains sugar. -the liver has the power of concentrating the sugar of the food, & hence we find sugar in its tissue. There is very little weight indeed in M. Figuier's argument. It always appears to me that those who call in question Bernard's fundamental doctrine, have never thoroughly studied the subject. — Without questioning the very questionable assertion that sugar existed in the tripe on which the subjects of experiment were fed. and without entering

(1) Robin et Verdeil - Traité de Chimie Anatomique. II. 543.
Paris. 1853.

(2) Nouvelle Fonction

into a minute discussion and adducing facts which might here be premature. I shall content myself with citing the two statements as under — the first showing the rapidity with which sugar disappears from the system, the second proving its existence long after any sugar introduced from the alimentary canal could have remained in the tissues of the body.

" Organic substances act on liver sugar in the blood, in the liver, in the urine, in the serosity of the pericardium, just as they do out of the economy. That is to say they cause it rapidly to undergo the lactic catalysis. In twenty-four hours or even less, the sugar which has existed disappears. &c." (1)

In the livers of dogs which were starved Bernard detected sugar in one case after twelve days of complete abstinence, and in another after fifteen. (2)

Apart from any other considerations, I think that M Foguier's hypothesis is quite invalidated by these observations of the above named authorities — We pass on therefore to ~~consider~~ enquire with Bernard — What amount of sugar

may be found in the human liver, and in that of the lower animals after death.?

Taking into account that the circumstances of death must have a grave influence on the processes of secretion, the investigations to determine the point in man were made either on criminals just executed, or on individuals who had met with a sudden & violent death. Bernard has put on record six cases of violent death, in all of which Sugar was abundant in the hepatic tissue, while none was to be found in any other organ. Even the contents of the Gall bladder gave no indication of Sugar, a circumstance remarkable when we reflect on the intimate & organic connection subsisting between it & the liver, & tending to show an antagonism between the secretion of Sugar, & the excretion of Bile. He has in three of these instances given us the following results.

1. Death by decapitation. Liver weighed 1 Kil 300 Grammes
2. do — 1 . 200 —
3. Killed by Musket shot. — 1 . 575 —

Sugar contained in 1st. Grammes 23.24
— 2nd — 25.704
— 3rd — 14.10

The Gramme is about 16 Grains. —

(1) Nouvelle Fonction p. 48

Experiments instituted in the case of sudden death - poisoning by arsenic for example - show a like agreement.

Bernard has given a long table (1) showing the vertebrate animals in whose liver he has found sugar. In most instances he has calculated the quantity contained. The underlined are extracted from this table.

Mammalia. Monkey liver contained 2·15 p 6ent. Sugar
Dog — 1·90 —
Cat — 2·10 —
Rabbit — 1·95 —
Sheep — 2·10 —
Cow — 2·65 —
Horse — 4·08 — during digestion

In the Birds Fishes & Reptiles the quantity of Glucose has not been sufficiently calculated to offer definite results.

The remainder of Bernard's work is devoted to certain accessory points. These are
1. The relation that subsists between the sugar of the liver & the sugar of the alimentary canal, & the relative importance of either variety.

2. The variations in the production of Liver Sugar following abstinence & digestion.
3. The origin of Liver Sugar.
4. The influence of Age. disease &c

As these will call for attention in various parts of this Essay, and as we are now beyond the range of Bernard's peculiar province, & since therefore greater ~~care~~ scope is afforded for variety of opinion, I shall take them up individually, and as may be convenient — I shall occupy the following section in discussing the first. —

The Sugar of the Alimentary Canal and Its Relation to Hepatic Glucose.

That the amylaceous ingesta require to undergo transformation before they can fulfil their purpose in the Economy, is an established doctrine in physiology. The many disputes which have arisen as to the place & means of their transformation, have led to the record of abundant proofs of the general fact. That the primary change

(1) Monats bericht der Acad. der Wissenschaften. 1841.

(2) Physiological Chemistry translated by Day. 1853.
II. 123.

(3) Arch. Gen. de Med. 1845. p. 245.

(4) Since writing this sentence I understand that Matteucci holds the opinion which I have ~~adopted~~. On what grounds however I do not know. as I have been unable to find a record of his views on the point. see also note page 42

which starch undergoes during digestion is its conversion into grape sugar. Such passages as the following testify.

"During the digestion of amylaceous substances we always find traces of sugar in the chyme from the stomach to the caecum." Mitscherlich.(1)

"The sugar found in the small intestines & sometimes even in the large intestine owes its origin to the action of the pancreatic juice on starch." Lehmann.(2)

"In rabbits the digestion of starch is begun in the small intestine & carried on in the caecal - it is resolved into dextrine, Glucose &c" Bouchardat.(3)

These observations leave us no doubt of the fact of the metamorphosis of starch into sugar, but what we wish principally now to determine is, whether this sugar is made subservient to the uses of the economy as such, or is absorbed & assimilated under another form.

Every author with whom I am acquainted seems to consider that sugar is absorbed as such almost entirely if not altogether.(4)

Lehmann says. "The sugar which is formed is very rapidly absorbed." & "the principal

metamorphosis

(1) Op. cit. I 289 + 295

(2) Letter. 1857. 376.

(3) Nouvelle fonction. p. 60

of Sugar occurs primarily in the blood." (1)

Liebig says "Grape Sugar disappears in the Blood with extreme rapidity so that it has only in a very few cases been possible to detect it in the Blood." (2)

Bernard would certainly seem to have entertained the same view in performing the very experiment by which he discovered the Sugar forming function of the liver. Since he says that he anticipated that the Sugar of the food of the animals experimented on, would enter the portal capillaries, & he maintains the same when he remarks "The passage of Alimentary Sugar by the liver is in fact an Anatomical & physiological necessity." (3)

Bouchardat & Sandras fed Animals on starch & found Sugar in their portal blood. Sommer and Lehmann have found Sugar in the Chyle of horses fed on grain. In short there is no doubt of the reception of Sugar into the circulation to a certain extent.

We leave these facts however in the mean time to investigate, whether Sugar in whole or in part submits to any change in the stomach & if we find that it does, to enquire what is

the change, and to what extent it takes place.

Since the natural catalysis of Glucose under such circumstances is the lactic, we naturally ask, does Lactic acid present itself in the alimentary Canal? Of its presence there is no question, but it may be argued that the lactic acid of the primae viae is due to the Gastric secretion & to it alone. That lactic acid is evolved from this source, & poured into the digestive passages we must admit, but if we can show that when Glucose is abundant in the intestine, while its existence can hardly be detected in the portal blood, and if at the same time lactic acid be present in the intestine under conditions in which it could not be affected by the acid of the stomach, it follows that Glucose is subjected to the lactic catalysis. This we hope to show to be actually the case. but we must first prove the presence of Lactic Acid of catalysis during primary digestion.

In the upper part of the small intestine an acid reaction due to lactic acid is invariably present during the digestion of mixed alimentary

matters

(1) Op. Cit. I. 122.

(2) Nouvelle fonction p. 68

according to Lehmann,(1) while as a general rule on the same authority, the contents of the ~~ileum~~ lower part of the ileum & large intestine give an alkaline reaction. In this latter position acid is always present during the digestion of amylaceous substances, as well as in the lower part of the small intestine. That this acidity was due to lactic Acid Lehmann satisfactorily proved in two cases of praeternatural anus in the ascending colon where he could procure it abundantly. The only possible source of lactic acid in this situation is the catalysis of the amylaceous ingesta.

Now what are the facts in regard to the absorption of Sugar? The most valuable data on this point are those given by Bernard to prove that the liver does not depend on any extraneous source for the sugar which it forms. He says "In normal states of the system, I have proved by experiment that the quantity of sugar in the liver is not sensibly augmented by amylaceous or saccharine alimentation."(2) in short that the nature of the food does not in the smallest add to, or detract from the

Amount

suggest, or conjecture;
or suppose.

of Sugar contained in the tissue of the liver. He also remarks. " When in an Animal fed on mixed diet the intestine contained a large quantity of Sugar, there was a mere trace in the portal vein. too little indeed to say how much there was."

Coupling these statements of Bernard with the facts as detailed by Lehmann, we can I think have little hesitation in assuming that the greater part of the Sugar of digestion enters the system under some other form. But I am inclined to go farther & to propose, that the presence of Glucose in the portal vein is due to mechanical causes solely, and ought never in reality to have entered the circulating fluid. Let us admit that Sugar is to found, what must be its next step towards performing its normal function? Are we to grant Bernard that this is its conversion in the liver, into the non-descript substance which he professes to have seen in the liver! - that Sugar is converted into this just as bees form wax from Sugar as M. Edwards has experimentally demonstrated? I think not. We know from Magendie's researches afterwards alluded to, that

the

(1) Comptes Rendus. Dec. 1850

† A French idiom. "that he has proved" is better

circulating fluid has eminently the power of bringing about the Lactic Catalysis of Sugar. & the whole rôle of hepatic Glucose depends on this catalysis as the first and principal condition.

It cannot be that Glucose is normally taken up in <u>indefinite</u> quantity. if it is to become fat in the liver as Bernard hints. Nature acts according to fixed laws, and in accordance with these, fat is formed from lactic acid, but only after this acid has had the opportunity of playing its own part in the Economy. as we shall afterwards explain. Bernard contends to have proved (!) that Sugar enters the circulation by the portal system only, and that it does so by a process of mechanical imbibition. Now the capillary lacteals are subject to the same mechanical laws as the venous radicles. and we may therefore safely infer that this imbibition takes place through both or through neither. And indeed we have direct evidence both by Lehmann & Frommer, that Sugar is occasionally present in the chyle. Lehmann writes thus "I have never been able to detect any sugar in the chyle of horses fed upon bran

(1) Op cit. II. 286.

(2) Op. cit. I. 95.

but the presence of this substance could be determined with certainty in the case of horses which I had fed for a considerable period on starch or highly amylaceous food, with due attention to all precautions, both by Trommer's & the fermentation test. "It would appear therefore as if sugar passed into the chyle in appreciable Quantities only when there was an excess of it in the intestine." (1)

One other point might perhaps have been here adduced, to render the proof of the absorption of lactic Acid complete. namely its existence in the chyle or portal blood. To prove the existence of lactic acid or of lactates in portal blood would be perhaps an impossibility for reasons which will be given in a subsequent chapter. and the only observation I have met with, as to lactic acid as a constituent of the chyle was made also by Lehmann, who recognised it with certainty in chyle obtained in two cases from the thoracic duct of the horse. — in the one case the animal had been fed with oats, two hours before being killed. in the other with starch balls. (2)

I have

× Sources

I have stated it as my conviction and endeavoured to prove, that alimentary Sugar does not as Sugar enter the circulation, and is not made subservient as such to the uses of the Economy. Taking this as granted may we by associating the fact with other established principles, suggest the following as the means used by nature to equalize the supply & nature of respiratory food in all classes of animals.

Lactic Acid we take to be the primary product of the catalysis of Sugar - We have no evidence of the formation of lactic acid from any Nitrogenous body - Lactic Acid by its transformations is the true originator of heat in the Economy. as explained in the Chapter on the Chemical Changes of Glucose. What origin then of this Acid have we in herbivorous Carnivorous and omnivorous Animals respectively? There are two primary sources common to all classes of Mammals. first the product of the catalysis of hepatic Glucose. Second the Acid of the Gastric secretion. The same conditions operate to call into play the function which in either case generates the Acid.

(1) Note. I find that Lehmann as well as Matteucci now holds that Sugar is not absorbed as Sugar. He quotes his statement "that the primary metamorphosis of Sugar takes place in the blood." The third volume of his work has recently been published & from a review of his chapter on digestion contained in the Brit. & Foreign Review for January 1855. I extract the following. "Lehmann does not infer that no Sugar at all is so much taken up by the intestinal capillaries, but feels himself justified in maintaining that only a very small quantity of Sugar can reach the vena portae from the intestines." Again Lehmann concludes "that it cannot be denied that Sugar is absorbed by the lymphatics but it is certain that the amount which enters these vessels is a very small fraction of the quantity formed in the intestines from starch." We may therefore regard the question as almost definitely settled.

Note II. I observe however in the Comptes Rendus of 5 February 1855 a paper by

It is a remarkable piece of Nature's economy that she uses the same acid for the digestion of food, as for the maintainence of heat.

But the varieties of element seem to present an unsurmountable obstacle to the equalising tendency. What however do we find? Lactic Acid exists abundantly not only as a product of vegetable matters, but also enters most prominently into, and in fact constitutes a most essential element of muscular tissue - the food of the carnivora, and this in the carnivora counterbalances the sugar & lactic acid as formed from Amylaceous substances in the intestinal system of the herbivora.

So soon as respiratory food leaves the alementary canal it is in both instances subjected to precisely the same conditions. The liver. lungs. & circulating medium afford in each the same facilities for destruction or for farther elaboration. It is unnecessary therefore to pursue the analogy. I think we may assert that it is hardly possible to conceive, how otherwise except through the agency of lactic acid, the respiration of classes of animals differing so widely in their habits, exhibits precisely the same phenomena. (1)

Longet detailing some observations which may be subversive of our conclusion to some extent if they be confirmed — These go to show that although sugar exist in the portal vein, its presence may be so masked by the product of digestion as to render all the ordinary tests useless. but as to this affecting the validity of the proposition of Bern. that the liver forms sugar — I consider no further disproof required than the fact that sugar may exist in the liver in abundance, while in the intestines none whatever ~~exists~~ can be demonstrated to be present

(1) Med. Soc. London. April 10. 1854.

The Origin of the Sugar of the Liver.

Having previously seen that the Liver gains nothing by the sugar of digestion, and is uninfluenced by the quantity of amylaceous or Saccharine material received into the system. we have now to ask whence is Liver formed sugar derived, & from what constituent of the Body is it formed. We are again compelled to fall back upon Bernard's researches, & he holds that hepatic sugar is as truly a secretion from the blood as is the secretion of the mammary or any other Gland in the body.

The only other observer as far as I am aware who has made observations on this subject is Dr Gibb of London (") who finding in the livers of Seals large quantities of Sugar while he finds but little in the active carnivora, argues that sugar is formed from fat because in the first case the liver abounds in fat, and in the second is comparatively destitute of this substance. I have elsewhere endeavoured to explain Dr Gibbs facts on grounds totally different,

I therefore make no account of them here, & adhere to Bernard's results which in truth it is impossible to set aside.

Bernard admits the many difficulties which present themselves in the study of such a question, of which he says. "that in the present state of Science they are almost unsurmountable." The first proposition which offers itself for examination is naturally — Is there a process going on the liver in virtue of which some element of the blood is split up, into Bile on the one hand & into Sugar on the other, or are bile & Sugar the products of two separate elements of the blood, and the product of the secretion of two distinct classes of cells? Bernard does not profess to have solved this question, but has given us the following details of experiments made with the object of determining out of what Materials Sugar is elaborated by the liver. and they are of great value as indicating the direction in which we are to look for further information.

Previous Experiment had shown him that

(1) Nouvelle Fonction. 73.

by withholding food from an Animals. after some time the Sugar began to disappear from the liver. Now he thought that if in such circumstances he added to the blood of the Animal by mixture with its allowance of water, a certain quantity of some alementary principle this would atone in some measure for the want of nutritive matter, & by varying the principle so added he hopes to arrive at an approximation to the true sugar-forming constituent. "In a word", he says, "all the conditions of impoverishment of the blood remained the same, with the exception of the substance superadded to the water, & it appeared to me legitimate to conclude that if in any case the sugar became increased in quantity, this was to be attributed to the principle so added." (1)

Four dogs were therefore chosen & treated as follows.

The first (adult) weighing 4379 grammes was starved for four days & then for the six days following had injected into its stomach 370 grammes of slightly tepid water, & at the end of that time was killed by strangulation an hour after the last injection. —

The second which weighed 4910 gr. was treated precisely in the same way with this exception that 20 gr. of Gelatine in solution were added to the water. In the third 20 grammes of Starch were substituted for the Gelatine it weighed 4865 gr.

The fourth dog (13.640 gr.) was starved for eight days & each day for the following six. 90 Cubic centimetres of liquid pork fat were thrown into its stomach along with 180 grammes of water. It was then killed as before. The results of these experiments were as under.

Sugar per cc in the Livers of the dogs.

Water alone.	water + fat.	water + gelatine.	water + starch.
0 gr. 13	0.54	1.35	1.50

As he expected a different result in the case of the dog fed on fat Bernard in case of error instituted a new set of experiments by directly feeding animals on Gelatinous, Amylaceous and fatty matters respectively, but again the same peculiarity was found. The percentage of Sugar in the liver standing thus

Dog starved 0 gr. 95. fed on fat 0.88. fed on Gelatine 1.65 fed on Starch 1.88.

The comparatively large amount found in the Animals fed on Starch Bernard thinks

"All the length" &c is not good English
"This is all", or, "this is the utmost, that Bernard
considers himself justified in conceding"

X then remarks

(1) Stowell function 4/9

due to direct absorption, in relation to the time of digestion during which they were killed. That the fatty matters were absorbed he satisfied himself & now being forced to regard Gelatenous matters or matters analogous as the true source of hepatic sugar, he quotes Lehmann to show that such substances do disappear in their course through the liver. who says. That the blood of the Portal Vein in traversing this organ loses a certain proportion of its azotised principles, and that its fibrin considerably diminishes. This is all the length the Bernard considers himself justified in going. He concludes by remarking " I must repeat what I said at the beginning of this paragraph, that the question is shrouded in the greatest obscurity. But in connection with my experience I am anxious to draw the attention of Anatomists Chemists & Physiologists to the question, for I consider that the assistance of them all is not too much for so vast & complex a problem."

May we therefore propose a theory of the formation of hepatic Sugar consistent with the indication which Bernard has pointed out.

(1) Op. cit. I. 292.

Many years ago Berzelius made the observation that animal tissues as well as vegetable tissues could be made to yield Saccharic & oxalic acids when treated with nitric acid. Lehmann says "Berzelius founding his hypothesis on the fact that protein treated with nitric acid yields Saccharic & oxalic acids indicates the possibility that protein may contain sugar." (1)
Such however is not the deduction we should draw from the above fact. We are inclined to regard animal & vegetable cellulose as one and the same, and as possessing the same chemical peculiarities. and I think that this assertion will be strengthened by a fact which we shall presently adduce. We consider lymph as the result of the solution of the solid portions of the albuminous tissues, and that the white blood corpuscle is in the lymphatic glands elaborated out of this material. The white blood cell we hold with the best authorities to be the originator of the red blood corpuscle, which we may call a liberated nucleus. That this last is a body destined very soon for excretion its structure is sufficient to show, since it has no internal germ by which its existence can be prolonged. What purpose it serves previous to its elimination

(1) Vide Gray on the Structure & Use of the Spleen. 1854.

it is not my business to inquire. If then this globule be destined for excretion, how is this excretion effected? Some say that it is broken down in the circulation. I am not aware that we have any positive evidence to prove that this is really the case. and I am disposed to consider that the Spleen is essentially the organ in which this disintegrating process takes place. All the latest authorities seem disposed to attribute to the Spleen an excreting function.(1) We look upon the kidneys and the Spleen as the primary excreting organs - the first adapted for the removal from the system of the soluble salts - the second for the elimination of the solid constituents. We have said that we regard the blood disk as essentially composed of cellulose. and that this body is thrown out of the economy by the Spleen. All writers now I think admit that the colouring matter of the bile is the effete colouring matter of the blood, but we have still to account for the cell wall. We shall go therefore to pathology to inquire whether from morbid influences the splenic excretion is ever retained, and if we find that it is, to investigate what is the true nature of the substance under examination.

1) Brit. + Foreign Med. Chir. Review. Oct. 1854.

I am inclined to believe the so called waxy degeneration, the result of a retention of the normal excretion, consequent (perhaps) on morbid states of the pulmonary tissue, and sympathy propagated backwards to the source of the supply of material for the normal accomplishment of the respiratory act. Now what is the nature of the substance which constitutes this waxy degeneration. Very recently Meckel has written a memoir on this condition, which he calls the Lardaceous or Cholesterin disease. He extract the following particulars of the chemical peculiarities of this body. "All drops made of a dark blue green colour by iodine & Sulphuric acid." "Oil drops simple or in concentric layers coloured at first beautifully violet. then blue. then dark brown by the same agents." "Cholesterin crystals not coloured directly by iodine, but exhibiting after the application of iodine & Sulphuric Acid. a beautiful play of colours. first violet. then for days indigo & cæruleau blue &c." "The lardaceous substance", says Meckel, "with the violet reaction is probably a combination of Cholesterin with other fats: The exact nature of the peculiar fat which plays so important a part in the composition of all these compounds is unknown. No other fat shows this reaction with iodine: Dr. Parker.

"just" here is not English. "We can only repeat"

" Handbook 390.

the reviewer remarks. "If it really appear that the so called lardaceous substance is within certain limits a stable chemical compound, and if it can be so easily distinguished by the test of iodine and Sulphuric Acid a new path of great interest is opened to pathologists. We must confess however that we are not at all convinced that Meckel has made out the propriety of the term. Cholesterine disease. Still our previous knowledge leads us to think that many of his facts are correct."

We shall have occasion subsequently to mention that we consider the spleno-hepatic diverticulum the channel by which fats are excreted from the economy but we just repeat with Meckel that no fat forms the reaction of which he speaks with iodine and Sulphuric acid. What substance does give this reaction? Dr Gregory says (1) Sulphuric Acid dropped on cellulose forms with it a jelly which is coloured blue by iodine." We therefore maintain that the sanguineous excretion of the spleen has nothing to do with the reaction, but that is owing simply to the presence of a solution of cellulose resulting from the breaking down of the red blood corpuscles, which have parted with their organic structure, and from this we may deduce that

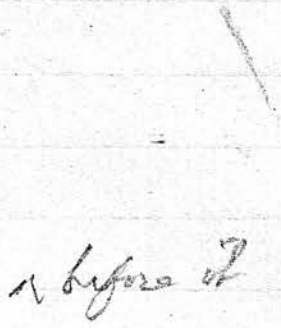
"composition" (They are certainly different in constitution, because, having nearly the same composition, per cent, they have yet different properties)

V. G.

a preparation for further chemical change is going on. We have cited Lehmann's observation that the blood of the hepatic vein differs materially from ~~that of~~ the portal blood in the amount of saccharine matters that it contains - We naturally assume that these matters have been consumed during their passage through the liver.

The close affinity that exists between Sugar & Cellulose, is shown by their being almost identical in constitution, and by the facility with which the latter is transformable into the former - The simple agency of temperature & of a dilute acid sufficing for the accomplishment of the transformation. That the hepatic tissue possesses within itself the requisites for bringing about the change we must assume, since we so invariably are able to demonstrate the abundant presence of Sugar in the Liver - Sugar in its origin quite independant of the alimentary supply.

Such we conjecture to be the mode in which hepatic Sugar originates. The theory is crude, & perhaps not worth further elaboration, still it is just what has suggested itself to my mind as possible, and in the absence of any better, I have ventured to propose it.



Notes. A. It will be said that if the red corpuscle be really composed of cellulose nothing will be easier than to demonstrate this by the ordinary tests. I have tried, & the tests have failed. why?- I believe from the presence of the colouring matter. I have added a little vermilion to starch jelly, & then I find that iodine gives no reaction. We must therefore decolorise the blood previous to testing. and this I have had no time or opportunity to do.

B. Whether the blood corpuscle furnish Glucose or not. Still I am inclined to hold that it is excreted by the liver after having undergone previous preparation in the Spleen. The abundant appearance presence of white blood cells in the splenic vein I consider to depend, not on their absolute increase, but as contrasted with the relative diminution of red disks. Why the Spleen should be classed with the blood preparing glands I never could make out. Is it not preferable to hold the opposite doctrine? How precisely does nature work. No sooner have the effete red corpuscles been got rid of in the liver, than the blood has a constant source of their rejuvenescence immediately presented to it by the thoracic duct, which mingles its contents with the hepatic blood before this has performed any duty, which might can after from its impoverished state, have been detrimental to the economy. Truly I think we may

call the Spleno-hepatic circulation a diverticulum for the purification of the blood.

C. If we hold the groundwork of our theory, does it not show how economically nature deals with the Economy in elaborating from substances otherwise effete, pabulum for the accomplishment of the many & important offices which we shall have to attribute to hepatic sugar in a subsequent chapter?

The normal Role of Hepatic Glucose in the Economy.

We have found a constant supply of Sugar poured by the hepatic vein into the torrent of the general circulation - this we have to follow to its place of disappearance, and we might deal with this part of our subject in a very summary manner, since in ordinary circumstances the part which hepatic sugar as such plays, is a very limited one indeed. & Since a subsequent section is occupied in considering its Chemical changes & uses in the Economy. But seeing that in certain conditions and these not of a pathological nature, Sugar finds its way not into the general circulation only, but into many of the fluids besides, we propose here to show under what conditions Sugar is normally to be found in these localities.

We ought however first to inquire by what agency the amount of liver formed sugar is increased or diminished - And again we are compelled to fall back upon the "Nouvelle Fonction du Foie" but now for the last time.

Direct experiment shows Bernard, that when an animal has finished the digestion of its food. perhaps six hours after being fed- just as much Sugar is thrown off from the Liver as can be consumed in the pulmonary organs, & none finds its way into the arterial circulation. Reception of food into the stomach acts as a stimulus to the abdominal circulation, and with its increased activity, increased secretion from all the Glands takes place, and during the whole continuance & maintainence of the stimulus the Liver elaborates & excretes Sugar in so considerable a proportion, as to overbalance the powers that combine to destroy it, & it may at such a period be detected even in the superficial veins of the Body, & even in the portal vein. Schmidt having found Sugar in the latter situation, & undoubtedly under such circumstances, objected to Bernard's deduction as to the Glucogenic function of the Liver, but experience abundantly testifies, that the Sugar found in the circulation invariably sets out from the hepatic organ.

The first observer who showed that Sugar was present in healthy blood would seem to have been

(1) Philos. Mag. 1845.

R. D. Thomson of Glasgow (1) altho' Mr M'Gregor of the same town in a paper which he published in the Med. Gazette for 1834 infers its existence from the fact noticed by him, that in those fed on vegetables diet Sugar could be proved to be present by fermenting the contents of the stomach, procured by the action of an emetic soon after taking such food. It was in the serum of his blood that Thomson ascertained Sugar to exist, after having fed the animals on porridge, and killed them three hours subsequently. He was led to perform his experiments in consequence of Tiedemann & Gmelin having asserted that fermentation could be set up by yeast in many of the fluids of the body. He determined the amount of Sugar present in two instances - in the one from 1000 Grains of Serum he got 2·57 Grains of Sugar - in the other 520 Grains Serum gave 4·19 Grains of Sugar. The statistics of quantity are of course of no value, still the fact itself is valuable as going to establish Bernard's statement that Sugar is present in the Blood during active digestion. Thomson's Conclusion was "that Sugar is found in

(1) Page. 189. 1846

the Blood of animals fed on Starch."

The year following we have a paper by Magendie in the Comptes Rendus (1), on the normal presence of Sugar in the blood. His experiments likewise arose out of his researches on the Catalytic properties of the tissues & fluids of the economy — he had found that Starch introduced into the circulation immediately changed to Glucose, but as this was altogether beyond the range of vital phenomena, he wished to know whether after feeding an animal on highly amylaceous diet, Sugar would exist in the circulation. He fed a dog for several days on cooked potatoes, & on killing it soon after the last meal, he examined the blood, and detected in it a Notable Quantity of Glucose. while the Urine of the animal contained no trace of it, Again with equal certainty Sugar was found in the blood of horses fed exclusively on corn — he goes on to say "I have not yet had an opportunity of experimenting on man, but as the phenomenon of which I speak is of a chemical Nature, I regard it as extremely probable that during

the digestion of starchy matters our Blood contains Sugar." These observations we class with those of Mr Thomson, regarding them merely as confirmatory contributions to the fact as Bernard has stated it.

It does not follow that because Glucose exists in the Blood, it should pass off by the Urine. The Blood must have reached a certain degree of saturation before the physical act of exosmose takes place. Forty grains of hepatic Sugar have been injected into the blood of a small dog without any of it being removed by the Kidney. Very recently Bernard has experimented on Rabbits to determine the effects of loss of blood on the sugar in their circulation - he finds that as the mass of blood diminishes, the urine becomes saccharine. If for example half a Gramme be injected, no Sugar will appear in the urine, but if the animal be previously bled, a certain quantity will pass off by the renal excretion. He very properly considers this merely as the result of a diminution which renders the Animal equivalent to an individual of smaller size, & therefore subject to the same chemical & physical laws with the latter.

Magendie

Magendie has given the following as the relative proportion in which various sugars require to be injected into the blood before being discoverable in the urine, or as the relative facility with which these undergo Catalysis in the circulation.

Cane Sugar 1. Milk Sugar 5. Grape Sugar 50. Hepatic 240.

So great is the fermentescibility of the last variety, that if we examine the parenchyma of the Liver even 24 hours after death, we may fail to find it, & its destruction may take place even within twelve hours if the temperature be high. This is no doubt one of the reasons why several persons have been unable to verify its presence in this & in other situations.

Bernard declares that in the Cephalo-rachidian fluid he has never failed to detect Glucose. His experiments were made on dogs, cats, & rabbits all in a state of health. There is one somewhat remarkable statement that he makes "that it was only after several days abstenence that the sugar began to fail." This by no means coincides with Bernards own views of the extreme ferment-escibility of hepatic sugar, for if we allow that

digestion

(1) Bulletin de l'Acad. de Médecine. Dec. 1852.

(2) Edin. London Philosophical ~~Trans.~~ Proceedings Jan 1854

is completed in these animals in six hours & that from that time the formation & destruction of Glucose is equalized, it follows according to Bernard that Sugar should immediately begin to disappear & be altogether removed within twenty-four hours if not much sooner.

Indeed the correctness of Bernards views on this point has been questioned. M. Buecy analysed a fluid from a fracture of the base of the Cranium, & having obtained a reduction of the blue protoxide to yellow suboxide of copper, concluded he had found Sugar. He ~~had~~ obtained similar results in the same fluid from the horse & dog, but having always failed to excite fermentation, he was inclined to believe that some substance other than Sugar was present, presenting the same reaction. (1)

An observation to the same effect, to which weight will be attached, is detailed by Mr Paget (2) who supports M Buecy from an analysis of fluid from a Spina bifida in a Child. Its sp. gr. was 1·006. He gives the particulars as under.

1. Heat produces opalescence. Heat & Nitric Acid a flaky

white precipitate. Nitric Acid also a precipitate.
2. Boiled with Liq. potas. there is a faint pinkish tint.
3. Heated in water bath with Trommer's solution, in a few minutes the red suboxide appeared.
4. Maumené's test gave no result.
5. No Gas was developed after standing some hours in a warm cupboard with Seiman Yeast.
On the fluid standing for some time Peroxide of Copper was not reduced. he adds.
"Thus only one test the most fallacious gave indication of Grape Sugar – the low Sp.gr. would in itself lead us to suppose no Sugar present."

It is quite possible that Bernard may be in error in supposing the reduction of the oxide of Copper due to Glucose, and it may be that this takes place from the presence of Leucin as Mr Paget suggests. which we know to have the property of bringing about the reduction. still I do not consider Mr Pagets deduction borne out by the facts as he has given them.
There is first as an objection the highly albumenous character of the fluid, which of itself materially interferes with the action of the tests, and may render them totally inapplicable. Hence Jones says

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in reference to testing for Sugar in Serum even in diabetic patients " It is essential first to get rid of all the albumen by evaporation to perfect dryness. Secondly to extract the Sugar from the albumen by treating it with water for a considerable time, & thirdly to be very careful not to add too much of the tests." (c)
Now Mr Paget gives us no proof of his ether having separated the albumen in this case, or of his having concentrated the fluid, ~~evaporated~~ yet notwithstanding Trommers admirable test is found to indicate Sugar, while simply boiling with potash gives a dark a coloration as we could be entitled to expect from the Credently small amount of Saccharine matter formed by the Sp. gr. of the fluid. Maumene's test altho' applicable enough where Sugar is in comparatively large quantity q. as an hospital test in diabetes, is obviously not sufficiently delicate in such an instance. & as to the fermentation test I am inclined to consider it more subject to fallacy than any other — if Carbonic acid be given off it proves little. Every organic tissue & fluid in its decay emits this gas. & had alcohol been formed in this case it would have been quite inappreciable. besides fresh yeast as procurable here, I have found to contain a very large quantity of Grape Sugar. therefore it was of little perhaps of no use.

Moreover from the appended circumstance which Mr Paget adduces, we should be induced to believe Glucose really present - The failure of Trommers test after the fluid had stood for some time is just what we should expect, as the Sugar must necessarily have undergone the lactic Catalysis. This was obviously not a fair case by which to test the accuracy of an observer. The Sugar was here clearly held in Solution by an immense amount of fluid. This being increased probably a hundred fold. Altogether although we must consider the question still undecided, we cannot consider Mr Paget's case as subversive of the statement of Bernard.

Instead of further tracing the existence of Glucose in other fluids of the economy at this stage, it will be more expedient to defer doing so till a future opportunity, and until we shall have enunciated certain general laws which regulate its presence, and which it would here be premature to introduce. We go on therefore to investigate what becomes of the liver-formed Sugar, and to what wants of the Body Sugar is subservient. —

Chemical Changes of Glucose in Normal States of the Economy.

We followed in the outset the Sugar of the alimentary Canal to its destruction, and place of disappearance, and in the previous section we determined where and under what circumstances Glucose was to be found in ordinary conditions. The part it played we showed to be a very limited one, its existence in the General Circulation being but the result of a special stimulus given to the hepatic organ, by the presence & absorption of nutritive matters of any description. We found that with the close of active digestion Sugar ceased to exist in the blood, except between the hepatic vein & left side of the heart, & hence inferred, that some cause operating in the pulmonary system brought about a change in virtue of which this disappearance took place.

At this point then our discussion of the chemical changes of Glucose begins, & it is natural to ask what processes go on in the Lungs which may determine the destruction

Glucose. Of these we propose to speak anon - in the meantime we may merely state, that according to the best authorities. while oxygen is taken into the pulmonary organs, Carbonic Acid is disengaged. Why & how this takes place we shall speak of presently.

That Lactic Acid is a normal constituent of arterial blood & that this is replaced in venous blood by Carbonic Acid we assume at present as facts. The source of Lactic Acid in arterial blood can be Grape Sugar only - that is in the intervals of digestion - and Sugar we have seen under all circumstances to be present between the Liver & Lungs & there alone. Hence we deduce that the Lactic Catalysis of Hepatic Glucose takes place in the pulmonary Capillaries constantly and invariably.

Let us inquire what is necessary for the accomplishment of this Catalysis, and whether the pulmonary Capillaries, afford us the Requisites for the transformation. To suit the case we may paraphrase Dr Gregory's description of the Lactic ferment. Keeping strictly to his own expressions. Thus ——

"When

(1) Handbook of Organic Chemistry. 378.

"When the Sugar of the Liver is brought
" in contact with an oxygenated ferment in the
" Lungs, the temperature of the Body being at
" its natural standard, a peculiar change takes
" place which has been called a fermentation.
" The Blood soon becomes Acid from the Sugar
" becoming Lactic Acid, & were the amount of
" free acid to reach a certain point the ferment-
" -ation would cease. But now the free acid is
" Neutralised by the addition of Carbonate of Soda
" brought hither by the Great Venous trunks —
" Lactate of Soda is formed, while the Carbonic
" Acid set free is exhaled, & fermentation continues." (1)

The discussion of several of the points in the above process implicates doctrines of the highest interest in physiology. and this summary involves my notions of the chemical changes which occur during the respiratory act, as these have been modified by my study of the question.

I do not stop to enquire what is the ferment which causes the catalysis. Magendie's experiments prove that in the Blood there exists a ferment which has eminently the power of bringing about

(1) Comptes Rendus 1845.

(2) Op. cit. I. 438.

catalytic action.(1) But we may here refer to the statement made above. "That the carbonic Acid of expiration is liberated by the lactic Acid of catalysis. and that Carbonic Acid exists in venous blood in the form of carbonate.

The latter part of our proposition has been most clearly proved by Lehmann. The experiments of Magnus showed that there was comparatively little difference in the amount of free Carbonic Acid in Arterial & venous blood. Liebigs opinion used to be that the Carbonate of Soda in the Blood was the means by which the Carbonic Acid was conveyed from the capillaries into the Lungs. Lehmann Sums up the results of his researches thus. "There can no longer be any doubt of the presence of Carbonate of Soda in the blood." (2)

We therefore bring up Carbonate of Soda to the lungs, & present to it free Lactic Acid, which is the essential result of the Lactic fermentation.— What must take place? Lehmann says, a few lines before, "No free Acid can be present with Carbonate of Soda" It follows that Carbonic Acid must be liberated

(1) Letters. 1857. 400.

and lactates formed by the combination of the acid with the base.

The idea that a free acid in the Body liberates the carbonic acid of the carbonats, is not a new one. for we find Liebig saying "The vegetable acids when they enter the Body decompose the alkaline carbonates in the Blood - the carbonic acid thus set free is given off by the Lungs." (1)

But as I have said the amount of free carbonic acid is generally granted to be as great in arterial as in venous blood. The first experiments of Magnus indeed (1837) gave a greater quantity for the former than for the latter. so that I am not inclined to admit that the gas discharged in expiration rests in the free state in the Blood. What I contend for is the existence of a free acid in the Lungs. The Lungs have invariably an acid reaction as may be readily verified. —

The only investigations as to the nature of this acid with which I am acquainted are those of M. Verdeil who has manufactured from the pulmonary tissue a new acid.

(1) Comptes Rendus. 1851. 604.

which he says is peculiar & proper to this tissue, & has given it the name of Pneumic Acid, & to it he ascribes the property of liberating the Carbonic acid of the Carbonates. (1)

I cannot give an opinion as to whether this acid results from the complicated process requisite for its isolation, & is merely a modification of the lactic. I think it at least possible, and we know the lactic acid to be present under all the conditions in which the pneumic is stated to be found - we know it also to be equally capable of fulfilling all the purposes ascribed to pneumic acid. We may therefore certainly doubt whether the presence of a second acid be essential.

Pneumic Acid says Verdeil is found from Youth to old age - so is the lactic. Pneumic Acid is found after death - so is the lactic. "We know nothing of how pneumic acid is formed." We know the details with precision as regards the lactic. We know little if anything of the existence of pneumates in the blood - the existence of lactates we are certain of. I therefore maintain that lactic acid as derived from

the catalysis of hepatic Glucose is the principal if not the sole agent in the disengagement of carbonic Acid from the Lungs.

By the metamorphosis therefore of hepatic Sugar, lactates are constantly furnished to the arterial circulation. In the nutritive ingesta we have previously found another source of lactates, whether furnished directly in the food of the carnivora, or the product of the catalysis of Starch Sugar. If these lactates be merely added to the former in the pulmonary capillaries, they can as yet have executed no function in the economy. It may have happened however that the division which has traversed the hepatic tissue has undergone a change in this situation this falls to be considered subsequently.

The phenomena which attend the introduction of food into the system are increase of heat, increase in rapidity of circulation, and in the number of respirations, and amount of Carbonic Acid expired. These phenomena we might explain in two ways - first by supposing with Bernard that the food acts as a special excitor to the Glucogenic function of the liver. in short that there is

(1) Op. cit. I. 96.

an increase in the amount of Sugar. thrown into the system, & hence a corresponding increase of lactates & carbonates, or Secondly we may suppose that the excretion of hepatic fluose remains the same while the lactates of the food form the source of the augmented supply. & this last is the view I myself would be inclined to ~~propose~~ adopt had we not Bernards assertions to the effect that he finds Sugar in the blood during active defestion & their Confirmation by Thomson. Magendie. & Figuier.

In either case the Carbonic acid exhaled is increased in quantity, and the accompanying exaltation of the circulatory & respiratory functions is perfectly explicable on the ordinary laws which regulate nervous agency. —

Two points we have taken for granted which ought now to be proved. first – that lactates do exist in arterial blood. Secondly – that lactates are converted into Carbonates in the circulation.

The following Quotations contain all that we can say, besides what we have already said in reference to the first of these ~~two~~ points.

Lehmann writes thus (1) "It is probable that we shall never obtain a positive demonstration

of the existence of alkaline Lactates in healthy blood by direct experiment – Nor is it surprising that the presence of lactic Acid has never yet been demonstrated in normal blood, since the combustion of the alkaline lactates – that is to say their conversion into Carbonates, exceeds in rapidity & extent their passage into the Urine." But again we have Lehmann remarking in the same page in reference to lactates in blood "The simplest induction proves they must be present there even if they remain in it for a very short period." ~~and again "Until we can prove that the lactic Acid which is accumulated & we must assume that it passes into the blood."~~ Again "We well know that chemical analysis has not yet attained such a degree of accuracy as to enable us to demonstrate the presence of lactic Acid in the blood with due Scientific precision." I may remark that all these statements were made before anything was known of hepatic Glucose.

Liebig's concurrent testimony is as follows "Sugar. Starch. & in general all those substances which in contact with animal matter

(1) Chemistry of food. 108.

are convertible into lactic acid, are converted in the blood into lactates which are destroyed as fast as they are produced."(*)

That Lactates then exist in arterial blood I take as a fact, but could we discover any indication by which their presence ~~of lactic acid~~ could be traced in the circulating blood this might afford us a valuable compensation for the deficiency of Chemical means of investigation. Does the following theory consist with fact, and if we entertain it does it afford us the desired indication?

Several circumstances lead me to believe that it is to Lactic Salts that the arterial blood owes its bright red colour. It is no proof indeed that the locality in which the blood assumes this hue is the same in which lactic acid is for the most part elaborated, nor does it altogether follow that because when we add lactates of Soda to venous blood ~~Lactic Acid~~ & it becomes apparently arterial, that the same takes place within the economy. The principal objection is that in the same locality oxygen is constantly absorbed, & that oxygen possesses the property we attribute

to Lactic Acid. But if we go to comparative anatomy or to pathological conditions, and if we show that where oxygen is deficient, & lactic Acid is proved to be superabundant, if we show that then & there the same law obtains, we shall then have some ground on which to base our hypothesis.

As an instance of the deficiency of Oxygen we take the case of the cetacea. That the supply of oxygen is truly deficient in these animals is perfectly apparent. It is by means of oxygen that lactates are destroyed & carbonate ~~Acid~~ produced. It is the slowness of the accumulation of Carbonic Acid which renders this class an exception to the rest of the Mammalia, in so far as that the cetacea can remain long under water, and that they are under the necessity of relieving their System of Carbonic Acid only at long intervals. The presence of fat implies the absence of oxygen, fat being as I believe the further catalysis of lactates, and occurring when from deficiency of oxygen lactates are incapable of resolution into Carbonates. This however I shall speak of subsequently. I now remark that in accordance with all the laws regulating our respiration we

should

naturally expect, that in animals remaining so long below water, the venous blood should be of pitchy blackness, as in a case of poisoning with Carbonic Acid. But this is not the case. An observation which I made last summer showed me exactly the contrary, and I was so struck with it at the time that I noted the circumstance, and it now serves me as an argument in favour of the present theory. I accidentally saw a porpesse cut up, and expected to see the blood dark as in ordenary conditions, but of the large amount of blood which streamed from it, all was of a bright crimson colour. I have made inquiry at some of my friends who have been in the Arctic regions and find that they remark the same of the blood of the whale.

The venous blood then of the porpesse is much brighter in colour than the same blood in the ordinary mammalia. Dr Gibb has shown that hepatic Sugar is very abundant in such animals; consequently Lactic Acid must also be abundant in their blood. and excluding oxygen I think that we are shut up to the conclusion that it is to the Lactic Acid that the crimson tint is due. —

and

(1) Mémoires de l'Académie de Médecine. VII. 232.

And all the more when we couple this circumstance with another which we borrow from pathological states of the body in man. I transcribe from the a paper in the Memoires de l'Academie as under in reference to the alterations of the blood in typhoid fever. (1) "Presque toujours il a été trouvé d'un rouge clair ou vermeil, offrant la couleur de vin de Bourgogne, de coraline, de gelée de groseilles (Huxham), de vermillon (Grant)." The author goes on to ask (page 234) "Is it true as Dr Blaney of Sunderland maintains that the blood in typhoid fever has lost the carbonic acid it contained in a state of health." We all know, he says, the importance they attach to this in England, and indeed they have founded on it a plan of treatment which they call specific. This is the addition to the blood of carbonic acid by means of aerated waters". But he adds we have no evidence whatever of the diminution of carbonic acid, and in fact the best observers eg. Nepton have proved that in place of being diminished under such circumstances the carbonic acid is increased.

What additional facts do we know regarding the blood in typhoid conditions?

Scherer

× If then lactic acid become free in certain typhoid states, we must consider that lactates are abundant in the circulation.

In acute Rheumatism we find generally that the venous blood becomes of an arterial colour. undoubtedly from the superabundance of Salts.

(1) Op. cit. I. 99.
(2) Chemistry of food. 103.

Scherer we may say has positively determined the presence of Lactic Acid having been able to separate it in quantity from the copious sweats of puerperal fever. while Lehmann has only twice found the blood give an acid reaction, and then in cases of pyaemia. × Taking all these things into account I think we are entitled to offer the proposition that the normal arterial blood owes to the lactates. ~~lactic acid~~ the bright tint which it invariably possesses.

Lactates pass to the state of Carbonates— what proof have we of this?. Laying aside all indirect evidence such as that formerly adduced. I mean that Carbonic acid is eliminated in proportion to the quantity of lactic acid furnished to the system, we can bring the testimony of the ablest Chemists in support of the fact "The following experiment instituted on myself" says Lehmann, exemplifies the rapidity with which Lactates in the blood are converted into Carbonates. Within thirteen minutes after taking half an ounce of lactate of Soda my urine had an alkaline reaction." (1) Experiments of the same kind made by Liebig & his assistants give similar results. (2) That the lactates in such instances did not become

carbonate in the primae viae Lehmann proved by injecting various quantities of lactate of Soda into the jugular vein of dogs, and found that the alkaline reaction was brought about in from five to twelve minutes. Such experiments are conclusive of the fact - but in what locality - under what circumstances - and by what agency the change is effected, remains to be shown, as also what purposes are served by the transformation.

In speaking of the changes in the pulmonary organs, we showed the existence of a free acid in their tissue - it is remarkable that we should meet with a free acid also in the tissues which are traversed by the ultimate capillaries for example in the muscular tissue and in the skin. We know from the researches of Berzelius that the free acid of the muscles is in a great measure the lactic, and to this Liebig gives his full assent. We know that almost invariably the exudations from the skin have an acid reaction which Berzelius ascribes mostly to lactic acid. This acid undoubtedly here performs the same function which we ascribed to it in the lungs. That is - that it sets free the carbonic acid which

is exhaled by the skin, and I think that this fact goes to establish my proposition that lactic acid - not pneumic acid - liberates the carbonic acid in the former situation, for we might as well manufacture an acid from the skin, and call it dermic, as from the lungs & call it pneumic. That the functions of the skin are vicarious with those of the lungs is well known. Why have we the abundant sweats in phthisis and other pulmonary lesions, with the attendant feverish condition? Merely I suppose from this, that the water and carbonic acid, from the blocking up of the air tubes, are unable to effect their elimination - they consequently seek another channel and find it in the skin. So also may we attribute the sweats which precede death to the pneumonic as agonizants of disease.

The change of lactates into carbonates must be regarded as the most important origin of animal heat in the economy, & Lehmann says of this "We know of no substitute which could better act in the blood as food for the respiration than the alkaline lactates. which we have seen undergo rapid combustion in the blood and are thus converted into carbonated alkali.

In

(1) Op. cit. I. 104.

(2) Op. cit. I. 256 + 258.

In a word nothing could be a better supporter of animal heat than the alkaline lactates." (1)

But we pass on to consider whether lactates are finally destroyed in supplying this animal heat, or whether through the medium of lactic acid sugar contributes further to the well being of the system. I propose to show that it does, and that it furnishes indirectly the most important maintainer of animal heat which the body possesses - I mean, fat.

We take as our starting point the following passage from Lehmann.(2) "As to whether the organism constantly exercises its power of forming fat does not admit of solution in the present state of our knowledge. Nor until a satisfactory answer can be given to the two following questions, namely what is the true seat of the formation of fat, & how & by what process, and in what chemical proportion is fat formed from starch or nitrogenous matters." We read in connection (page 208). "The third question as to how fat is formed would next engage our attention if the preceding consideration did not show that we are entirely deficient in the materials necessary for

(1) De genesi adipis. 1843.

(2) Nouvelle fonction du foie.

(3) Lettres. 3/8.

affording a satisfactory answer. For so long as we are ignorant of the grounds on which a process is based we must defer all idea of a scientific explanation."

The ideas of physiologists in regard to the means by which fat is formed are in general very vague, and their opinions are very conflicting — Thus A. Mechel says that the bile has the power of transforming saccharine matters into fat.(1) Bernard cites the experiments of Dumas & M. Edwards by which they proved that Bees formed wax from sugar alone, and conjectures that the sugar of the alimentary canal is in a similar manner changed into fat, by the liver.(2) Liebig speakes thus "The opinion that this transformation is determined by a ferment in the liver which behaves towards sugar in the production of fat as saliva does towards starch &c, & hence that the liver is the seat of this process is not destitute of probability."(3) Liebig formerly held that Starch and other substances were transformed into fat in the primae viae. Robin & Verdeil while they assert that the liver is undoubtedly a fat forming organ, consider fat as formed also wherever we find it, and that the

(1) Traité de Chimie physiolog. 1853. III. 40.

nature of the fat is modified by the situation in which it occurs, and that fat may be produced by the fermentation of Saccharine or azotised matter.(1)

The views of these last physiologists come nearest to my own on this subject & these I may now state. I may first mention that I consider the Liver to have an intimate relation with fat, but not in the manner which the above named authors suppose - in fact I believe with Lehmann that the Liver is a fat destroying organ, and that it is by this channel that the superfluous fats are eliminated from the system - but to enter into the question I think the two following evidences may suffice to show that we have some ground to go on - first the observation of Simon, Schultz, & Schmidt that the blood of the portal vein differs from all other blood by its large quantity of fat. Bernard however says the same of the blood of the hepatic vein - I cannot conceive how this blood could be procured without inflicting such lesion on the liver and of its nervous supply as to ensure destruction of its normal function and so falsify the experiment. Our second argument is that in disease of the liver fat is invariably present in large quantity in the blood,

(1) Annals of Philosophy. V. 199.

gas?

and is in amount invariably proportionea to the secretion of Bile. Dr Traill showed this in Hepatitis (11) and he has been confirmed by Ecanu, Lassaigne, Becquerel & Rodier &c.

The theory that Sugar is transformed in the liver is then destitute of foundation in proved facts, and of the view we started with in the outset, that the sugar of the alimentary canal never normally reaches the liver as Sugar, be adopted. we may set it aside altogether. What theory then of the formation of fat are we disposed to adopt?

The Sugar of the digestive passages we left in the primae viae as lactates when we started with the examination of the Sugar of the Liver and this reduced also to lactates, we traced to the ultimate Capillaries. A certain Amount of Oxygen is essential for the resolution of these lactates as before seen, and if this is not furnished the lactic Acid must undergo a X Catalysis the nature of which will be regulated by the amount of oxygen afforded, and the nature of the catalytic Agent. For instance if we have three equivalents of lactic Acid, and

(1) Note. — Dr Gibb as I have previously stated has shown that the liver of Seals and the Cetacea contain fat in abundance. Why this should be what I have just said, shows — and I believe that exactly on the same broad principle the coexistence of fatty liver with phthisis is to be explained —

oxygen sufficient merely for the reduction of one, the remaining two will resolve themselves. Thus

$2(C_6H_8O_6) = C_8H_8O_4 = \text{Butyric Acid} + 4CO_2 + H.$

By this contrivance of Nature the economy is spared the immense exertion which would otherwise be thrown upon the respiratory organs by the necessary attempts at the introduction of oxygen — But so far as I am aware we know of no means by which fat can <u>directly</u> be made subservient to the <u>production</u> of animal heat, and fat would necessarily be a substance destined for excretion did not nature again interpose to prevent such prodigality, and render it <u>indirectly</u> useful to the Body as a <u>maintainer</u> of the heat generated by its progenitor lactic Acid.

Wherever we find oxygen deficient either in Consequence of the comparative Slowness of breathing for example in Stall fed animals or in Geese artificially crammed and deprived of air and exercise, or our old illustration the cetacea and their Submersion- (1) in all these cases the carbon and hydrogen of the lactic Acid must shift for themselves, and the more deficient the oxygen, the denser, the more fixed, and the more capable of sustaining the animal heat

is the fat which results - all this time the elimination of carbonic Acid and water remaining nearly. perhaps altogether the same as if no fat were formed at all.

I do not intend to enter into details as to the facts. Dr Gregory's well known table supplies all the requisite information. We see as we ascend in the scale that the oxygen remains always the same while the hydrogen & carbon continually increase. — We have nearly all the fatty Acids of the body included in this list. many in number. Now I think it an impossibility that any organ such as the liver can have the power of elaborating fats so varied in their composition and properties, and there is undoubtedly some special ferment inherent in special tissues which operates in conjunction with the conditions afforded to produce each individual class of fats in the Economy.

Such we take to be the normal Rôle of Glucose in the human Economy. We have traced it in its origin, its transformations, and its elimination from the system, and we have shown to how many and how varied wants of the body it is subservient. We now proceed to the Second part of this Dissertation.

Sugar in the Economy in Disease.

Sugar in Pathological states of the Economy.

Sugar may present itself as an abnormal constituent in the excretions, in various forms, and in various conditions. We may find it as true hepatic Glucose. as Glucose the product of the transformation of the amylaceous ingesta in the digestive passages, and thirdly as Lactine, the result of a vicarious metastasis of the mammary secretion.

In following Glucose to its destruction in the economy in the previous chapter, we showed that the great and primary step towards its disappearance was the lactic catalysis. — It is obvious then that whatever tends to check or to put a stop to this catalytic change, must bring about a redundant and abnormal accumulation of Glucose in the system, and consequently cause its appearance in one or other of the excretions. Sugar we have said is furnished to the system through two great channels. The relation which either of these varieties of Sugar bears towards the other is peculiar, so that while both are

Subject

to the same general laws which regulate their catalytic changes, circumstances may combine to prevent catalysis in the one case without as a matter of necessity implicating the sugar in the other.

In endeavouring therefore to draw up a summary of the conditions under which sugar may be present in consequence of some pathological state of the Body, we must keep in view that want of catalysis is the primary cause of its existence, but we must also look to variety and locality as influencing the form in which sugar may occur.

We shall afterwards discuss the question as to whether sugar is ever produced in the Economy to an exaggerated degree, a proposition on which most theories of diabetes mellitus depend. We take it for granted in the meantime that it is not, and so we take no account of it in our Category.

How then may we group the pathological relations of sugar consistently with the statement that these result from the non-fulfilment of the lactic catalysis? What are

the requisites for this catalysis we have previously had occasion to specify, so that it is unnecessary again to detail them. I think that under the three heads as below, we embrace the whole range of causes which may operate to bring about the appearance of Sugar in the excretions with one exception, that is in the case of pregnant females in whom we very often meet with Sugar under circumstances which show it to be but the milk Sugar which seeks a mode of exist when superabundant in the system, or repelled from the mamma.

I may however just repeat what I have said before, that because Glucose exists in the circulation even in excess it does not follow that it must be found in the excretions. Since the Blood must have become to a definite degree charged with Sugar before the physical act of Exosmose can take place.

Sugar may exist in the Body and be eliminated, in consequence of

a. Deficiency of Oxygen in the pulmonary capillaries.

b. Excess of Acid in the System, whether

derived from the catalysis of Sugar. or from the transformation of other organic substances within the Economy.

c. Something taken in from without, which tends to check catalysis. This may be as above an acid mineral or organic, or a chemical substance whose presence precludes fermentation. for example, arsenic.

It is clear that the sugar of the primae viae is not subjected to the first of these conditions, which applies therefore to hepatic Sugar alone. The sequel will show how far I consider both classes of Glucose as affected by the Decoct – and in the third case I think it is impossible to say, how much of the Sugar of Urine is due to hepatic and how much to alimentary Glucose.

It will be observed that I have not named nervous lesions as determining a morbid elimination of Sugar from the System. And this would indeed be a very grave omission on my part seeing that immense importance has of late years been attached to irritations of the nervous System as causing

Who are these?

Diabetes both temporary and permanent. I have however given to the discussion of the question, the amount of attention which I considered it deserved, altho' I have at the same time assigned to it a secondary position, from the conviction, that however important nervous agency be for the due performance of physiological function, and however by the exaltation of nervous force this physiological function may be excited to unnatural activity, still that in the case in point most exaggerated ideas have been entertained by certain very eminent physiologists. Nothing is more common now-a-days than for a person on being asked on what the excretion of sugar depends, to reply - on lesion of the floor of the fourth ventricle. French physicians have noted the appearance of grey spots upon the floor of the fourth ventricle, and called them the cause of diabetes, in the subject of their examination, while others again have found diabetes to depend on the increased volume of the ganglia of the sympathetic. If Diabetes can be explained otherwise than by

having recourse to pathological phenomena so problematical and so little satisfactory as these, I think we are justified in rejecting the observations altogether, and I have therefore laid them aside entirely in framing a theory of Diabetes.

In pursuing this second division of my subject, I shall make two subdivisions. The first will include all the pathological relations of Sugar, with the exception of true Diabetes. — The second will consist of an inquiry into the pathology and treatment of Diabetes.

Pathology of Saccharine Excretion.

Part. I.

Reasoning on the fact as propounded by C. Bernard, that in ordinary circumstances just as much sugar is afforded to the economy by the Liver as can by the facilities provided in the pulmonary capillaries, be resolved into Lactic Acid, it took no great exercise of intellect to deduce, that if any obstacle to resolution were presented

(v) Comptes Rendus. 1851. XXXIII.

in this situation, hepatic Sugar would be found in the circulation and excretions. Indeed I had myself drawn the deduction and verified it by experiment, before I became aware that M Rayneau had promulgated the same doctrine, and had announced that whatever embarrasses respiration causes the appearance of Sugar in the Urine!" It was not to the Urine however that I directed my first investigations, but to another excretion. Considering that the same mechanical law which we saw brought to bear on the passage of Saccharine fluids through the coats of the intestinal canal, ought to hold good in reference to the more delicate texture of the pulmonary air cell, I anticipated that when any morbid state determining an exudation or the blocking up of the air cell vesicle supervened, in the fluids thrown out, I should find Sugar more or less in proportion to the amount of substance involved. — It is not always easy to procure Sputum which we can guarantee to be absolutely free of Sugar introduced from the food or from the syrups almost constantly prescribed for those who expectorate. I have however endeavoured

as far as possible to avoid such sources of fallacy, and from the constancy with which it occurs, and from the eminent fermentescibility of the Sugar itself, I have no hesitation in ascribing the saccharine impregnation to true hepatic Glucose. The first case in which I put my hypothesis to the test was that of a patient treated last July in the Clinical wards for double pneumonia — The reduction of oxide of copper which I obtained in this instance was quite equal to that in ordinary diabetic urine — The method of testing which I adopted for this sputum was that recommended by Bence Jones for the discovery of Sugar in albuminous substances - namely to evaporate to dryness, and then to treat the residue with water to extract the Sugar, filter, and apply Trommers test thus — to about half a drachm of the fluid, add twice as much of Aq. potassæ with one or two drops of a saturated solution of Sulphate of Copper and gently heat the mixture, when as the heat rises if Sugar be present a yellow haze

will appear which increases, so as to form a thick deposit of Suboxide of Copper — The Sugar in this case underwent Catalysis, and totally disappeared from the Solution in a few days. — I may just cite another example of Saccharine Sputum in which I took especial care to procure it freed from foreign admixture, and used a different mode of procedure for the detection of the Sugar. I examined (Dec 14th) the Sputum of a patient in advanced phthisis from Dr Gairdner's ward — The expectoratum was received into a clean jar, was procured in the interval between meals, and the sole medicine made use of was a bitter infusion with hydrocyanic acid. I boiled with water and filtered, & immediately got reduction by Trommer's test. I then, as recommended by Bernard for liver decoction, threw down the animal matters present by acetate of lead, neutralised the fluid, and again filtered — and on again applying the test there was instant and most characteristic reaction — On Dec 18th (four days afterwards) Sugar could no longer be shown to be present —

(1) Lib. V. 59. (1494)

in the filtered Solution.

I have mentioned these cases more particularly because I find no record of similar observations. Nor am I aware of the fact having been noticed. I find however the following in the works of Frank. "De curandis hominum morbis". is it not a confirmation of my Statement? "Nota est phthisicorum plurimorum Sub fine morbi lethalis insignis et ad Nauseam usque molesta Dulcedo Sputorum." (1)

Reynoso we have said was the first to announce that he had found Sugar in the urine of persons labouring under impediments to respiration. — He says "I have determined its presence in the urine of the tuberculous in quantity proportioned to the intensity of the inflammatory symptoms, I have found it also in pleurisy, Chronic bronchitis, asthma, hysteria & epilepsy." He gives as his mode of testing that which we have specified above, namely the treatment by Acetate of Lead with filtration, and concentration. In answer to M Reynoso's invitation to the Profession to put the accuracy

(1) Pathological Transactions. V. 1854.

of his allegation to the test, M. Michea denied that in such conditions Sugar could be ascertained to be present by the ordinary tests, whereupon the former undertook to prove to M. Micheas satisfaction, the real existence of Glucose in the states of the system above specified. And he seems perfectly to have succeeded in his demonstration, for in the Comptes Rendus for 1853. (page 230) we have a joint communication by these two Gentlemen, showing the invariable occurrence of Sugar in the circumstances as stated by M. Reynoso. It is only within this comparatively short period that Sugar has come to be acknowledged as an ordinary ingredient of the urine in such cases. Several Chemists and Physiologists have however added their experience, and as a model of the means which should be used to investigate the subject. I cannot do better than subjoin a few sentences from a paper by Dr Garrod on the presence of Sugar in the urine in a case of Acute Bronchitis. (1)

"It occurred to me," he says. "that the ca

(1) Note. There is an important paper by Dr Hassall (Lancet. Jan. 1853) on the fallacies which are apt to complicate Trommer's test, and especially the influence of the normal constituents in this respect. The summary of which however it would be tedious to introduce.

would be a good one to test the accuracy of the theory which has been propounded viz. that Sugar in the Urine is dependent on the imperfect performance of the function of respiration."

"Examination of Urine. Abundant urate deposit of pink colour, cleared by a temperature of 100° Fahr. when heated above 200° again became cloudy from precipitation of albumen, not redissolved by nitric acid. — precipitate occupied about one third of the height of fluid in the tube. Sp. Gr. at 60° 1021. and full acid reaction."

"As much albumen and urates were present it was useless to depend on Moore's test with potash, or on the copper test without previously removing most of such matters.(1) I therefore added to the Urine a solution of the tris-acetate of lead in slight excess, and after filtration treated the clear fluid with powdered bicarbonate of Soda & refiltered. The resulting solution was clear and colourless, and was tested thus:—

"A portion boiled for a minute or so with strong solution of hydrate of potash gave an orange yellow coloured fluid equal to that produced by one grain of Glucose in an ounce of water

when treated in the same way."

"A second portion was treated with the solution of the tartrate of copper dissolved in an excess of potash; decolouration of the fluid and a very distinct precipitate of red oxide of copper took place on boiling for a few seconds" &c

Trommer's test was applied with equal success.

"Another portion $\frac{30}{100}$ cubic inch was placed in a tube with a piece of German Yeast – it was found to yield $\frac{2}{100}$ cubic inch of Carbonic Acid Gas."

Even before the addition of the lead Yeast discovered the presence of Sugar. Dr Garrod recommends that the urine should not be concentrated, since on evaporating in this instance to one fifth he got no indication of Sugar.

I may just remark that Dr Garrod falls into one error in reference to the nature of the Sugar in this instance, since he assigns as his reason for anticipating to find Sugar in the urine, the fact that his patient had during the night taken some arrow root and remarks also that Sugar appears in the urine from deficient action of the respiratory function. "whereby the Sugar normally formed from Starch

or <u>Amylaceous matters</u>, is incapable of being further changed and broken up into Carbonic Acid, Water &c.
Now we have shown that alimentary Sugar is never found in the circulation in normal conditions, and never reaches the pulmonary organs for the purpose of resolution, and that alimentary Sugar can never be prevented from resolution by any cause operating in the Lungs. In short the Sugar of excretion in all cases of impeded respiration is true hepatic Sugar, since it is this variety of Sugar alone which is subjected to catalysis in the Lungs, and therefore is alone liable to be affected when the organs of respiration is withheld. Even apart from merely theoretical grounds we might from the remarkable rapidity with which such Sugar disappears from the fluid in which it is held in Solution, infer it to be hepatic Sugar - three or four days at most suffice for its total disappearance, while I have kept diabetic urine for six months, & still Sugar was abundant.

From Bernard's researches we know that even during intrauterine existence, the liver secretes Sugar. At what period this glico genesis

(1) Comptes Rendus 1850. II. 659

× There is no difficulty whatever in satisfying ourselves of the real presence of sugar in the fœtal fluids. Since I have got at once a characteristic reduction by Trommer's test without any preparation,

(2) Comptes Rendus 1850. II. 629.

commences it is impossible to say - in the human foetus Bernard has reason to think that it begins about the fifth or sixth month of pregnancy. In the lower animals of course it varies with the period of uterogestation. The amount of sugar in the liver increases up to the period of birth.

Bernard has also shown that sugar is present in the fluids of the amnios and allantois during a considerable period of pregnancy.(1) The fluids of the cow, the sheep, and the sow were those ~~animals~~ on which his experiments were conducted.* It is a remarkable fact that in the last weeks of intrauterine life the sugar disappears.— The causes which lead to this it might be interesting to investigate.— M. Stas confirms Bernard.(2)

Now what gives very great weight to M. Reynoso's statement is the observation also made by Bernard that along with the formation of sugar by the foetal liver we have the simultaneous appearance of it in the urine of the foetus. and this is just what we should expect from the circumstances in which the foetus is situated if the proposition made by Reynoso be a true one.

It seemed to me in following out the consideration of M. Reynoso's fact. that if the real cause of the presence of Sugar in the urine were the deficiency of the supply of Oxygen, and Knowing as I did from Bernard's experiments that Sugar even in the circulation underwent catalytic change, it seemed to me that it was not Sugar so much as the products of Catalysis we should expect to find excreted by the kidneys. The detection of minute quantities of Sugar was never attempted till within a very recent period, and in fact neither Bernard's researches nor Reynoso's deduction were known to Lehmann when he wrote his treatise on Physiological Chemistry. But I have been enabled to confirm my suggestion by reference to this most accurate work. To have attempted the detection of Lactates would have entailed much trouble, without probably leading to any very definite result. but if we go on the authority of Lehmann, and a higher authority is not to be found, I think the proposition can be established. and I therefore quote the two following sentences, which must be read in connection. "Numerous investigations," he says, "have led me to the following results

(1) Op. cit. I. 46.

(2) Op. cit. I. 100.

When the Respiratory process is in any way disturbed we most frequently observe a most copious excretion of Oxalate of Lime." (1) and "there is an almost universal occurrence of lactic Acid in urine containing Oxalate of Lime so that by a microscopic examination of a specimen of urine a conclusion may often be drawn regarding the presence or absence of lactic Acid." (2)

Prout too remarks in reference to unhealthy urine that it often contains the saccharine principle in imperfectly developed forms, and says that to such urine the lactic Acid imparts the smell of Sour milk. He does not specify the conditions in which he met with this, sufficiently to enable us to draw conclusions from his statement. We may however say, and in all likelyhood future investigation will bear out the statement that lactic Acid of Catalysis as well as Sugar itself exists in the urine when oxidation of the system through the respiratory function of the lungs fails of its due accomplishment.

Bernard while he admits the fact, denies that the phenomena in question arise from the causes assigned by Raynaud, & ascribes

them solely to the exaggeration of the glucogenic function of the Liver resulting from the irritation of the nervous supply of the pulmonary organs and consequent sympathy. The Sugar of the liver like every other product of the Animal economy presupposes as a condition of its existence a certain influence of the nervous System, & when we reflect on the complex structure of the gland. the peculiarities of its vascular relations, and the variety of Stimuli which call its functions into Action it will appear that the laws which regulate its secretion, and its nervous affinities, are more complicated than might at first sight be anticipated. Bernard illustrates his views of the nervous affections of the Liver by taking the visible instance of the Salivary glands — If, he says, we cut the lingual nerve and irritate the peripheral extremity no result takes place, but if we irritate the central, there is an instant flow of Saliva from the duct of the Gland. as if some Sapid substance previous to section had been placed on the tongue, Thus showing that there had been through the nervous centre, a reaction by the Sympathetic on the vessels of the organ and on its peculiar

secreting tissue – What the lingual nerve is to the tongue the vagus is to the liver – following Bernard – while the great sympathetic presides over and regulates the formation of Sugar and its amount. It follows then that the origin of the vagus is the nervous centre from which emanates the power of the liver to produce Sugar.

All physiologists agree in considering the Medulla oblongata as the centre & regulator of the movements of respiration. Flourens moreover has found that there is a very limited portion of the bulb which is the true seat of respiration and this in the rabbit corresponds to the origin of the eighth pair of nerves.

Bernards reply to Reynoso's statements is as follows "Recently, he says, some have recently thought to bring the Chemical theory of incomplete combustion in the Lungs to bear on this question, by announcing that whatever tends to cause diminution of respiration by asphyxiating the animal may cause Sugar to appear in its urine. This however does not prove that the passage of Sugar into the urine depends on

the incomplete combustion of it in the lungs for in short one of the most certain and most powerful means of lessening respiratory energy, is to cut the two Vagi Nerves as they pass through the neck, and never in such a case, adds Bernard, have I seen sugar appear in the urine."

Reynoso had experimented on rabbits by way of counter experiments to those of Bernard. Bernard can render rabbits diabetic very rapidly by causing lesion of the above specified portion of the nervous tissue. He can in twenty minutes show the presence of sugar in the urine of the subject of his operation. And he can regulate its amount by the depth or shallowness of his puncture. Of the facts there can be no doubt. Bernard explains them by supposing an increase of hepatic sugar, and its accumulation in the system in such quantity, as to overbalance the powers which combine to destroy it. Reynoso maintains that he can produce the same results by simple compression of the trachea in the same animals.

The

The question at issue is simply this. Is hepatic glucogenesis the only means which can bring about the presence of Sugar in the urine. or are the chemical causes operating in this case sufficient to account for the phenomenon. The latter is the view of the case which I am disposed to take. Since we have no evidence of the increase in the system of liver Sugar, Nor do we know with sufficient accuracy under what stimuli this takes place. — We proceed therefore to inquire how far Bernard's reply is satisfactory, taking the facts as he himself has stated them.

Bernard founds his objection on the well known law that irritation of a nerve causes increased of function in the part to which it is distributed, but what is remarkable he seems to forget the latter part of the proposition. Namely that destruction of a nerve puts a stop to the processes which go on in the same organ, when he argues. That because after Section of the two Vagi nerves we find no sugar in the urine and ~~that therefore~~ since respiratory energy is most powerfully lessened in such a case Reynoso's

doctrine

does not hold. And yet of this fact he has himself afforded us the most perfect illustration when he remarks in reference to wounding the Rachidian bulb "if my lesion was too severe no sugar whatever was formed." As to his remark that he had never seen sugar appear in the urine after division of the Vagi nerves in their course through the neck we need do no more than place alongside it this statement written by Bernard himself "If we cut the Vagus nerve the production of Sugar by the Liver immediately ceases, and it instantly begins to disappear from the economy, and if we have previously rendered the animal diabetic the sugar disappears from its urine." Bernard then I apprehend has no ground to go on in raising the above objection to Reynoso. But when we come to the matter from a different point of view altogether. I mean to the phenomena manifested in the rabbits employed by Bernard in the establishment of his opinion, I think we have most conclusive evidence that sugar does not exist in the urine in disordered states of the respiration from an

additional amount being added to the circulation.

What phenomena then do the rabbits operated on present, after having the floor of the fourth ventricle injured by the manipulation? Bernard says: "the time during which the subject of operation remains diabetic is generally forty-eight hours, and during this time the animals are extremely restless, the respiratory movements are hurried, the arterial blood presents almost a venous tint, the quantity of carbonic acid being augmented. — The temperature of the body is nevertheless diminished several degrees.

It is perfectly obvious from reading the above that whether this determined the existence of sugar in the urine or not. The respiration was extremely embarrassed — and that the normal chemical change did not take place, we infer from the allusion to the venous tint of the arterial blood — Bernard holds that the vagus is the afferent nerve from the liver, and that the sympathetic is the regulator of its secretion through its controlling influence on the hepatic capillary circulation — but in the details of the experiments we have no proof of hepatic congestion.

(1) Note. Indeed I am not sure but that I have somewhere read that the shock of some severe lesion such as amputation will cause in an animal the stoppage of Glucogenesis. Just as John Reid remarks of the Gastric secretion.

I question how far Bernard's analogy between the lingual + vagus nerve holds. The first being a nerve of Special Sense, and of limited distribution, while the second of it really presides over hepatic secretion, must regulate a very great number of other secretions as well, all of which are equally liable to be affected with the hepatic, when such a cause as that above specified comes into operation. I think that John Reid's experiments in regard to the influence exercised in the gastric secretion by section of the eighth pair of nerves, are equally applicable to the hepatic secretion, and that Bernard is therefore probably wrong in attributing to the integrity of the Vagus the Glucogenic function of the liver. (5) But as we said before these questions are too complex to be advantageously discussed and it appears to me that all the above phenomena are much more satisfactorily accounted for by keeping in view that the Vagus is an efferent as well as an afferent nerve, which Bernard seems to forget, + by attributing especially to the recurrent nerve + its injury the respiratory difficulties which we have above enumerated. —

The

The last fact mentioned by Bernard — the accompanying diminution of temperature — appears altogether at variance with our notions of the purposes served by hepatic Glucose in the economy. If Glucose be truly formed for respiration and for the support of animal heat — if the increase of this sugar in the system be the cause of elevation of temperature — if the special stimulus of digestion call forth the glucogenic function of the liver, and if this be accompanied by the diffusion of warmth throughout the Body. How comes it about that when the same sugar is thrown into the circulation in great quantity in the present case, the temperature of the Body falls? There is a manifest inconsistency. If we grant Bernard that respiratory impediments have no effect upon the catalysis of hepatic Glucose, the animal heat ought still to be maintained at its highest standard, altho' the system have sugar over and above, to spare & excrete, since if there be no obstacle to catalysis all the conditions favouring the production of heat are present in their highest degree of perfection. — The fall of temperature we must

look upon as arising from a want of respiratory material. Sugar is but a foreign body in the system. Sugar as Sugar is subservient to no end - it is to the catalytic changes of Sugar that the importance of Sugar in the economy is due. Sugar which does not undergo the catalytic transformation is inevitably destined to excretion, and this we take to be the nature of the Sugar in the present instance.

I may just add that it takes but a slight degree of perturbation to upset the vital functions in the rabbit, and these animals are therefore ill suited to demonstrate the effects of nervous lesions. John Reid never laid any stress on arguments drawn from observations made on rabbits. The fact indeed of the ease with which rabbits could be rendered diabetic seems to have been known long ago. I find in the article on diabetes published many years ago, in the Cyclopaedia of practical Medicine the statement that Bernei of Halle, had shown that if rabbits were fed for some time on flour, Sugar was readily to be detected in their urine.

[1] Comptes Rendus. ~~XXXIII~~. 606.

Reynoso ascribes to certain Chemical substances the power of producing Sugar in the urine "by preserving a part of the blood from the action of oxygen." (1) He more particularly specifies anaesthetic agents such as ether + chloroform, and tonics such as arsenic and quinine. Bernard as in the former case maintains that the Sugar presents itself merely in consequence of its increase in the circulation from augmented glucogenesis in the liver consequent on irritation of the vagus nerve. We consider that the sole cause of its increase in the circulation, is want of catalysis. Now have ether and chloroform the property of stopping catalytic action? - that they have is a fact well known to chemists. When therefore hepatic sugar and the vapour of these bodies meet in the pulmonary capillaries are we to expect that the laws of Chemistry are to be broken? certainly not - it follows as a matter of necessity that the Sugar can not undergo catalysis, & must therefore present itself in the excretions. We have even a more interesting illustration of our statement that Chemical agents act within the economy so as to prevent

catalysis with equal certainty as in the laboratory, in the physiological effects on the Body of arsenic quinine &c. taken as medicinal agents. Reynoso by a series of investigations on dogs satisfied himself that under the continued use of these substances sugar appeared in the urine. That arsenic instantly stops fermentation is a fact noted in every work on Chemistry - how it acts we shall consider immediately. I am not aware of any record which shows that arsenic acts on man as Reynoso showed it to act on the dog and as I have had an opportunity of proving that it does, I note the following particulars of the case. A Man (Lemm) was admitted to Dr Gairdner's ward suffering from a skin disease. Some time afterwards I happened to visit the ward, and Dr Gairdner called attention to the state of the patient as exhibiting well marked symptoms of the physiological effects of arsenic on the constitution - suffusion of the eyes, headache &c. The man had for some days previously been taking half a drachm of Fowler's solution three times a day. It struck me that this would be a favourable opportunity for putting

the accuracy of Reynoso's statement to the test. and on examining the urine taken directly from the patient, Sugar proved to be present in considerable abundance. that is to say. in quantity sufficient at once to reduce the oxide of Copper, without any preparation of the urine.

Now then do such substances as Arsenic and Quinine act to produce their therapeutic effects upon the Economy? and is the following theory of their mode of action admissible? We have positive demonstration as above that arsenic prevents Catalysis in the system. What other properties in relation to the tissues does it possess? The fact of the Hungarian peasantry rendering their bodies plump and fair by the use of this drug is sufficiently attested. but as an instance more to the point I may mention the following which came under my observation in our hospital. but as it appeared occurred before I took an interest in it, or was aware of the sugar-eliminating property of arsenic, I cannot definitely say Sugar existed in the urine in this case, although

(1) Note. I understand that last summer this patient again returned & amputation was thought to be had recourse to, in consequence of the ulcer having broken out anew & threatening to prove fatal from hemorrhage. This however does not invalidate the fact as I have stated it.

I have no doubt that it did. In autumn 1858 there was under Mr. Syme's care a woman whose forearm had been amputated a few months before, for a circular ulcer deemed incurable. She had now returned to the infirmary with an ulcer quite identical in character with the first, surrounding the entire arm a few inches above the stump. Mr Syme despaired of cure even by a second amputation, which might have terminated fatally from the cachectic state of the patient. At this period however an East Indian practitioner happened to visit the hospital, and Mr Syme asked his opinion of the case, & I remember well that he said "I have seen this often in India, give the woman ten drops of Fowlers solution three times a day and you will cure her." The emaciated woman from that time gained flesh. The ulcer healed, and she left the house in excellent health, and ruddy in complexion. (s)

I may remark that the arsenic had on several occasions to be intermitted from the production of its physiological effects.

From the above relation it is clear that

(1) ~~Annales de chimie 1853~~ Journal de Pharmacie, 183

Arsenic is a preserver of the tissues. Do we know the same of quinine? I do not know of any direct evidence, but if we substitute for quinine a substance extremely analogous - Caffeine - we can bring a very weighty authority to bear on the question. Lehmann has published (1) an elaborate series of investigations on the physiological effects of caffeine on the human body, and the result of these goes to show that caffeine is a preserver of the tissues - that is prevents to a certain extent the wasting of the tissues when they are called into play. Now if the debris of the textures be the ferment in the blood which determines catalysis it is obvious that if comparatively little debris be formed, or at least if the quantity of debris furnished to the blood be insufficient for complete catalysis, such catalyses as those of Sugar into lactic Acid must be proportionally retarded, and the quantity of Sugar excreted will be proportioned to the retardation. We have formerly seen how under the augmentation of the normal amount of Glucose in the circulation. the

balance

of production and destruction was lost - the quantity of Sugar exceeding the equivalent of ferment. In the present instance although the Sugar does not increase, the diminution of the ferment brings about exactly the same result as in the former case.

In the case of this woman treated with arsenic, in the case of the Hungarian peasantry and in general when Arseni is given to produce its so called tonic effects, we consider that it acts by enabling the tissues to resist the slow combustion which is constantly going on, just in the same manner as it enables the Sugar to resist its further resolution. The consequence of this is that as the nutritive processes go on as before, instead of the nutritive matter having to expend itself in supplying the waste of the tissues, it is added to their substance. and thus they not only maintain their integrity but increase in vigour besides.

The utility of the Sangore arsenical pill of India as a specific against the typhoid condition which is apt to supervene after the bites of poisonous serpents is recognised equally by

* That is. the normal ferment with the poison superadded.

natives & Europeans, while of the wonderful effects of quinine as a specific against malarious influences Dr Bryson's experience on the African coast among boats crews on river service it gives testimony as unequivocal as astonishing. The mode of action of such remedies under such circumstances we take to be this - That they prevent the tainted ferment from multiplying itself in the circulation, and secondarily counteract the mordant effects of the imbibed poisons on the tissues themselves. in both cases precluding the formation of morbid material the existence of which according to the speciality of the case would cause marsh fever on the one hand or typhoid on the other.

If the primary contact of the morbid ferment * with the fermentescible body takes place in the lungs & if we have positive evidence that one fermentation which is constantly & normally going on there is hindered by such agents as arsenic & quinine, it is just what we should expect, that when the system is impregnated with such substances the imbibed poison should be unable to multiply itself beyond a certain point & that the liability to be attacked, and the severity of the attack should be proportioned to the degree of saturation of the system, with the antiseptic. ——

(1) Brit. & Foreign. Review. Jan. 1855. p. 274

(2) Müller. Archiv. 1864. (41

It is certainly to be desired that the means of ascertaining the actual presence of small quantities of Grape Sugar, were more certain than those which we at present possess. Disputes are constantly arising as to whether certain substances which answer Bommer's test are not really to be regarded as the reducing agents in impeded respiration. We have seen that Mr Paget suggests leucin in the case of the cerebro-spinal fluid - Valentiner has discovered leucin in the urine of an epileptic patient.(1) Frerichs considers that the reaction is owing (sometimes, at any rate) to the presence of allantoin, as this substance was found in the urine of two dogs the action of whose lungs was artificially impeded by injecting oil into the bronchi, and since allantoin has the power of causing the precipitation of the oxide of copper. No allantoin however could be found in human urine in several individuals suffering from various disorders of the respiratory functions (2) If our suggestion however regarding the presence of lactic acid be taken into account, I think this may afford us the means of ascertaining the reality

(1) See Med. Chir. Review. Jan. 1853.

of the presence of Glucose.

There is an allied condition in which from failure in the vital processes, Sugar is stated to be present in the urine. Dechambre refers to his researches into the condition of respiratory organs of the aged, described in the Arch. Générales. 1835. These exhibited lateral depression of the thorax, projection of Sternum forwards, rigidity of the costo-vertebral articulations, ossification of the cartilages, and a diseased condition of the pulmonary parenchyma, in which the cell-walls were found thinned or ruptured, and the capillary vessels obliterated. The defective haematosis which results from these physical changes should favour the production of Glucosuria, and experiments performed upon the urine of a considerable number of the aged women of the Salpetrière have so constantly exhibited it, that M. Dechambre considers himself justified in asserting that Sugar exists habitually in the urine of the aged. Although it is possible that its presence may be explained on some other hypothesis. (1)

The very interesting inquiry as to the origin

of milk Sugar Circumstances have prevented me from entering on. The question - under what conditions does lactine find its way into the urine -, admits readily of solution by any one who has the opportunity of making the investigation. It is not to be wondered at that we should find the milk Sugar eliminate itself by the Kidney, when it exists in a superabundance in the circulation, either when repelled from the mamma by Morbid influence, or as a result of too copious secretion, especially since we know that it is a substance little liable to become changed in the Economy.

I may just mention two cases which have come under my notice. The first - a woman named Henderson - was admitted to the clinical ward. Suffering from rheumatism of the Scalp. She had been suckling a child born five months before, and after her admission the breasts became distended and painful to such an extent that it was necessary to withdraw the milk in consequence of the irritation. On taking the Sp. Gr. the clerk finding it to be 1035 tested for Sugar and recognised

[1] ~~Du diabète sucré. Paris. 1845.~~ Op. cit. 289. I.

its presence by Moore's and Trommer's tests. The day following, the urine passed in the morning still presented some traces, but in the evening the Sp. gr. had sunk to 1020 and it was impossible any longer to detect Sugar. Carrying out the view suggested by the above case, in the only private case in which I ever had the opportunity of making the examination, I at once determined the presence of Sugar in the urine on the third day after delivery the breasts being swollen, and slight feverish symptoms present. Schmann records an observation exactly similar - he says. "I once met with Sugar in the urine of a puerperal woman in whom on the fifth day after delivery the secretion of milk was suddenly suspended. I was led to the discovery by observing the formation of Yeast cells in it. The Sugar only continued in the urine of this woman for four days." (') Although these three cases are scarcely sufficient to establish the principle, I have no hesitation in considering it of almost universal application in such circumstances as I have detailed. ——

(1) Du diabète sucré. Paris. 1845

The Pathology of Diabetes Mellitus.

To give any history of this disease or to enter into any detail of the many theories which have been propounded concerning it, would be foreign to my purpose. It will suffice that I point out briefly the characteristics of the complaint, and then attempt to demonstrate on what the various symptoms depend, and what indications are to be pursued for their alleviation consistent with the advance of pathology & chemistry. In carrying out this plan I must of course touch upon the theories which seem to me most worthy of consideration, and endeavour as far as possible to make a just adjudgement of their merits. and then state the view which to me appears most satisfactory.

M. Bouchardat defines Diabetes thus (1)

"Diabetes mellitus is a disease characterised by by a very abundant excretion of Urine, containing always a saccharine crystallisable matter analogous to starch sugar, accompanied by a notable

increase of appetite, by unquenchable thirst, and progressive emaciation.

The predisposing causes and the phenomena which mark the accession of this malady are by no means evident. It is met with from early youth to old age, and seems to affect both sexes alike, while season & climate apparently exercise but little influence on its production. England is said by French authors to be the country most subject to diabetes probably merely on account of a statement by R. Willis that a friend of his had at one time thirty three cases under his care. Another writer in the Dict. des Sciences Med. for 1812 says that more theses have been written in Edinburgh on this disease than in any other city in the world, and he fancies this to be owing to its extreme prevalence here. — Sir Geo. Lefevre has met with no record of such a complaint in any Russian register. while Sir James Wylie found no example in two millions of Russian soldiers who had come under his inspection. I do not know what amount of credit we are to give to these assertions, as proving the

non-existence of this disease in Russia, since going southward we can trace it in Germany France, Italy, Egypt. East Indies, and Ceylon, and we find it to be present in much the same proportion in all.

As to occasional cause - the enumeration of these by authorities is endless, almost every individual case indeed adding another to the list. This we can hardly wonder at when we consider the insidious invasion of the complaint — We have no data to go on to determine whether diabetes supervenes gradually or suddenly. The patient is often troubled with indigestion during the first stages - with general uneasiness. with dryness in the throat, and sometimes with headache. But as a general Rule he experiences no local pain and his attention may be called to his state by mere accident, as in an instance cited by Rollo, where a voracious appetite alone led him to detect diabetes in the individual, or that mentioned by Watson in which the patients attention was drawn to his urine by the swarms of wasps & bees which its sweetness had attracted.

& The Amount of the urinary excretion too can hardly at first give any indication, for Frank, Watt, Prout, Copland & have given instances in which Sugar was present in large quantity, altho the urine did not exceed in amount that passed in a state of health. The question as to whether the immense volume of water sometimes excreted, exceeds much that taken by the mouth is still debated. I should be inclined to consider that it did not. —

The phenomena of a characteristic case of Diabetes are very well summed up in M. Contours definition given above. and when we inquire whether these depend on organic lesion, pathology answers decidedly that they do not. What are the peculiar anatomical lesions met with in diabetes? The Kidneys are usually hypertrophied, flaccid, pale, and soft. at other times congested. The Stomach and intestines are frequently dilated. The Lungs are generally extensively diseased and it is by phthisis that diabetic patients are usually carried off. but Watson has seen in

several post mortem examinations not a trace of tubercle. Some French Physicians since Bernard published his experiments on nervous irritation, ~~have~~ since profess to have detected dark spots on the floor of the fourth ventricle. and others have recognised an increase in volume of the great Sympathetic. Leaving these last assertions out of the question, it is clear that none of the other morbid appearances are sufficient to account for the symptoms which manifest themselves, the dilatation of the stomach, and the hypertrophy of the kidney, being but the result of the stress laid on them by the increase of the ingesta.

We therefore look to Chemistry, and we must endeavour to find out, whether the non fulfilment or perversion of Chemical Change in the Economy can give us a satisfactory explanation. We proceed therefore to inquire what Chemical theories of Diabetes have been advanced, which are at present regarded as standard, and as the basis of Rational treatment. But before proceeding to the

more

modern authorities. It would be unjust not again to mention the elegant treatises of Dobson and Rollo which although written in the last century are almost worthy of the present day.

The first theory we take up is that of M. Bouchardat. He holds that starchy matters are alone converted into sugar, and that the agent of the transformation is a principle which exists in the Economy of Diabetes which would have on starch an action similar to that of diastase. He has always found the quantity of sugar in the urine in direct relation to the quantity of bread &c consumed by the patient, and says that it would disappear were the patient altogether to abstain from such food. To explain whence comes the increased amount of diastase in diabetes, the author has recourse to another and somewhat problematical hypothesis. Namely that the Malady shows itself first by a sudden interruption to the acid secretion of the skin in consequence of which the glands of the intestine ordinarily secreting an alkaline fluid now throw out an acid one, and observation shows him that

"Wherever

(1) On diseases of the stomach &c 1840. 31.

(2) Treatise on food and diet. p. 500.

(3) Comptes Rendus. 1844 & 1845.

organic Acids exist in large proportion, we are sure to meet with this modification of albumen which acts by transforming Starch into Sugar, and of this we have an instance in the ripening of fruits as shown by Thenry &c." It was hardly worth while to mention this theory since it merely attempts to show whence may possibly be derived the Sugar of diabetes. and even in this it perfectly fails. We may object to two of the fundamental propositions by the two quotations as under. Prout says." I have seen many cases of confirmed diabetes in which this symptom (dryness of Skin) was wanting and in which perspiration and even profuse sweating was induced by slight exercise." (1)
Pereira says of diabetic urine." I have never seen this secretion lose its saccharine condition by even the most rigorous adoption of animal diet." (2) Besides this transformation of starch into Sugar is not a phenomenon peculiar to diabetes, but is part of the normal role of amylaceous substances in the alimentary canal as we have before seen.

Mialhe's theory of diabetes (3) is the one

(1) Guide du Médecin prat. III. p. 562. 1853.

which has gained most credit on the Continent as the following remarks on it by M. Vallejx testify.

" Perhaps it may be said that it is not supported by a sufficient amount of facts. but I am altogether inclined to believe that new facts well observed will go to confirm the above, and if, as we can hardly suppose it will, the theory of M. Mialhe be not shaken by these, it will remain the most satisfactory and the most complete." (')

Mialhe begins where M. Bouchardats theory ends by asking why do those troubled with diabetes give off by the urine, the Sugar absorbed from the surface of the digestive passages although no such occurrence takes place in the healthy constitution.

The Blood, says Mialhe, normally is very alkaline now if we put Starch or Sugar in Contact with an alkaline fluid, this sugar undergoes a change of condition, as may be seen by its acquiring a power to deoxidise. Eg. if the attempt be made to procure a Reduction of the oxide of copper by means of Sugar in an acid Solution it will fail, but if again the same experiment be repeated in an alkaline Solution the desired result will take place. What is the exact

Vide

of Sugar in the circulation, says M. Mialhe, we do not know but it is clear that if the blood be not sufficiently alkaline this cannot be accomplished. Since the change of Glucose into the deoxidising body cannot take place. But he says it will be objected that sometimes in diabetes the blood is strongly alkaline, either from the disease not having reached its height or from the effects of treatment - but in such a case let us suppose. taking atom for atom. that the quantity of Sugar is to the alkali as 4 to 2 it is evident that the half of the Sugar absorbed will not be changed and will therefore pass into the urine. Mialhe agrees with Bouchardat in considering the suppression of the acid secretion of the skin the cause of the blood being deficient in alkalinity. He has however cited an interesting case in which diabetes was excited by the continued use for several months of acid drinks as refrigerants.

This brings us down to the period of Bernard's discovery and instead of raising objection as we might do to the above theory it will be more advantageous at once to offer

such a theory as seems to me borne out by the recent advances of physiology and chemistry. Several of the more modern speculations as to the pathology of Diabetes are incorporated in what follows — I may mention those of Bernard, Gibb, and Bence Jones. They are introduced for the most part as furnishing facts for the elucidation of the theory proposed. I trust that I shall not draw a conclusion unless I shall previously have brought forward facts, of weight sufficient to give support to the assertions which I may find it necessary to make.

Theory of Diabetes.

A theory necessarily presupposes a certain number of facts or hypotheses as the basis on which deductions are founded — and the more complete the chain of facts and the greater the plausibility of the hypotheses so much the more probability is there of the theory being a true one.

Before proceeding to farther detail

it will be necessary to show the true origin of of the excreted Sugar in diabetes. Since so many conflicting Statements have been made on the subject.

Bernard's theory of diabetes we have sufficently discussed in our inquiry into the relation subsisting between the integrity of the medulla oblongata, and the production of liver sugar. Bernard maintains that the Sugar of diabetes ~~is true~~ is true hepatic Sugar, and that its increase in the system in consequence of some nervous irritation constitute diabetes - This is completely disproved by pathological evidence, and by the decreased temperature of the diabetic. We know moreover that the amount of carbonic acid exhaled is notably diminished in this disease, which shows that the chemical processes for the production of animal heat are deficient in activity: and that less pabulum is consumed than in a state of health. We have no reason whatever to conclude that more Sugar is manufactured in the economy of the diabetic, than in that of the healthy individual. but this we are

Juice of. That a considerable portion of the Sugar of catalysis passes off by the faeces as Bernard has recently found, altho' the fact was perfectly known to M'Gregor in 1837, the system even at this early stage seeming to regard Sugar as excrementitious, and confirming our statement that Sugar is absorbed from the primae viae only after being changed to lactic Acid. But the greater part of alimentary Sugar is unquestionably admitted into the circulation in a case of confirmed diabetes, as is proved by the disappearance of a considerable proportion of the Sugar from the urine when the patient is restricted to animal diet alone. We have thus the two varieties of Sugar existing at the same time in the Blood. The cause which operates to prevent the further resolution of these two classes of Sugar must be one applicable to hepatic as well as to alimentary Glucose. How do we know this? Simply from the fact which we may just repeat as it is stated by Pereira. namely. "I have never seen diabetic urine lose altogether its saccharine condition by even the most rigorous adoption of animal diet."

(1) Medical Society London. Jan 27. 1855. reprinted in Lancet. Mar 9th.

Our deduction therefore is that the Sugar of diabetes has two distinct Sources of derivation.

In connexion with the question of the origin of diabetic Sugar, I may advert to a somewhat startling doctrine which I perceive Dr Gibb has propounded a few days ago.(1) namely. that diabetes is essentially characterised by paralysis of the Sugar forming function of the Liver. He founds his assertion on the supposed fact that in the liver of diabetic patients Sugar is never found after death. and his theory is that the special function of the Liver is paralysed by more gastric Sugar being sent to that organ than it can assimilate. In diabetes Dr Gibb contends that the liver cannot form more Sugar than in ordinary circumstances. For, says he, the the saccharine function is abnormally active only in fatty liver - which he assumes that he has proved - while in diabetes the liver is quite destitute of fat. Not to enter on the latter portion of Dr Gibbs statement which we have sufficiently discussed, and I think disproved, in a previous chapter, we may remark that there is not even probability much less certainty

in the proposition that the liver ceases to form sugar. We know of no means by which in the intestine nitrogenous matters are convertible into sugar, and we know that much sugar exists in the excretion altho' animal food have constituted the sole diet of the patient. If the fermentescibility of sugar constitute its value to the economy, and if non-fulfilment of Catalysis constitute diabetes, and if both varieties be equally subject to the operation of the cause which hinders Catalysis - taking into account the comparative fermentescibility of hepatic and alimentary sugar. it is obvious that were the supply of the former to be stopped, the person would die ~~as soon as if~~ very speedily from the failure of a necessary for existence since if in diabetes the eminently fermentescible hepatic sugar can only in part undergo Catalysis no part of the simple alimentary sugar, which in point of fermentescibility is to the hepatic sugar as 1 to 5, can undergo the requisite change. I consider therefore that in diabetes almost the sole source of the demonstrable animal heat is hepatic Glucose.

In reference to Dr Gibbs statement

that he has been unable to detect Sugar in the liver of diabetic patients after death, I hold it as of no importance whatever as constituting a proof that the liver does not form Sugar in diabetes. When a patient dies from diabetes the Sugar almost invariably disappears from the urine some days before death.— A spontaneous cure has been effected. The pabulum for the formation of hepatic Sugar has ceased — the patient dies of starvation.— Necessarily the Sugar has disappeared from the hepatic tissue also. in many other chronic diseases. when the patient dies of exhaustion not a trace of Sugar is to be found in the liver. When death was occasioned in dogs by starvation Bernard found that the liver ceased to perform its Glucogenic function for about three days before death ~~took~~ was expected to take place. From all this I consider Dr Gibbs doctrine to be quite untenable.

We may again repeat the proposition that Glucose must. to be subservient to the wants of the Economy. submit to a certain rôle in the circulation. This we have shown to be its conversion into lactates. and the further transformations

of these into Carbonates or fats according to the circumstances of the case. Glucose if not so metamorphosed is a foreign body, and as such destined to excretion.

In diabetes a certain quantity of Glucose does not submit to catalysis, and therefore fails to perform its function, as is evinced by decrease of temperature in the diabetic and by the constant craving of his body for respiratory food, which is displayed by his voracity and by his system still remaining unsatisfied although Animal food have been supplied in large quantity. In diabetes therefore the Sugar must be excreted.

We assume that Sugar exists as Sugar in the blood and urine of diabetic patients, as the result of its not having undergone the lactic Catalysis, and that therefore the agency which ~~produces~~ prevents this catalysis constitutes the true source of diabetes. What circumstances then may conspire to produce diabetes by permanently interrupting the lactic Catalysis?

We found in a previous discussion of this question that the most certain means of checking this catalysis, was by the acid formed

(1) Handbook 379

ceasing to be counterbalanced by the amount of alkali present. I quote from Dr Gregory. (1)
"The liquid soon becomes acid from the conversion of sugar into lactic acid, but when the amount of free acid reaches a certain point the fermentation is thereby checked." and that permanently unless we shall have added an alkali to neutralise this acid. Applying this statement to the catalysis as it takes place within the body, ~~we should call diabetes~~ and if we prove it to be applicable we may specify diabetes as a condition of the economy during the whole persistence of which there is the constant presence of an acid — what that acid is remains to be shown - which operates equally on alimentary and hepatic sugar so as to retard or prevent their catalysis, & hence inducing every one of the concomitant symptoms, with their morbid tendencies.

It will be said that this just the theory of Mialhe — it is not. Mialhe imagined that the suppressed acid of the skin acted on alimentary sugar — of the existence of hepatic sugar he was of course ignorant & therefore considered with Bouchardat that diabetic glucose was solely

(1) Note. That is altered the nature of the Sugar

(2) Op cit. II. 122.

of extraneous origin — and impressed on the Sugar itself (1) such a character that it was incapable of performing a function in the economy - a function of which he says we know nothing. The idea that an acid has something to do with the non-resolution of alimentary Sugar, I find to be stated by several writers, but there is nothing definite stated by any one that I am aware of. I find for example that one persons says that diabetes is disease of the stomach which consists of an increased secretion of acid from the mucous membrane, "which prevents the fermentation of Sugar just as in the Laboratory." This gives us no explanation of the cause of the disease & is merely repeating what we find Lehmann states as a perfectly known fact when he writes." In the normal state the existence of lactic acid in the duodenum cannot depend on a lactic fermentation. Since any such fermentation is prevented by the Gastric juice." (2.)

What we propose to show is something very different and accordant with Physiological truth as well as with the laws of Chemistry.

(1) Note. I make this remark merely because I have had no opportunity of examining the urine e.g. in pyaemia & puerperal fever, or other such cases in which we know the blood to have an acid reaction. nor can I find any record of such an examination having been made.

(2) On Stomach & Urinary diseases. 1840. 62.

(3) Op. cit. p. 64.

And previously to endeavouring to show on what Acid in particular diabetes depends we may instance a few cases by way of illustrating the fact that the existence of any free Acid in the blood is as a general rule coexistent with Sugar in the excretions. altho' Chemical condition may perhaps combine to prevent its being appreciable in all cases.(1)

I quote a few sentences from Prout to show the coexistence of Saccharine urine with the Oxalic diathesis - this is a tendency to acidity in the system in which oxalates appear in the urine.

"The Urine is often of considerable specific gravity, and contains Sugar as well as Oxalic Acid." (2)

"The Class of individuals (affected with the Oxalic diathesis) is often liable to boils which in infeebled habits are apt to degenerate into Carbuncles." and "Diabetes very frequently (as far as my personal experience always) accompanies Carbuncles and Malignant boils allied to Carbuncles. (3)

This fact is mentioned also by several of the older writers. eg. by Cheselden who

(1) Cheseldens Anatomy XI. Edit. 1778. pp. 139.

(2) Physiological Chemistry. I. 289.

(3) Medical Gazette. June 1831.

(4) Medico. Chir. Trans. 1853. XXXVI.

writes thus "Membrana adiposa is all that membrane immediately under the skin which contains the fat in cells - This membrane is the usual seat of imposthumations and boils." he then mentions two varieties of boil and Carbuncle and says in referenced to the discharge from them. "At the latter end the matter has a bloody tincture and a bilious smell exactly like what comes from an ulcer in the liver, and both these cases are attended with sweet urine as in a diabetes." (1)

Lehmann in speaking of Sugar in the Saliva casually remarks that it was in a case of acute Rheumatism that he found it. (2)

Prout has the following statement "A Saccharine condition of the urine in a minor degree is by no means an unusual occurrence in various forms of dyspepsia, more especially in old gouty subjects." (3)

One of the best illustrations of our assertion, that a Saccharine condition of the urine coexists with, and depends on an acid state of the system is furnished by a paper published lately by Bence Jones (4) and as this paper is likely to assume a standard character I shall here make

a short analysis of it.

Jones commences his communication entitled "on Intermitting Diabetes." as follows "it will be my object to point out some phenomena connected with diabetes which I do not find to be dwelt on by other authors." Now I think that the undernoted tabular view will at once suggest that in this communication its author merely gives cases in illustration of the old but important fact so well known by Prout, that in the uric and oxalic diatheses sugar as well as the salts of those acids is present in the urine, and that these are not specimens of diabetes at all, but of the above diatheses. We have the record of seven cases.

1. The urine contained Urates, Oxalates & Sugar
2. ——— Urates, Oxalates & Sugar
3. ——— (acids not specified) Sugar
4. Urine was highly acid, & gave 30 gr Sugar pr oz
5. The urine Contained Urates, Oxalates, & Sugar.
6. ——— Urates, Oxalates & Sugar.
7. ——— Urates Oxalates & Sugar.

Animal diet & alkalis caused in all these instances the total disappearance of the Sugar.

$\overset{x}{\wedge}$ it is deduced from the above examples

I may note Bence Jones theory of diabetes just as he himself gives it. He says "ordinary indigestion shows itself in a want of action on the sugar and starch taken as food, in consequence of which excessive acidity is produced - that is the changes in the non-nitrogenous food are imperfect. Imperfect changes also occur in the nitrogenous food - This is made evident by an excess of urea and urates in the urine and perhaps also by the formation of oxalate of lime. In diabetic indigestion the effect may also be traced on the two great classes of food. At first from the non-nitrogenous food sugar is formed in place of acids. Ultimately, if not simultaneously sometimes the arrest of healthy changes extends to the albuminious food, and instead of an excess of urates and urea other products are formed one of which is sugar."

If I understand the above theory rightly it seems to me the doctor simply attempts like M. Bouchardat to account for the origin of sugar in diabetes, and argues that because sugar is not digested therefore

it passes into the urine. and in the commencement of diabetes coexists with the products of the non-digestion of nitrogenous matters, while in confirmed diabetes these nitrogenous bodies are themselves converted into Sugar, So that we do not meet with urates oxalates or urea, the products of their non digestion. We might raise objections on many grounds. amongst others, because we are not told why in diabetes Sugar is not digested. because there is a gratuitous assumption that Sugar may be, or is formed from Nitrogenous food, because the urea has been found by the best authorities to be often immensely increased in diabetes. I think that we can show a tolerably satisfactory reason for the absence of urates & oxalates the result of deficient digestion, without assuming that albuminous bodies are converted into Sugar. — This we shall mention very soon. Altogether I do not think that the suggestion is worthy to be entertained.

Now from all that we have said, and

(1) Op. cit. p. 66

(2) Valleri Guido, III, 662.

and from the evidence which we have adduced I think that we are entitled to deduce, that if we can show in true and confirmed diabetes, the existence of an acid which has a constant source of regeneration within the economy. if we can show that this acid operates on the sugar of the Economy, both hepatic and alimentary, to prevent its catalysis. I say that if we prove this we demonstrate the true exciting cause of diabetes Mellitus.

I cite three passages to support my assertion that prolonged Acidity of the System induced by any cause may be perpetuated by this acid of which we shall presently speak, and so constitute true diabetes.

First. Prout says. " The oxalic diathesis sometimes passes into the diabetic " (1)

Second. Mialhe says " Acids drinks had been taken for several months as refrigerants, and the patient having persisted in their use notwithstanding the supervention of diabetes the disease made very great progress." (2)

Third. I find Thomas Willis ascribes diabetes to the indulgence in acid wines. he says. "Novi quemquam vino Rhenano pro potu ordinario

(1) Opera omnia. Genevae. 1680. I. 105.

(2) In Chabetes 1798. p. 19.

per 20 dies usum Diabetem incurabilem contrahisse." (1)

Let us look then to the digestive system in the diabetic to show that an acid does exist and what that acid is.

We begin with the Teeth. I cannot do better than simply copy Rollo's description of their condition. Of Captain Meredith he says "the teeth feel loose to him, and as on edge, or like the sensation from sharp acids - he has lost two." (2) He remarks the same in the case of the General. p. 63. Home gives a case in which the patient lost 16 teeth in a short time. Similar facts are recorded by Cotton, Prout, & others. in fact the phenomenon is almost universal.

The Saliva. As this secretion is the only one in which we have direct evidence that in diabetes the glandular secretions have an acid reaction, and that this reaction is due to the acid which we consider the perpetuator of diabetes - namely the lactic - it is most satisfactory that the proof is furnished by the highest authority on Lactic acid and its tests - that is by Lehmann and the demonstration

(1) Op. cit. I. 94.

(2) Med. Chir. Trans. XXXVI. 419.

may therefore be deemed conclusive. I quote from Lehmann verbatim. "In all cases of Diabetes mellitus which I have observed the Saliva has had an acid reaction (it is ordinarily alkaline). Associated with this symptom and intense thirst we sometimes find a copious secretion of Saliva which we have thus a good opportunity of analysing. As the Saliva of such patients sometimes contains sugar, I took care that it should flow from the mouth directly into alcohol, so ~~that~~ as to avoid any possible formation of lactic acid from the Sugar. The Zinc salt which was obtained showed very distinctly the crystalline form of the lactate." (1) No comment is required since no observation could possibly be more complete.

We pass on to the Stomach. Bence Jones says. The diabetic usually expresses himself thus "I used to have excessive disorder of the Stomach - I could hardly eat any thing in consequence of the acidity and uneasiness which I suffered but now since the water has increased the disorder of the Stomach has disappeared" (2)

(1) Op. cit. III. 671. 1853.

(2) Op. Cit. p. 32.

Although the uneasy sensations of the patient may in many cases be of no great intensity still we know that this is by no means invariably the case, and is the exception rather than the rule. Valleix remarks "When the disease has made great progress, the patient has gnawing sensations at the stomach which he compares to those which a corrosive acid would produce - This we explain by the great degree of the acidity of the gastric fluid." (2)

Again Rollo says of Captain Meredith "He threw up by the emetic an acid greenish matter, and the morning following the urine was evidently more urinous. The acid green matter thrown up after so entire a diet of animal food shows the strongest disposition of the stomach to acidity." (2) This was on 17 Nov 1797. The same remarks is made of the stomach of the Seneral, and of the Gastric secretion.

Now taking all this into account I do not think that there is any necessity to account for the absence of urates and oxalates from true diabetic Urine by supposing the nitrogenous

food to be transformed into Sugar. We know that the action of the gastric juice is solely to effect the reduction of such matters. Indigestion we know in most instances to be owing to the deficiency of this gastric acid secretion. How much more reasonable then is it to account for the absence of urates and uralates — the products of the deficient digestion of nitrogenous substances — by inferring that the increased & superabundant supply of lactic Acid has thoroughly inverted and rendered assimilable the animal food consumed by the patient. The fact indeed that the diabetic can assimilate much greater quantities of nitrogenous aliment than the healthy individual, is positively determined, so that we may say that he does not suffer from indigestion at all.

That the catalysis of Sugar does not and cannot take place in the upper part of the alimentary canal in consequence of the presence of lactic Acid we maintain and again cite Lehmann's casual remarks to confirm the assertion namely. That the lactic Acid of the duodenum <u>cannot</u> depend

(1) Op. cit. II. 122.

for its existence, on a lactic fermentation of Sugar. "Since any such fermentation is prevented by the gastric juice."(1) Much less then is Sugar apt to undergo Catalysis when the acidity of the duodenum is greatly increased.

We have shown proof above that the alkaline Saliva has invariably an Acid reaction in the diabetic, it follows naturally that other Glands which in ordinary circumstances possess an alkaline Secretion, in the diabetic condition pour out a Secretion rendered Acid by the same Acid, which we stated was found in the Saliva - that is the lactic -. Under this designation come the Pancreas and probably others of the intestinal Glands. If then an alkaline State of the digestive Canal be essential to the fulfilment of the normal rôle of Glucose, can we be surprised that this is not accomplished when we take into account the opposing Agency in the System of the diabetic? —

The Sugar of digestion therefore enters the circulation and again seeks the means of Catalysis. Liver Sugar continues

- as we have previously seen to be elaborated as before, and is therefore added to the former and both seek to become subservient to the uses of the economy through their catalysis. But it is obvious that precisely the same obstacle stands in the way of their resolution as in the digestive passages, for lactic acid previous to its excretion by the glands, which we have specified must have been present as such in the blood. The intensity of the disease is commensurate with the amount of the acid, and this we reckon to be greater or less according to the ~~amount~~ quantity of sugar which escapes catalysis, taking always of course into account the nature & amount of the nutritive ingesta.

In speaking of the chemical changes of hepatic Glucose we showed how in the pulmonary capillaries a constant formation of lactic acid took place. — We showed how by the action of the free acid, the carbonates — themselves the result of transformations of the lactates — were split up into carbonic acid and

their base. — Now it is clear that if the free acid exist in quantity more than sufficient to become united to the base. a certain amount must become free in the circulation, and as the formation of lactic acid from hepatic sugar is uninterrupted from birth to death the condition must be permanent if means be not used to obviate the tendency. It may have been any acid which originally provoked the disease - we have proved that acids taken as refrigerants have induced diabetes — also that saccharine urine may coexist with the uric and oxalic diatheses. and that these also may terminate in true diabetes. but unless the source of the acid be unfailing diabetes cannot be persistent. Lactic acid as derived from liver sugar has an unfailing source - Lactic acid we have shown on the highest authority to be an abnormal constituent of certain glandular secretions, and to be an invariable accompaniment of diabetes. — Therefore we hold that the true pathology of diabetes mellitus is as we have stated above, an acid state of the economy

due to, and dependent for its perpetuation on lactic Acid derived from the glucogenic process carried on throughout life in the hepatic Capillaries. —

What objects are to be pursued in accordance with the above theory in carrying out a system of treatment of this disease.

To strike at the root we should cut off all sources of lactic Acid from the economy. It is questionable if we in any measure effect this by the removal of all saccharine and amylaceous matters from the food, since we have no evidence that in diabetes any portion of such substances ever does exist as lactic Acid in the circulation. Do we know then of any means by which the formation of the sugar of the liver - the source of the lactic Acid in diabetes - can be arrested? To answer this question we ought first to be certain, out of what materials this sugar is elaborated. but since we do not know this with certainty, we must content ourselves with conjecturing. That the failure of the pabulum for its elaboration must inevitably stop the glucogenesis,

Now the fact is well known that Sugar almost always disappears from the urine ~~Shortly~~ before the fatal termination of diabetes. This I consider due to the failure of the supply of hepatic glucose to the system. just as Bernard showed to be the case in dogs starved to death. from deficiency of the pabulum for its formation.

In accordance with our theory, a decrease in the quantity of lactic acid formed, necessarily attends the diminution of glucose. — the lactic acid ~~however~~ remaining in the system is however excreted and transformed in as great quantity as before. and consequently, between the continued excretion on the one hand, and the limited formation on the other, there is the tendency in the system to return to its normal state of alkalinity.

With the gradual return to alkalinity the sugar disappears from the urine but the vital powers of the patient are exhausted, and he is in all probability the victim of some organic lesion. — for it is by phthisis that the great majority of diabetics die — and so he sinks.

Such we take to be manner in which nature effects a spontaneous cure of diabetes. if we may call it so.

Can we imitate nature so as to effect the cure of diabetes without producing a fatal issue? Can we cure diabetes by restricting the patient solely to an animal diet? We can cause by this means no doubt the disappearance of a considerable portion of the Sugar from the urine of the patient. and we can diminish his thirst and so cause the amount of urine excreted considerably to diminish. But I look upon neither the diminution of Sugar nor of urine under such circumstances, as affording any proof ~~diminution in~~ of the diminution in intensity of the diabetes. The disease is essentially as severe as before, and with the renewed addition of saccharine material to the food, there again supervenes the intolerable thirst with increased excretion of alimentary Sugar - the cause of the thirst - and of water, the result of increased potation. This remedy therefore we consider as simply palliative, and as acting by relieving the system of the presence of Sugar of digestion. a substance altogether foreign to the circulation and calculated from its presence to add to the intensity of every case of diabetes.

× Small T repeated

Bloodletting[x] has been much recommended by some as a palliative in this disease. Does it act by taking from the liver the material out of which, according to our hypothesis, hepatic sugar would be formed? Would absolute starvation have a similar effect? To carry out either of these measures so completely as to effect a radical cure, would in all probability be impossible.

If then we cannot lessen the quantity of lactic acid furnished to the system, by acting directly on its source, we must attack it when formed, and endeavour to eliminate it under another form. and it is obvious – if our theory be a correct one – that if we throw into the circulation an amount of base sufficient to counterbalance the amount of acid present we may render the system alkaline to such an extent as that its acidity shall no longer interfere with the normal catalysis of hepatic sugar, and in short do away with the diabetic condition altogether. – It is not by giving alkalis in even moderately large doses. that we should expect to succeed in removing

diabetes. Ordinary doses of alkali would in the diabetic never affect the circulating fluids at all. They would be swallowed up entirely in the primae viae. It is only by supersaturating the system with alkali, and by keeping it so for a definite period, that we should expect a radical cure to follow.

We have said that our theory depends for confirmation in a great measure on the results of such treatment, and fortunately practical experience does not invalidate our proposition. It so happens that we are led much to the same conclusion as Mialhe as regards our treatment, although from different theoretical considerations, and we have therefore the results of his practice to guide us. I believe that the reason why we have not a more extended series of facts is that from the failure of several points of M. Mialhe's theory, practitioners have been unwilling to afford his treatment a fair trial, or have probably misunderstood the treatment and its objects altogether. But one fact such as the following is worth many

(1) Op. cit. 1853. III. 589.

negative results - it is given by a most trustworthy Physician M. Vallex. (c) he says "I could cite several examples, but I shall content myself with citing the following which is very remarkable from the extremely rapid effects of the alkaline treatment." - The prescription for the patient was as follows. 20 Grammes Bicarbonate of Soda - 5 Grammes of Calcined magnesia - two bottles and a half of Vichy water - all to be taken in the course of twenty-four hours. The urine which contained 80 Grammes of Sugar in the pint, and which had a density of 1040 On the following day presented not the slightest trace of Sugar, and its density was no more than 1026. The treatment was continued, and the patient was completely cured." Mialhe has given cases also in which complete cure was effected. for instance that of a man with diabetes of eighteen months standing, and with the most aggravated symptoms. Mialhe recommends the gradual saturation of the system with alkali yet in six weeks this mans urine was completely

(1) Bull. de l'Acad. Juillet 1844

free from Sugar, and he was cured. This case was without organic complication, but judging from Mialhe's description, a case more confirmed or with a greater tendency to a fatal termination could not have been met with. (') Andral has cited two cases in which he says the alkaline treatment failed — This is not at all to be wondered at when we read that the greatest amount of Soda taken in the day by these diabetics was 8 Grammes.

I should be inclined with Valleix to proceed at once with the saturation of the diabetic by administering at short intervals - say every hour or so - from half a drachm to a drachm of bicarbonate of Soda allowing him at the same time to drink lime water ad libitum. and I should continue the treatment till some decided effect was produced. I should not feel myself called on to restrict the patient to animal diet entirely, believing as I do that with the return to the normal state of alkalinity the normal rôle of Sugar in the digestive

passages will be completed.

I expected to have had an opportunity of seeing the above recommendation put in practice in the hospital here. I requested Dr Robertson through his clerk to try the effect of the prescription of Valleix on a patient who had been in the hospital for very many months. He refused however to give the remedy a trial. If our principles of treatment be correct, I can conceive of no means more calculated to perpetuate the disease than were pursued in this case. namely - the continued exhibition of tincture of the muriate of iron. With what object this universal remedy was given I was unable to discover. The clerk said he imagines it might act by improving the general state of the system & might possibly enable it to throw off the disease. Iron is one of that class of substances such as arsenic. Quinine &c. which in the economy prevent the catalysis of Grape Sugar. The administration of free muriatic acid in a case of diabetes induced primarily by the acidic diathesis perhaps, or by the use of vegetable or mineral acids. is but adding fuel to the fire. unless the

administration

act on the Hahnemannic principle "Similia similibus curantur." If again our theory be correct, and if the line of practice consistent with this, be the only consistent one, it is obvious that this man never could have got well, and that any good effects likely to result from other hygienic measures must have been certainly counteracted by the simultaneous use of the drug.

Whether we are to conclude that Diabetes is in every case uncomplicated with organic disease, a disease quite amenable to treatment, remains to be seen. Theoretical Considerations would certainly lead me to draw this inference. If practitioners get impressed with the idea that Diabetes is an incurable disease dependent for its existence on lesion of the brain, then truly their patients will have but little chance of recovery. But if as we believe, and as our well authenticated instances of recovery satisfactorily attest, this is not and cannot be its true pathology, and if, by directing our remedies in the channel which we have indicated, the results we

hope for be attained, then indeed rational medicine has received an important accession. If not - and if the riddle of diabetes be still unsolved then must this disease remain as one of the opprobria of our profession, until more perfect knowledge, and more extended experience, have cast on this malady that light which it is our trust and expectation that they will one day spread over every department of Medicine.

I have now discussed all the questions which I proposed to myself in the beginning of this essay. The subject is one of the highest interest whether we regard it simply as forming a topic of scientific inquiry, or as furnishing us with a basis on which to ground our therapeutic endeavours. In worthier hands, and by more extended observation, the physiological department will doubtless yield results of no little interest in Science; while the pathological will continue to present its knotty points for consideration, till these have been definitely settled in some way or other.

I am well aware of the crudity of many of the suggestions which I have offered, Still when I had not the speculations of others to guide me, I, same considered myself justified in offering speculations of my own. There is a great deal to be done in human physiology and to the onward progress of our knowledge it is the privilege of every student of Science to contribute; it is at the same time his duty to keep up with the advance of the times, and while he pays due respect to what is old, not to keep his eyes shut to the exclusion of what is new. for what was true long ago, is true at the present day as well —

"tempora mutantur, et nos mutamur in illis."

James Lumsdaine Bryden.

Edinburgh
March 31/55.