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 and 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 deemed 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, and 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
which has gone furthest to strengthen former theory, while it has added to physiological science facts at once new and 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, and of the modifications of its role under motived influences, using as my groundwork the general Institutes of Liebig, and the facts as promulgated by Bernard—that we have throughout life within the body a constant and never-failing source of sugar for its uses. My endeavour has been to make use of well grounded chemical and physiological facts 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 and arrangement my aim has been to give continuity and integrity to the subject of my dissertation.

(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, present
a barrier at which even the most sagacious
stumbles. The vagueness of the ideas entertainned
of the Role 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. Prior
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. Mont's hands, ( & no man
has been more of this malady, since he says
in the last edition of his work, that he has
had upwards of 100 cases under his care)
the most approved treatment has been found
unavailing. & he remarks (2) "the general
progress..."
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 characterized 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? It 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 materials, and as a foreign ingredient in certain of the normal excretions, as these were recognised and 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, and it is not my intention in the sequel, to enter into any minuteness as to the place and 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, and more especially those of the French school. The results of whole researches are recorded for the most part in the Annals of their Academy.
(1) "Quod autem plerique Authores potius aut parum aut nihil immutatum peddi atque sunt, a vero longipene dictat: Quoniam urina in omnibus, quos singulam me novitatem antiquitatis credo sit in universae hujusmodi tum a potis singulo, tum a quovis humore in corpore nostro gigni solito plurimum differens, quasi melle aut saccharo imbata mire dulciscebat."

Thomas Willis, Opera omnia. Geneva 1680

I. 101.


(3) Vol. IV. 290. 1788.
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. It translated from him as follows.

"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 (or I believe the fact to be of universal application) the urine has been of wonderful sweetness, as if in that impregnated with honey or sugar and in this respect differing most essentially, not from the patients drank only, but from every fluid which we know to be generated in our system in ordinary conditions."

Cheselden made the remarks that Carbuncle,

"are attended with sweet urine as in a diabetes." (2)

Thomas Lawley gets the credit of first showing the sweetness of diabetic urine to be due to sugar. His observations are contained in the London Medical Journal.
Medical observations and inquiries. 1779. V. 295, 296.

(a) page. 305.

(b) page. 304.

(c) page. 309.
There he certainly makes no such claim. He gives in his paper an excellent digest of the theories of the older physicians, of 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: "The white cake which remained after the evaporation of two quarts of this diabetic urine, weighed 31 3/4. It smelled sweet like brown sugar, neither could it by the taste be distinguished from sugar." He adds further: "The serum of the Blood was sweetish, but I thought not so sweet as the urine." 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." He anticipates Siedemann and Gmelin when he asks "Does it not appear that saccharine matter is a product of the Animal Economy?" or that as various spirits are the product of the Various 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


(4) Recherches sur la déjection. trad. par Goudineau.
of sugar during the "Vegetative Fermentation" of
grain, + the maturation of fruits.

Fermentation does not therefore deserve the merit
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 view,
since he first published his theory as a note to

a French translation of Rolle's well known +
admirable treatise on diabetes, who in Dobson's

principle showed the great advantage to be obtained
by withholding amylaceous substances from the food
in this disease. (1)

Frank. (J.R.) showed that there was not

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
Serius Consueverat, non minueret Deus nostris." (2)

The revival recognizes diabetic sugar to be

identical with grape sugar. (3)

Sedemann Smelis first absolutely demonstrated

the presence of sugars in the Prima Vae, during

the digestion of grain + in various classes of

Animals. (4)
(1) London Medical Gazette. 1831. 185.

(3) Comptes Rendus 1845. XX. 143. 328. 1026.

(4) Comptes Rendus 1845. XX. 1347.

(5) Philosophique Mea. 1845. 323. 418.

(6) Comptes Rendus 1846. XXIII. 189.

(7) Nouvelle Fonction du Foie, "Pajot."
Plant found Sugar in the Urine in Gout &ct. 1831
Ambrusini extracted Sugar from Alabetic Blood. 2
Bouchardat has published numerous papers on Alabete in many Parisian journals. I do not see that he has gone beyond Dibson either in fact or theory. His opinions are discussed subsequently, as also those of Mialhe.

1844

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

Lassaigne allowed the pancreas possessed the property attributed to it by these observers, but denied that the saliva could act on Crude Starch. (4)

1845

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

Majendie confirmed this statement and showed that the blood had the power of causing the resolution of Starch into Sugar. (6)

Bernard proved that animals as well as 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 role of sugar in the economy, and bring about its appearance in the equations.
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 as 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.

I 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 vs. animals — the continual formation of starchy or saccharine matters by the first, and their continual destruction by the latter — led all chemists and physiologists to conclude, that it was to the vegetable kingdom and to it alone, that animals were indebted for the sugar which under certain abnormal conditions was found in their excreta. Nor indeed was this inference to be wondered at, for chemists had never yet fabricated except from amiable substances a sugar truly fermentable, 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 fermentable sugar had nearly two centuries before been discovered in the urine, from which circumstance the
add the specific name of melilias 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 inconceivable. This belief was no doubt countenanced and 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 their nutritive matters, and 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 exercised. 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 Journal des \textit{Journaux} and more recently (1853) been published in a separate form under the title of "Nouvelle Doctrine du \textit{Foie}" and in this work he undertakes to prove that in the liver we have a constant \textit{fabrication} of \textit{Glucose taking place}, not in man only nor in mammals, but in every animal \textit{vertebrate} or \textit{invertebrate}, which possesses a liver. The experiments by which he supports his assertion have been conducted with the strictest regard to \textit{logical accuracy}, it 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 and suggestions as we have to offer, and taking into consideration certain objections which have very lately been brought forward, calling in question the accuracy of the deductions of Bichat.

The mode in which the discovery was made is not devoid of interest. Bichat had resolved to ascertain in what organs 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 and 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 and 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
in the body an organ which originated there. It was necessary by way of counterproof to show, that the sugar so found in the hepatic vein was really the sugar derived from the alimentary materials. 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 in examination of the blood of the hepatic vein, just as much sugar as the blood of the dog fed on saccharine matter only. Here was a fact altogether new, and the establishment of it was in future the chief end of all Bernard's researches. The experiments were at once repeated, and they have been repeated again and again by many physiologists besides Bernard, on animals which have subsisted for many months or for absolutely years devoid of amylaceous or saccharine substances, and 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 precluded by the invariable examination of the contents of the cecum.
of the spleen, mesentery, and 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 manufactures alcohol from it. In solution it causes the deviation of polarized light to the right, while the tests of Mme. T. Frummer 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 fermentable 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 urine, does not necessarily come from without – it must be formed within the
for me meet with it in the hepatic tissue independently of saccharine or any other 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 materials."

He supports these propositions by such experiments as the following: — A dog was fed for eight months on tripe exclusively, it 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 contained from 1 to 2 parts per cent of hepatic sugar. I have said that every experiment 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 being a liver-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 same substance
of the objection is this. Bernard's experiments
on dogs submitted to animal diet for months
lose their significance, and M. Figuier holds
that sugar exists in food as procured from
the stomach. 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. + Read 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 tissue on which the
subjects of experiment were fed, and without
considering
(1) Robin et Viallet. Traité de Chimie Anatomique. II. 343.
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 live sugar in the blood, in the liver, in the urine, in the abortion 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 entered disappears. etc." (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. Figuier's hypothesis is quite invalidated by the observations of the above-named authorities. We pass on therefore to consider inquire 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 in criminals
just executed, or in individuals who had met
with a sudden and 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
bile bladder gave no indication of sugar, a
circumstance remarkable when we reflect on the
intimate of organic connection subsisting between
it and the liver, tending to show an antagonism
between the secretion of sugar and the secretion
of bile. He has in three of these instances
given us the following results:

1. Death by decapitation. Liver weighed 1 lb. 3 oz. Gramme

2. — — — 1. 200 —

3. Killed by musket shot. — — 1. 575 —

Sugar contained in 1st. Gramme 23.24
2nd. — 25.10
3rd. — 17.10

The Gramme is about 16 grains.
(1) Nouvelle fonction, p. 478
Experiments instituted in the case of sudden death—poisoning by arsenic for example—show a like agreement.

Bernard has given a long table showing the vertebrate animals on whose livers he has found sugar. In most instances he has calculated the quantity contained. The condensated acre extracted from this table.

Mammalia. Monkey livers contained 2.15 pound sugar

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<td>Cow</td>
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In the Birds, Fishes, and 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 fluid of the livers and the sugar of the alimentary canal, and the relative importance of certain varieties.
The variations in the production of liver sugar following abstinence & digestion.

3. The origin of liver sugar.

4. The influence of age.

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 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 complex processes require to undergo transformation before they can fulfill their purpose in the economy, is an established doctrine in physiology. The many debates 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
(1) Monatsbericht der Akad. der Wissenschaften. 1841.

(2) Physiological Chemistry translated by Day. 1853.


(4) Since writing this sentence, I understand that Matteucci holds the opinion which I have stated. But on what grounds however, I do not know, as I have been unable to find a record of this view in the papers. See also Note page 44.
which starch undergoes during digestion is its conversion into grape sugar. Such passages as the following testify:

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

"The sugar found in the small intestine is sometimes even in the large intestine over 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, is carried on in the caecum, it is resolved into dextrose, glucose etc." Boucharat. (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 the sugar is made subservient to the uses of the economy as such, or is absorbed and 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

(2) Letter. 1861 295

(3) Nouvelle fonction. P. 60
of sugar occurs primarily in the blood." (1) Lichâz says, "Sugar disappears in the blood with extreme rapidity so that it has only in very few cases been possible to detect it in the blood." (2)

Blandan would certainly seem to have entertained the same view in preparing the key 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 elementary sugar by the liver is in fact an anatomical & physiological necessity." (3)

Bouchardat & Sandras fed animals on starch, and found sugar in their portal blood. Sommer and Elhamann 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 wheat or in fact submits to any change in the prima via. If we find that it does, to inquire what is
The change, and to what extent it takes place.
Since the natural catalysts of fructose under such circumstances as the lacte, we naturally ask, does lactee acid present itself in the alimentary canal? Of its presence there is no question, but it may be required that the lactee acid of the fermenturia be due to the lactee reaction, and to it alone. That lactee acid is evolved from this source, if passed into the digestive passages we must admit, but if we can show that fructose is abundant in the intestine, while its existence can hardly be detected in the portal blood and if at the same time lactee acid be present in the intestine under conditions in which it could not be affected by the acid of the stomach, it follows that fructose is subjected to the lactee catalysts. This we hope to show to be actually the case. But we must first prove the presence of lactee acid of catalysis during primary digestion.

In the upper part of the small intestine the acid reaction due to lactee acid is usually present during the digestion of mixed elementary matters.

(2) Nouvelle fonction p. 63.
According to Lehmann, "while as a general rule on the same authority, the contents of the lower part of the ileum and large intestine give an alkaline reaction. In this latter protein 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 foetal natural airs in the ascending colon. Whereas 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. In short that the nature of the food does not in the smallest affect it, 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 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 Rénaud
with the facts as detailed by Thénaux, 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 further & to propose, that the presence
of Glucose in the portal vein is due to mechanic
causes solely, and ought never in reality to
have entered the circulating fluid. Let us admit
that Sugar is so found, what must be its next
step towards performing its normal function? The
we to grant Rénaud 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
away from Sugar as M. Edwards has experimentially
demonstrated? I think not. We know from
Mangoni's researches afterwards alluded to, that
(1) Comptes Rendus, Nov. 1856

1 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 role of hepatic glucose depends on this catalysis as the first and principal condition.

It cannot be that glucose is normally taken up in indefinite 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 vessels, 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 and Sommer, that sugar is occasionally present in the chyle. Lehmann wrote thus: "I have never been able to detect any sugar in the chyle of horses fed upon bran"

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 Porrera's or 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)

The other point might perhaps have been less 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 Ehrmann, who recognised it with certainty in Chyle obtained in two cases from the 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 stated it as my conviction and endeavoured to prove, that elementary 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 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 transformation 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. Blood. 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 Malteucci 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, and from a review of his chapter on Digestion contained in the Brit. and Foreign Review for January 1855, I extract the following. "Lehmann does not infer that no Sugar at all is as such taken up by the intestinal capillaries, but feels himself justified in maintaining that only a very small quantity of Sugar can reach the venamission 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." He may therefore regard the question as almost definitely settled.

Note II. I observe a paper 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 maintenance of heat:
But the varieties of element seem to presage
an insurmountable 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 Carbohydrans
Substances in the intestinal system of the Herbivora.
So soon as Respiratory food leaves the
elementary canal it is in both cases subject
to precisely the same conditions. The cleverly
Circulating medium affords in each the same
facilities for destruction or for further 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, whilst precisely the
same Phenomena.
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 any lacerous or saccharine matter received into the system, we have now to ask whence is Liver formed, Sugar derived, and from what constituent of the Body is it formed. We are again compelled to fall back upon Bernard's researches, for 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. Gilt of London (who finding in the livers of Stal's large quantities of Sugar while he finds but little in the active carnivore, 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 endeavored to explain Dr. Gilt's facts on grounds totally different.
I therefore make no account of those here, but 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, and into sugar on the other, or are bile, sugar the product 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.
by withholding food from an animal. 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 elementary principle this would alone in some measure for the want of nutritive matter, or by varying the principle so added, he hoped to arrive at an approach 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 be 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 and treated as follows:
The first (adult) weighing 137.99 grammes was starved for four days. Then for the next day following had injected into its stomach 136 grammes of slightly tepid water, and at the end of that time was killed by strangulation an hour after the last injection.
The second which weighed 4.910 g. was treated precisely in the same way with this exception that 20 g. of Gelatine in solution were added to the water. In the third 20 Grammes of Starch were substituted for the Gelatine it weighed 4.865 g.

The fourth class (12.640 g.) was steamed for eight days at each day for the following six. 90 Cubic Centimetre 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 packets in the Liver of the Dog.

<table>
<thead>
<tr>
<th>Water alone</th>
<th>Water + Fat</th>
<th>Water + Gelatine</th>
<th>Water + Starch</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.57</td>
<td>0.39</td>
<td>1.35</td>
<td>1.50</td>
</tr>
</tbody>
</table>

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 Gelatine, Amylase, and fatty matters respectively, but again the same peculiarity was found. The percentage of fat in the liver standing thus

Dog Warren 0.9735 fed on Fat 0.378 fed on Gelatine 1.65 fed on Starch 1.88.

The comparatively large amount found in the animals fed on Starch Bernard.
All the breadth: *to is not* good English.

"This is all," or, "This is the utmost, that Bernard

considers himself justified in concluding."

"Then remarks:"
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 of now being forced to regard gelatinous matters or matters analogous as the true source of hepatic sugar, he quotes Leixeder to show that such substance does disappear in their course through the blood, who says that the blood of the fat hog in traversing this organ loses a certain proportion of its fatty ex. principles, and that its film 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 are is not too much for so vast a 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 and oxalic acids when treated with nitric acid. Schwann says "Berzelius finding his hypothesis in the fact that protein treated with nitric acid yields saccharic and 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 and 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 corpuscles is in the lymphatic stands elaborated out of this material. The white blood cell we hold with the best authorities to be the originator of the red blood corpuscles, 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 gum by which its existence can be prolonged. What purpose it serves previous to its elimination.
(1) R. E. Gray on the Structure and Use of the Opleon. 1837.
it is not my business to inquire. If then this globule be destined for execution, how is this execution affected? 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. 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 corpus as essentially composed of cellulose, and that this body is thrown out of the economy of the spleen. All writers now I think admit that the colouring matter of the bile is the chief Colouring Matter of the Blood, but we have still to account for the cell wall. We shall go therefore to pathlogy to inquire whether from morbid influence the splenic evacuation is ever retained, and if we find that it is, to investigate what is the true nature of the substance under examination.
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 sympathetically 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 Michel has written a memoir on this condition, which he calls the Cardiacous-Cholesterine disease. We extract the following particulars of the chemical peculiarities of this body: "All drops made of a dark blue green colour by iodine + sulphuric acid. "All drops simple or in concentric layers coloured at first beautifully violet then blue then dace brown by the same agents. "Cholesterine 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 + carbuncle blue etc. 
"The Cardiacous substance," says Michel, "with the vital reaction is probably a combination of Cholesterine 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 refer."

[Handbook 390]
The reviewer remarks: "If it really appear that the so-called cardiacous 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. All 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 spleen phlegm divertiunum.

The canal by which fats are evacuated from the economy, but we must repeat with Meckel, that no fat gives the reaction of which he speaks with iodine and sulphuric acid. What substance does give this reaction?

Dr. Gregory says: "Sulphuric acid dropped on cellulose forms with it a jelly which is coloured blue by iodine." We therefore maintain that the deplorable situation 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, &c. &c., they have yet different properties.)
a preparation for further chemical change is going on. We have cited Alhmann’s observation that the blood of the hepatic vein differs materially from that of the portal blood in the amount of gelatinous matter 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 and 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 or of a dilute acid sufficing for the accomplishment of the transformation. That the hepatic tissue possesses within itself the requisites for 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 independent 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 corpuscles be really composed of cellular matter nothing will be easier than to demonstrate this by the ordinary tests. I have tried, and 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 decolourize the blood previous to testing, and this I have had no time or opportunity to do.

B. Whether the blood corpuscles furnish glucose and still I am inclined to hold that it is secreted by the liver after having undergone previous preparation in the spleen. The abundant 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 corpuscles. 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 liver has a constant source of these rejuvenescence immediately presented to it by the thoracic duct, which mingle its contents with the hepatic blood before this has performed any duty, although it might from its impoverished state been detrimental to the economy. Truly I think we may
Call the spleno-hepatic circulation a diverticulum for the purification of the blood.

O. If we hold the groundwork of our theory, does it not show how economically nature deals with the economy in elaborating for substances otherwise effectual, the function 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 current of
the general circulation - thus we have to follow
its place of disappearance, and we might
deal with this part of our subject in a very
summary manner. Since in ordinary circumstances
the fact which hepatic sugar as such plays is
a very limited one indeed. Since a subsequent
detail 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 "sourceless
function du froid" but now for the last time.
Direct experiment shows Bernard, that when an animal has finished the digestion of its food, perhaps 24 hours after being fed, just as much sugar is thrown off from the liver, as can be conserved in the pulmonary organs, and 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 of maintenance of the stimulus the liver elaborates and secretes sugar in so considerable a proportion, as to overbalance the powers that combine to destroy it. It may at such a juncture be detected even in the superficial veins of the body, as even on the porta vein. Schmidt having found sugar in the latter situation, I undoubtedly, under such circumstances, objected to Bernard's deduction as to the place from which it was eliminated and abundant, abundant testifies that the sugar found in the circulation invaded, and not from the hepatic organ. The first observer who showed that sugar was present in healthy blood would seem to have been
(1) Phila. May. 1845.
P. D. Thomson of Glasgow, in an address to Mr. M. Gregor of the same town in a paper which he published in the Med. Gazette for 1834 inferred its existence from the fact noticed by him, that in those fed a vegetable 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 this 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 Lotenmann and Snellius 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—i.e., the one from 100 grains of flour he got 2.53 grains of sugar—i.e., the other 520 grains flour 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 Bernhardi's statement, that sugar is present in the blood during active digestion. Thomson's conclusion was That sugar is found
page 189 1846
The blood of animals fed on starch."

The year following we have a paper by Viennadie in the Comtes Rendus, on the normal presence of sugar in the blood. His experiments likewise arose out of his researches on the catalytic properties of the tissues of the body - he had found that starch introduced into the circulation immediately changed to sugar, but as this was altogether beyond the range of vital phenomena, he wished to know whether after feeding an animal on a highly amylaceous diet, sugar would exist in the circulation. He fed a dog for several days on cooked potatoes; at on killing it soon after the last meal, he examined the blood, and detected in it a notable quantity of sugar. 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 Starch partly matters our Blood contains Sugar. These observations are allied with those of Mr. Thomson, regarding them merely as confirmatory contributions to the fact as Bernhard 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 excretion takes place. Forty grains of Saponce Sugar have been injected into the blood of a small dog without any of it being removed by the Kidney.

Very recently Bernhard 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 of Sugar 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, and therefore subject to the same chemical and physical laws with the latter.
Magenta 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:

<table>
<thead>
<tr>
<th>Sugar</th>
<th>Nebular 240</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Sugar</td>
<td>1</td>
</tr>
<tr>
<td>Milk Sugar</td>
<td>3.5</td>
</tr>
<tr>
<td>Grape Sugar</td>
<td>50</td>
</tr>
</tbody>
</table>

So great is the fermentability 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 in doubt one of the reasons why several persons have been unable to verify its presence in this or in other situations.

Bernard declares that in the cephalorachidial fluid he has never failed to detect glucose. His experiments were made on dogs, cats, and rabbits all in a state of health. There is in me somewhat remarkable statement that he makes "that it was only after several days' abstinence that the sugar began to fail." This by no means concurs with Bernard's own views of the extreme fermentability of hepatic sugar, for if we allow that

is completed in these animals in 204 hours. From that time the formation and destruction of Glucose is equalised, it follows, according to Bernard, that Sugar should immediately begin to disappear and be altogether removed within twenty-four hours, if not much sooner.

Indeed, the correctness of Bernard's views in this point has been questioned. M. Bucyey analysed a fluid from a fracture of the base of the Cranium, having obtained a reduction of the blue protoprotein to yellow Subsodium of Copper, concluded he had found Sugar. He had obtained similar results in the same fluid from the Horse's head, but having always failed to excite fermentation, he was inclined to believe that some substance other than Sugar was present, presenting the same reaction.

An observation to the same effect, to which weight will be attached, is detailed by Mr. Tagel, who supports M. Bucyey from an analysis of fluid from a Vagina biforma in a Child. Its p. f. was 100%. He gives the particulars as under:

1. Not produce Opalescence. Not V. Nitric Acid a Flatus
white precipitate. Nitric acid also a precipitate.

2. Boiled with Ag. nitric. There is a faint faintest

3. Heated in water bath with formic solution, in a
few minutes the red oxide appeared.

4. Mauncri's test gave no result.

5. No gas was developed after standing some hours
in a warm cupboard with seminal scent.
On the fluid standing for some time the oxide of
Copper was not reduced. He adds.

"Thus only one test the most fallacious gave
indication of Grape sugar - the low H of fructose
in itself lead us to suppose no sugar present."

It is quite possible that Remon may be
in error in supposing the reduction of the oxide of Copper
due to Scurvy, and it may be that this takes place
from the presence of lenticul as Mr Raimist suggests, t
which we know to have the properties of bringing about
the reduction. Still I do not consider Mr Raimist's deducti
borne out by the facts as he has given them.

There is first as an objection the highly albuminous
character of the fluid, which of itself materially
interferes with the action of the tests, and may
render them totally inapplicable. Prince Jones says
"Mr. Clark's Transactions 25
XXVI"
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, and thirdly to be very careful not to add too much of the tests." Now Mr. Paget gives us no proof of his either having separated the albumen in this case, or of his having concentrated the fluid, notwithstanding his having used an amiable test that is found to indicate sugar, while simply boiling with potatoes gives a colour a dilution as we could be entitled to expect from the density of an average amount of saccharine matter contained by the Urine of the fluid. Mauve's test also appliance enough where sugar is in a comparatively large quantity as an inoperative 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 if proves bitter. Every organic tissue and fluid in its decay emits this gas; it had alcohol been formed in this case it would have been more inappreciable. Besides, fresh yeast is precarious. Here I have found to contain a very large quantity of fresh sugar. Therefore it was of little perhaps of no use.
Moreover from the appended circumstance which Mr. Prits
adduces, we should be induced to believe Glucose really
present - the failure of Frummer's test after the fluid
had stood for some time is just what we should
expect, as the Sugar must necessarily have undergone
the lactic catalysts. 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 altho'
we must consider the question still undecided, we
cannot consider Mr. Pritts 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 uncovered
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
lau-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 the place of its appearance, 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 or 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 and left side of the heart, from which inference, that some cause operating in the pulmonary system brought about a change in virtue of which this disappearance took place.

At this point how our discussion of the Chemical Changes of Glucose begins, it is natural to ask what processes to be in the lungs which may determine the destruction
Success, if these we propose to speak soon in the meantime we may merely state, that according to the best authorities, while hydrogen is taken into the pulmonary organs, carbonic acid is desengaged. 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 besides the liver & lungs & these 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 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 fermentation would cease. But now the free acid is neutralised by the addition of Carbonate of Soda brought hither by the Great Venous Trough. Lactate of Soda is formed, while the Carbon acid set free is wholesome & fermentation continues."

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 there have been modified by my study of the question.

I do not stop to inquire what is the ferment which causes the catalysis. Many of the experiments prove what in the Blood there exists a ferment which has eminently the power of bringing about
(1) Comptes Rendus 1846.

catalytic action. (1) But we may here refer to the statement made above: 'That the Carbonic Acid of inspiration 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 Thaumast showed that there was comparatively little difference in the amount of free Carbonic Acid in Arterial and Venous blood. Liebig's 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, and 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 carbonate is not a new one. For me I find, Ogilby 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 greater 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 respiration 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 which I am acquainted are those of M. Verdet, who has manufactured from the pulmonary tissue a new acid.
which he keeps as peculiar to this tissue, it has given it the name of Pneumic Acid, and to it he ascribes the property of liberating the carbonic acid of the carbonates.

I cannot give an opinion as to whether this acid results from the complicated process requisite for its isolation, it is merely a modification of the lactie. I think it at least possible, and we know the lactie 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 lactie. Pneumic Acid is found after death—as is the lactie. "We knew nothing of how Pneumic Acid is formed," we know the details with precision as regards the lactie. We know little of anything of the existence of pneumates in the blood—the existence of lactates we are certain of. I therefore maintain that lactie 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 tissues, 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 exercised 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 specific irritant to the glucogenic function of the liver — in short, that there is
an increase in the amount of sugar thrown into the system, it hence a corresponding increase of lactate & carbonates. Secondly we may suppose that the excretion of hepatic glucose 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 had we not Bernard's assertion to the effect that he finds sugar in the blood during active digestion & their confirmation by Thomson, Magendie, & Signor. In either case the carbonic acid, while increased in quantity, and the accompanying vasation of the circulatory & respiratory functions is perfectly explainable 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. Second—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 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 lacte acid has never yet been demonstrated in normal blood. Since the combustion of the alkaline lactates—that is to say, their conversion into carbonates, proceeds in rapidity and extent their passage into the urine.” But again we have Schimann remarking in the same paper in reference to lactates in blood: “The simplest induction proves they must be present there even if they remain invisible for a very short period.” And again: “Until we can prove that the lacte 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 lacte acid in the blood with due scientific precision.” I may remark that all these statements were made before anything was known of hepatic glucose.

Lactie concurrent testimony is as follows: “Sugar, starch, and in general all those substances which, in contact with animal matter
Chemistry of Food. 10s.
are converted 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 or lactates could be traced in the circulating fluids 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 decisive indication?

Several circumstances lead me to believe that it is the Lactic Salt that the arterial blood loses its bright red colour. It is no proof however 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 to venous blood lactate acid it becomes apparently arterial, that the same lactate place within the economy. The principal objection is that in the same locality oxygen is constantly absorbed, and 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 and there the same rule 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 and carbonates have 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 inspiration we...
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 Carminic 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 Porpoise cut up, and expected to see the blood dark as in ordinary conditions, but of the large amount of Blood which streamed from it, all was of a bright Crimson Colour. I have made inquiry of one 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 Porpoise is much brighter in colour than the same Blood in the ordinary Mammalia. Toldt has shown that Lactic Sugar is very abundant in such animals; consequently Lactic Acid must also be abundant in their Blood, and including oxygen, I think that we are shut up to the conclusion that it is the Lactic Acid that the Crimson tint is due.
(1) a 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 Mémoires de l'Académie as under in reference to the alterations of the blood in typhoid fever. "Presque toujours il a été trouvé d'un rouge clair ou vénitien, offrant la couleur de vini de Bourgogne, de Cordène, de gélée de groseilles (Strachan), de cermillon (Grant)."

A few pages on to ask (page 234) "Is it true as it

Wemyss 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 place 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 of Kepes 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?
If true lactu acid become free in pyoheic 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.

(2) Chemistry of food. 108.
There are many ways has positively determined the presence of lactic acid; having been able to separate it in quantity from the excretions of purerect fever. While Lehmann has only twice found the blood give an acid reaction, and then in cases of jaundice. Taking all these things into account, I think we are entitled to offer the proposition that the normal arterial blood owes to lactic acid the bright tint which it invariably possesses.

Lactates pass to the state of Carbonates.

What proof have we of this? Lying 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, "simplifies the difficulty 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." Experiments of the same kind made by Liebeh & his assistants give similar results. That the lactates in such instances did not
carbonate in the formae was 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 Perselius that the free acid of the muscles is in a great measure the lactate, and to this Liebig gives his full assent. We know that almost invariably the exudations from the vein have an acid reaction which Perselius ascribes mostly to lactate acid. This acid undoubtedly here performs the same function which we ascribe to it in the lung. That is—that it acts free the carbonic acid.
is exhaled by the skin, and I think that this fact goes to establish my proposition that lactic acid, not pneumonic acid, liberates the carbonic acid in the former situation, for we might as well manufacture an acid from the skin, and call it cutamic, as from the lung. Call it pneumic. That the functions of the skin are coincident with those of the lung is well known. Why have we the abundant sweats in pleuritis and other pulmonary diseases, 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 affect 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 a precursor of death.

The change of lactates into carbonates must be regarded as the most important source 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 inspiration than the alkaline lactates, which we have seen undergo rapid combustion in the blood and are thus converted into carbonated alkaline."
(1) P. c. 1. 104.

(2) P. c. I. 256 + 258.
In a word, nothing could be a better support of animal heat than the alkaline lactates. (1) But we must go on to consider whether lactates are finally destroyed in supplying this animal heat, or whether through the medium of lactic and sugar the latter contributes further to the well-being of the system. I propose to show that it does, and that it furnishes indirectly the most important maintenance of animal heat which the body possesses - I mean, fat.

We take as our starting point the following passage from Lehmann (2): "In so far as 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, and how, by what process, and in what chemical proportion is fat formed from starch or nitrogenous matters? We read in connexion (page 258). 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
(1) Léon Gambon décédé 1843.

(2) Nouvelle fonction au Ton.

(3) Lettre 348.
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. Michel says that the bile has the power of transforming Bicharne matters into fat. (1) Bernard cites the experiments of Blussas and W. Edwards by which they proved that fats formed were from sugar alone, and conjectures that the sugar of the alimentary canal is in a similar manner changed into fat by the liver. (2) Leslie speaks 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, is, hence, that the liver is the seat of this process is not destitute of probability. Leslie formerly held that Starch and its Substane were transformed into fat in the peritoneum, Robin and Verdeli while they assert that the liver is undoubtedly a fat forming organ, consider fat as formed also wherever we find it, and that the
Société de Physiologie. 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 Sarcharine - agitated matter.\(^{(a)}\)

The views of these last physiologists come nearest to my own on this subject. There 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 Schonberg that the Liver is a fat destroying organ, and that it is by this channel that the superfluous fats are eliminated from the system - Not 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 much 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.
Annals of Philosophy. V. 199.
and is in amount inversely proportionate to the secretion of bile. Dr. Schwatck showed this in hepatica. and he has been confirmed by Sehnau, Savaigne, Mequenel, and Rodier etc.

The theory that sugar is transformed in the liver is then destitute of foundation in proved facts; and if 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 prime vice 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 catalyse 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. Leif as I have previously stated has shown that the livers of seals and the cetaceans contain fat in abundance. Why this should be what I have just said, I mean, and I believe that exactly on the same broad principle the incidence of fatty liver with syphillis is to be explained.
oxygen sufficient merely for the reduction of one.
The remaining two will resolve themselves thus:
\[ \text{C} \cdot \text{H} \cdot \text{O} \rightarrow \text{C} \cdot \text{H} \cdot \text{O} = \text{Butyric acid} + \frac{1}{4} \text{CO}_2 + \frac{1}{4} \text{H}_2 \]

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 directly be made
subservient to the production of animal heat,
and fat would necessarily be a substance useless
for exertion did not nature again interpose to
prevent such prodigality, and render it indirectly
useful to the Body as a Maintainer of the heat
generated by its progenitor Lactic Acid.

Whenever we find oxygen deficient either
in consequence of the Comparative Slowness of Breathing
for example in Sluggish Fast Animals, or in those artificing
Crammed and deprived of air and exercise, or our
old illustration the Cetacea and Their Submission
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 frozen,
and the more capable of sustaining the animal heat.
of 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 role 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. It 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 lactose, the result of a vicious metamorphosis 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 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...
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 do we take no account of it in our Category.

Now when may we speak 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 circulation, with one exception. That is 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 excreta. Since the Blood must have become to a definite degree charged with sugar before the physical act of exsostasis can take place.

Sugar may exist in the Body and be eliminated, in consequence of a.
1. Deficiency of Oxygen in the Pulmonary capillaries.
2. Excess of Acid in the System, whether
Derived from the catalysis of Sugar, or from the transformation of their organic substance within the economy.

C. Something taken in from without, which tends to check catalyses. 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 visae is not subject 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 Second, and in the Third Case I think it is impossible to say how much of the Sugar of the spine 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, although 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 excitement of nervous force the physiological function may be excited to unwonted 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 in what the secretion of urine depends to reply — in lesion of the floor of the fourth ventricle. French physicians have noted the appearance of gray 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 Nervous.

Part I.

Reasoning on the fact as founded by 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
(c) Comptes Rendus. 1851. XXXIII.
in this situation, hepater sugar would be found in the circulation and effusions. Indeed it had
myself as pure the reduction and verified it by experiment before I became aware that M. Boreau
had formulated 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 secretion. Considering that the same mechanical law
which we saw brought to bear in the passage
of saccharine fluids through the coats of the
intestinal canal, ought to hold good in defense
to the more delicate texture of the pulmonary
air cell, I anticipated that when any morbid
state determining an occlusion or the blocking
up of the air cell vessel supervened, in the
fluid thrown out, I should find sugar more or
less in proportion to the amount of substance
involved. It is not always easy to ensure
system which we can guarantee to be absolutely
free of sugar introduced from the food or from
the excreta almost constantly prescribed for
those who expectorate. I have however endeavored

as far as possible to avoid such sources of fallacy, and from the constancy with which it occurs, and from the ancient ferment
resibility of the Sugar itself, I have no hesitation in accrediting the Saccharine
impregnation to true hepatic Sugar. 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 that instance was
quite equal to that in ordinary diabetic
urine — The method of testing which I
adapted for this purpose was that recom-
manded by Pence 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 Froumeyer test fluid — to about
half a dram of the fluid, add twice as
much of Ag. Nitricae with one or two drops
of a saturated solution of Sulphate of Copper
and gently heat the mixture, when as the
heat rises of 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 Spatulum 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 Spatulum of a
patient in advanced Phthisis from O'Shaunbey's
ward — The expectoration 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, and
immediately got reduction by Somme's test. I then, as
recommended by Beinard for liver detection,
threw down the animal matters present by
acetate of lead, neutralized the flux, and
again filtered — and on again applying the
Test there was instant and most characteristic
reaction — On Dec 18th (four days afterward)
Sugar could no longer be shown to be present
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 work of Franci: "De curandis hominum morbis," as it not a confirmation of my statement. "Nota est pathologicorum plerorumque tabulam morbi lethalic insignis et ad Museum usque molestar Dulcedo Sputorum." (1)

Reynolds 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 phthisis, chronic bronchitis, asthma, leprosy, and 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 Mr. Reynolds's invitation to the profession to put the
(1) Pathological Transactions. V. 1854.
of his allegation to the test, Mr. Michan
denied that in such conditions sugar could be
ascertained to be present by the ordinary tests,
whereupon the former undertook to prove to Mr.
Michan's satisfaction, the real existence of glucose
in the slate of the system above specified.
And it seems perfectly to have succeeded
in his demonstration, for in the Cheque Books
for 1833 (page 230) we have a joint com-
munication by these two gentlemen, showing
the invariable occurrence of sugar in the
circumstances as stated by Mr. Reynolds. It
is only within this comparatively short space
that sugar has come to be acknowledged as
an ordinary ingredient of the wine in such
cases. Several chemists and physiologists
have however added theirexperience, 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 of Dr. Garrod on the presence of
sugar in the wine in a case of acute
bronchitis. (1)

"It occurred to me," he says, "that
(1) Note. There is a paper by R. Hassall (Lancet, Jan. 1853) on the fallacies which are apt to complicate forensic texts, and especially the influence of the normal constituents in this respect. The absence of alcohol, however, it would be better to introduce.
would be a good one to test the accuracy of the theory which has been
proposed to be a test of the presence of sugar in the urine.

*Examination of Urine.* Abundant white deposit of ferric oxide, cleared by
a temperature of 100° Fahr. when heated above 200° again became clear,
from precipitation of albumen, not redissolved by nitric acid. Precipitate
occupies about one third of the height of fluid in the tube. Sp. gr. at 60° 1024,
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.
I therefore added to the urine a solution of the trisulphate of lead, in slight excess, and after filtration
treated the clear fluid with powder of bicarbonate of soda, &c. The resulting solution was
clear and colourless, and was tested thus:

A portion boiled for a minute or so with a
strong solution of hydrate of potash gave an
orange yellow colored fluid equal to that produced
by one grain of glucose in an ounce of water.
when heated in the same way."

A second portion was treated with the solution of the tartrate of copper dissolved in an excess of potash; this colored the fluid, and a very distinct precipitate of red oxide of copper took place on boiling for a few seconds. A Somers test was applied with equal success.

"Another portion 26 cubic inch was placed in a tube with a piece of German Yeast - it was found to yield 26 cubic inch of Carbonic Acid Gas."

Even before the addition of the lead yeast disclose the presence of Sugar. Mr. Garrow 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 Mr. Garrow 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 portion; whereby the Sugar normally formed from starch
or amylaceous matters, is incapable of being further
changed and broken up into Carbonic Acid, Water, & Sugar.
Now we have shown that alimentary 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 imputed
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 outflow of inspiration
is withheld. Even apart from merely theoretic
grounds we must from the remarkale 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 Saccharic Wine for six months, it
still Sugar was abundant.

From Bernard's researches we
know that even during intrauterine existence,
the liver possesses Sugar. At what period this
Glucogenesis...
(1) *Comptes Rendus* 1850. II. 659

There is no difficulty whatever in satisfying ourselves of the real presence of sugar in the polar fluids, since I have got at once a characteristic reduction by 

(2) *Comptes Rendus* 1850. II. 629.
commences it is impossible to say — in the human
fetus Bernard has reason to think that it begins
about the fifth or sixth month of pregnancy.
In the lower animals of course it begins with
the period ofuterogestation. 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 luminis 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
uterine life the sugar disappears. The causes
which lead to this it might be interesting to
investigate. M. Bay confirms Bernard. (2)

Now what gives very great weight
to M. Reynolds's statement is the observation
also made by Bernard that along with the formation
of sugar by the fetal liver we have the simultaneous
appearance of it in the urine of the fetus.
and this is just what we should expect
from the circumstances in which the fetus is
situated if the proposition made by Reynolds
be a true one.
It seemed to me on following out the consideration of M. Regnese's fact, that if the real cause of the presence of sugar in the urine were the deficiency of the supply of sugar, and knowing as I did from Bernarr's experiment that sugar even in the circulating blood underwent catalytic change, it seemed to me that it was not sugar so much as the products of catalysis we should expect to find ejected by the kidneys.

The detection of minute quantities of sugar was never attempted till within a very recent period, and in fact neither Bernarr's researches nor Regnese'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. So have attempted the detection of lactate would have necessitated 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.

When the respiratory process is in any way disturbed, we most frequently observe a most copious eversion of urate of lime. And "there is an almost universal occurrence of lactic acid in urine containing urate 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." 1

Great too remarks on reference to unhealthy urine, that it often contains the saccharine principle in imperfectly developed form, and says that in such urine the lactic acid imparts the smell of sour milk. He does not specify the condition in which he met with this, sufficiently to enable us to draw conclusions from his statement. We may however say, and in all likelihood future investigation will bear out the statement that lactic acid of lactic acid as well as lactic itself exists in the urine when irritation 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 Lagrange, et seq.
From solely to the exaggeration of the glandular function of the liver resulting from the irritation of the nervous supply of the pulmonarv organs and consequent sympahty. The liver is like every other product of the animal economy presupposes as a condition of its existence a certain influence of the nervous system, and when we reflect on the complex structure of the gland, the peculiarities of its muscular 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 affinities 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 salpin substance prevents the 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 precedes over and regulates the formation of sugar 
and its amount. It follows then that the 
organ of the vagus is the nervous centre from 
which emanates the power of the liver to 
produce sugar.

All physiological agree in considering 
the Medulla oblongata as the centre of regulator 
of the movements of respiration. Helene Wisseau 
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.

Bernard's reply to Baynes's statement 
is as follows: "Recently," he says, "some have 
recently thought to bring the ancient theory 
of incomplete combustion in the lungs to bear 
on this question, by announcing that whatever 
tends to cause diminution of respiration by 
asphyxiation 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 that case, adds Bernard, have I seen sugar appear in the urine."

Regnoue had experimented on rabbits by way of counter experiments to those of Bernard. Bernard can render rabbits diabetic very speedily by causing lesion of the above specific section 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 fact 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 power which combines to destroy it. Regnoue maintains that he can produce the same results by simple compression of the trachea in the same animals.
The question at issue is simply this: is hepatic glycogenesis 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 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 since, that therefore respiratory energy is most powerfully lessened in such a case Raynor'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 hæmatoidiun 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 vaga 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 vaga 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 apprehends has no ground to go on in raising the above objection to Pappenheim. But when we look to the matter from a different point of view altogether, I meant to the phenomenon manifested in the rabbit employed by Bernard in the establishment of his opinion, I write we have most conclusive evidence that sugar does not exist in the urine in disordered states of the circulation 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 veins
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 on the details of the
experiments we have no proof of hepatic congestion.
"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 inflamogenesis just as the renal remnants of the fetal secretion."
I question how far Bernard's analogy between the
tongue and vagus nerve holds. The first being a
nerve of special sense, and of limited distribution,
while the second, if 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 on 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
dner. 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 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 food 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 glycogenic 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, although the system have sugar over and above, to spare for excretion, 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 over
look upon as arising from a want of respiratory material. Sugar is but a foreign body in the system. Sugar as sugar is indigestible to we 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 eviction, 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 affinities 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 observation made on rabbits. The fact indeed of the case with which rabbits could be rendered diabetic seems to have been known long ago. I find in the articles on diabetes published many years ago, in the Encyclopaedia of Practical Medicine the statement that Thunier of Stelle had shown that if rabbits were fed for some time on flour, sugar was readily to be detected in their urine.
1) Compte Rendus. XXXIII. 606.
Resinosa 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. It more particularly specifies anaesthetic agents such as Ether, Chloroform, and Tonic such as Amin and Quinine. Brande 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. He considers that the sole cause of its increase in the circulation, is want of Catalyst.

Now have ether and Chloroform the property of stopping Catalytic action? - that they have is a fact well known to Chemists. Then therefore Hepatic Sugar and the Vapors 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, it must therefore present itself in the Urine. We have then a more interesting illustration of our statement that Chemical agents act within the economy as to prevent.
catalysts with equal certainty as in the laboratory, in the physiological effects on the body of arsenic, quinine &c. taken as medicinal agents. Regnart, 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 early 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 Regnart 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 (London) was admitted to Dr. Gardner’s ward suffering from a skin disease. Some time afterwards I happened to visit the ward, and Dr. Gardner 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. The man had for some days previously been taking half a dram of iodine’s solution three times a day. It struck me that this would be a favourable opportunity for putting
the accuracy of Repress'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 previously demonstrated 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 stumpy and fair by the use of this thing is sufficiently attested, but as an instance due 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 was one of the sugar-diminutive property of arsenic, I cannot definitely say sugar existed in the urine in this case, altho'
(1) Note. I understand that last summer this patient again returned, & amputation was urged to be the last resource to, in consequence of the ulcer having broken out anew & weakening himself to prove fatal from hemorrhage. This, however, was not in abatement the fact as I have stated it.
I have no doubt that it did. In autumn 1858 Miss was under Dr. Syne'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. Dr. Syne despaired of cure even by a second amputation, which might have terminated fatally from the cachectic state of the patient. At this juncture however an East India passenger happened to visit the hospital, and Dr. Syne asked his opinion of the case. I remember well what he said. "I have seen this often in India. Give the woman ten drops of Fowler's 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 happy in complexions. I may remark that the arsenie had on several occasions to be intermittent from the production of its physiological effects. From the above relation it is clear that
Arsenic is a preserver of the tissues. Do we now 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 an elaborate series of investigation 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 Catabolism, it is obvious that if comparatively little debris be formed, or at least of the quantity of debris furnished to the blood be insufficient for complete Catabolism, such Catabolism as those of Sugar into Lactic Acid must be proportionately retarded, and the quantity of Sugar excreted will be proportionate to the retardation. We have formerly seen how under the augmentation of the normal amount of Glucose in the circulation, the
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 arsenic is given to produce its so-called toxic 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 Jangne arsenical pill of India as a specific against the typhoid condition which is apt to supervene after the bite 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 influence. Dr. Ross's experience on the African coast among boat's crews on river service & 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 secondary, counteract the mortifying effects of the imbibed poisons on the tissues themselves in both cases precluding the formation of morbific material the existence of which according to the speciality of the case would cause marsh fever on the one hand or bilhaemia on the other.

If the primary contact of the morbific ferment with the fermentative 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 bismuth & 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 proportionate to the degree of saturation of the system, with the antidotes.

(2) Müller. Archiv. 1864. (4)
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 Sommer's test are not really to be regarded as the reducing agents in impeded respiration. We have seen that Mr. Faith suggests leucin in the case of the cerebro-spinal fluid. Valentinus has discovered leucin in the urine of an epileptic patient. I, believe, considers that the action is owing (sometimes, at any rate) to the presence of allantoin, as this substance was found in the urine of two also the athlete of whose lung 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 function. If one suggestion however regarding the presence of lactic acid be taken into account, I think this may offer us the means of sustaining the reality.
of the presence of glucose.

Here is an allied condition in which
from failure in the vital processes, sugar is
stated to be present in the urine. Alchambe
refers to his researches into the respiratory
organs of the age, described in the Arch.
Generale, 1835. These exhibited lateral depression
of the thorax, projection of sternum forward,
rigidity of the chest, vertebral articulation, obliteration
of the cartilages, and a sacrified condition of
the pulmonary parenchyma, in which the
cell-walls were found thinned or ruptured, and
the capillary vessels obliterated. The defective
hemorrhages which result from these physical
changes should favour the production of
glycosuria, and experiments performed upon the
urine of a considerable number of the age
formed of the sulphuric acid so constantly
exhibited it. That Dr. Alchambe considers
himself justified in asserting that sugar exists
habitually in the urine of the age, although
it is possible that its presence may be explained
on some other hypothesis.

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 anyone who has the opportunity of making the investigation. It is not to be wondered at that we should find the milk sugar eliminated itself by the kidney, when it exists in a superabundance in the circulation, either when rejected from the mamma by morbid influences, or as a result of too copious secretion, especially when we know that it is a substance 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 Clinic's 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 tests for sugar and recognised
Au domicile de M. Paris 1845. P. W. O.F. E.
its presence by Moore's and Sumner's tests. The day following, the urine passed in the morning still presented some traces, but in the evening the 
Sp. Fr. had sunk to 1020 and it was impossible any longer to detect sugar. Carrying out the views 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. Altmann records an observation exactly similar - he says. "I once met with sugar in the urine of a precipitate 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.
" " De la 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 adjustment of their merits, and then state the view which to me appears most satisfactory.

M. Couteau defines Diabetes thus:

"Diabetes mellitus is a disease characterised by a very abundant excretion of urine, containing always a saccharin crystallisable matter analogous to starch, sugar, accompanied by a"
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 not rare from early youth to old age, and seems to affect both sexes alike, while season and climate apparently exercise but little influence on its production. England is said by French authors to be the country most subject to diabetes, probably much on account of a statement by B. Willis that a friend of his had at one time thirty-three cases under his care. Another writer in the Dict. des Maladies Med. for 1812 says that more cases 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 there. Sir Gen. Lepers has met with no record of such a complaint in any Russian register, while Sir James Willoughby Sample in two volumes 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
necessity of this disease is its causing death, as we can trace it in Greece, 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 differs among another to the last. 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 lassitude, 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 some accident, as in an instance cited by Rolfe, where a moraceous appetite alone led him to detect diabetes in the individual, or that mentioned by Watson in which the patient's attention was drawn to his urine by the swarms of wasps and bees which its sweetness had attracted.
The amount of the urinary excretion too can hardly at first give any indication, for Franks, Watt, Brown, and Eland to have given instances in which sugar was present in large quantity, although the urine did not exceed in amount what 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 Mr. Cantor's 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, however, profess to have detected dark spots on the floor of the fourth ventricle and others have recognised an incense 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
According to medical authorities, it would be unjust not to mention the elegant treatises of Dobson and Rolls which, although written almost in the last century, are worthy of the present day.

The first thing we take up is that of M. Duchardet. 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 in March an action similar to that of acidosis. He has always found the quantity of sugar in the urine in direct relation to the quantity of bread 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 acidosis in diabetes, the author has recourse to another and somewhat problematical hypothesis. Namely, that the diabetes 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
(1) An absence of the stomach in 1840. 31.

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

(3) Compte Rendus. 1844 and 1845.
organic Acids exist in large proportion, we are
likely 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 Fleming. It was
hardly worth while to mention this theory since
it merely attempts to show where it may possibly
be derived. The Sugar of diabetes and even in
this it perfectly fails. It 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 (diabetes of Skin) was wanting
and in which perspiration and even profuse
sweating was induced by slight exercise." (1)
Bierce 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 Substance in the alimentary canal
as we have before seen.

Mink's Theory of Diabetes is the
(3) École du Médecin prat. III. p. 612. 1853.
which has gained most credit on the continent as
the following remarks on it by Dr. Valleix 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 will
obviously will go to confirm the above, and if, as
we can hardly suppose it will, the theory of Dr.
Malhe does not shatter by these, it will remain
the most satisfactory and the most complete."

Malhe begins where Dr. Bouchardet's 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 Malhe, 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 deoxidize. E.g. if the attempt be
made to procure a reduction of the Bride 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
re
of Sugar in the circulation, says M. Malthe, 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 absorbing 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 1 to 2 it is evident that the half of the Sugar absorbed will not be changed and will therefore pass into the urine. Malthe 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 Pierard'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, Gifs, and Bedec Anes. 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 hypothesis, so much the more probability is there of the theory being a true one. Before proceeding to further detail
it will be necessary to show the true origin of
of the secreted Sugar in Diabetes. Since so many
conflicting statements have been made on the
subject.

Bernard's theory of diabetes we have
differently 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
is consequence of some nervous irritation instilled
diabetes—this is completely disproved by
pathological evidence, and by the decrease 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 fuel is consumed than in a
state of health. We have 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.
Sure of, that a considerable portion of the Sugar of catalysis passes off by the faces as Bernard has recently found, although the fact was perfectly known to W. Gregor in 1837. The system even at this early stage seemed to regard Sugar as an excrementitious, and confirming our statement that Sugar is absorbed from the juices via 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 dissolution of these two classes of Sugar must be the 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 Glaire, namely: "I have never seen diabetic urine lose altogether its saccharine condition by even the most rigorous adoption of animal diet."
Our deduction therefore is that the sugar of diabetes has two distinct sources of derivation.

In connection with the question of the origin of diabetic sugar, I may advert to a somewhat startling doctrine which I perceive Dr. Giff has promulgated a few days ago, namely, that diabetes is essentially characterized by paralysis of the sugar-forming function of the liver. He found his sanction in the supposed fact that in the liver of diabetic patients sugar is never found after death. And his theory is that the specific function of the liver is paralyzed by more gastric sugar being sent to that organ than it can assimilate. In diabetes, Dr. Giff contends, that the liver cannot form more sugar than in ordinary circumstances. For, says he, the sugar-forming 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. Giff's 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 of the animal food have constituted the sole diet of the patient. If the fermentability of sugar constitute its value to the economy, and if non-fulfilment of catalysis constitute diabetes, and if both be equally subject to the operation of the cause which holds catalysis, taking into account the comparative fermentability of hepatic and elementary 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 fermentably fermentable hepatic sugar can only in part undergo catalysis, no part of the simple elementary sugar, which in point of fermentability 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 diminished albumen heat is hepatic sucrose.

I refer to Gibbs's statement.
That he has been unable to detect sugar in the
liver of diabetic patients after death, I take 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 liver 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 (as was expected to take place). From all
this I consider Gill's doctrine to be quite
untenable.

We may again repeat the proposition
that glucose must, to the advantage of the events
of the economy, submit to a certain role in the
circulation. This we have shown to be its
conversion into lactates and the further transformation
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 reversion.

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 has been supplied in large quantity. In diabetes, therefore, the sugar must be reverted.

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 interfering the lactic catalysis?

It is found in a previous discussion of this question that the most certain means of checking this catalysis, was by the acid formed
ceasing to be counterbalanced by the amount of alkali present. I quote from Dr. Gleyzay: 

"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 permanency 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 please 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, and hence inducing every one of the concomitant symptoms, with their moral tendencies.

It will be said that this is not the theory of Diabetes—it is not. Mabre imagined that the suppressed acid of the skin acts on alimentary sugar—of the existence of hepatic sugar he was of course ignorant. Therefore considered with Duchardt that diabetic glucose was solely
(1) Note. That is alter the nature of the Sufis.

It is extraneous origin — and impressed on the body itself, such a character that it was incapable of performing a function in the economy — a function of which we say 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 a 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. It is merely repeating what we find Blumen 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.
Note. I make this remark merely because I have had no opportunity of examining the urine, as in syphillis, 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 and Urinary Diseases. 1840. 62.

And previously to endeavouring to show on what aid 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 consistent with sugar in the excretions, all the chemical condition may perhaps combine to prevent its being appreciable in all cases.

I quote a few sentences from quaint

"to show the existence of dextrorotary sugar in the sugar diathesis - this is a tendency to acidity in the system in which acetates appear in the urine.

"The urine is often of considerable specific gravity, and contains sugar as well as acetic acid." (2)

"The class of individuals (affected with the sugar diathesis) is often liable to boils which in unhealthy 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, e.g. by Cheselden.
(1) Cholecemi Anatomy. XII. Edin. 1798. p. 139.

(2) Physiological Chemistry. I. 289.

(3) Medical Gazette. June 1831.

(4) Medici. 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 impregnations and boils." He then mentions two varieties of boil and Carbuncle and says in referred to the discharge from them: "All the latter and the matter has a bloody texture and a bilious smell; water like what comes from an ulcer in the liver, and both these cases are attended with sweet urine as in a Diabetes."

Thomann in speaking of Sugar in the Saliva casually remarks that it was in a case of acute Rheumatism that he found it.

1. Point 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 Hypokraemia, more especially in old, youthful subjects."

One of the best illustrations of our assertion, that a saccharine condition of the urine coexists with, and depends on, the state of the system, is furnished by a paper published lately by "Rome's Annals," and so this paper is likely to assume a standard character I shall have to make..."
Dr. Jones commences his Communication entitled "on Diabeting 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 tubular view will at once suggest that in this Communication its author merely gives cases, in illustrations of the old but important fact so well known by Priest, that in the leaven and starchy diabetes sugar as well as the salts of these acids is present in the urine, and that these are not specimens of diabetes at all, but of the above diseases. We have the record of seven cases.

1. The wine contained Water, Ralato, Sugar.
2. Water, Ralato, Sugar.
3. (acid not specific) Sugar.
4. Wine was highly acid, and gave 30 gr. Sugar per.
5. The wine contained Water, Ralato, Sugar.

Animal diet; alkalies caused in all these instances the total disappearance of the Sugar.
It is deduced from the above examples
I may not, Alfred Jones' theory of diabetes just as he himself states it, "the digestive and excretory organs being in a state of acute irritation, the sugar and starch latter as food, as consequence of which excesses 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 uric and urates in the urine and perhaps also by the formation of urate of lime. In diabetes, digestion, the effect may also be traced in the two principal classes of food. At first from the non-nitrogenous food sugar is formed in place of Acids. Ultimately, if not simultaneously, sometime, the arrest of healthy changes extends to the albuminous food, and instead of an excess of urates and uric acids other products are formed, one of which is sugar.

If I understand the above theory rightly, it seems to me the low simply attempts, like Mr. Bouchardat to account for the origin of Sugar in Diabetes, and relieve that because Sugar is not digested, therefore
it passes into the urine, and in the commen-
tation 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 of phosphates or water,
the products of their non-digestion. We
might raise objections on many grounds.
amongst others, because we are not told why
this diabetes sugar is not digested, because
there is a gratuitous assumption that sugar
may be, or is formed from nitrogenous food.
It has been found by the best
authorities to be often immensely increased in
diabetes. I think that we can show a
satisfactory reason for the absence of
urates or oxalates, the result of deficient
digestion, without assuming that albuminous bodies
have 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. at. p. 16

(2) Valenti Girardi, III. 352.
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 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.

1st. Priest says, "The oxalic acid is sometimes found in the diabetic." (1)

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

3rd. Now I find Thomas Wells assure diabetes to the indulgence in their wines. He says, "Novi quenquam erit Rhenani propria ordinaria..."

(2) De Diabetes 1798. p. 19.
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 Rollie's description of their condition. 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 Couteau, Prunt, & others, in fact the phenomenon is almost universal.

The Saliva. In 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 perpetrator of diabetes - namely the lacti - 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

may therefore be deemed Conclusive. I quote
from Lehmann's treatise. "In all cases of
Diabetes mellitus which I have observed the
Saliva has had an acid reaction, it is
ordinarily alkaline in association with this
symptom and intense thirst. Next we sometime 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
it 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. (*) No comment is
required since no observation could possibly
be more complete.

We pass on to the Stomach. (Now)

Thus says. The diabetic usually expresses himself
Thus. I need to have overcome disorder of
the Stomach. I could hardly eat anything
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)

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. Vallée remarks, "When the disease has made great progress, the patient has growing 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 Rolfe says of Captain Meredith, "He threw up by the kinetic and biliary greenish matter, and the morning following the serious was evidently more serious. The green matter thrown up after an entire diet of animal food shows the strongest disposition of the stomach to acidity." (2)

This was on 14 Dec 1797. The same remark is made of the stomach of the General, 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 nitrogene...
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 secretion. Now much more reasonable then is it to account for the absence of urates and uricacites — the products of the deficient digestion of nitrogenous substances — by inferring that the increased or superabundant supply of lactic acid has thoroughly converted and rendered assimilable the animal food consumed by the patient. The fact indeed that the diabetic can assimilate much greater quantities of nitrogenous material 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 Lehman's casual remark to confirm the assertion. Namely, that the lactic acid of the duodenum cannot depend
(") Π. στ. II. 122.
for its existence, on a lactic fermentation of Sugar. "Any such fermentation is prevented by the gastric juice."

Much less then is Sugar apt to undergo Catalysis when the density 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 fluids which in ordinary circumstances possess an acid reaction, in the diabetic state, tend to pour out a secretion rendered acid by the same Acid, which we stated was found in the Saliva—that is the lacteal secretion. Under this designation come the pancreas and probably others of the intestinal glands. If then an alkaline state of the intestines be essential to the fulfilment of the normal role of Sugar, 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. Ever 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 lactu acid previously 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 quantity of sugar which undergoes catalysis, taking always of course into account the nature and 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 lactu 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
This page - 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 life birth to death the condition must be permanent if means be not used to abate the tendency. It may have been any acid which originally provoked the disease - we have proved that acids taken as refuquents have induced diabetes - also that saccharine urine may coexist with the uric and oxalic acidness, 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 Alcina from the Glucogenic process carried on throughout life in the Hepato Capillaries.

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

Struck 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 Sacchaons and any faceous matter 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 the Sugar is elaborated. But since we do not know this with certainty, we must content ourselves with conjecturing that the failure of the labilum 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 is considered due to the failure of the supply of hepatic glucose to the system, just as Bernhard showed to be the case in dogs starved to death from deficiency of the pabulum for its formation.

And according 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 lowered, excreted and transformed in as great quantity as before, and consequently, between the continued secretion of 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 pohties that the great majority of diabetic die — and so he sinks.

Which we take to be manner in which Nature effects a spontaneous cure of diabetes, if we may.
Can we imitate nature so as to effect the case 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 this 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 dissipation 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 supervenues the intolerable thirst with increased evacuation of alimentary sugar - the cause of the thirst - and of water, the result of the need rotation. 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.
Blood letting 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 lacteal 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 alkalies 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 at all, they would be swallowed up entirely in the former urine. It is only by super-saturating the system with alkali, and by keeping it so for a definite period, that we should expect a medicinal urine 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 M'Intosh 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'Intosh'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) Pr. at. 1853. III. 589.
Negative results — it is given by a most trust-worthy physician Mr. Wallace. 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 Vick's 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. Mialho 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. Mialho recommends the gradual liberation of the system with alkali. Yet in six weeks this man's urine was completely
(1) Bull. de l'Acad. Sculitter 1874
free from sugar, and he was cured. This case was without organic complication; but judging from Maithe's description, a case more confirmed or with a greater tendency to a fatal termination could not have been met with. (1) Andru 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 Willig 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 for dinner some 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 role of sugar in the digestive
passages will be complete.

I expected to have had an opportunity of seeing the above recommendation full in practice in the hospital here. I requested Dr. Robertson through his clerk to try the effect of the prescription of Vallet 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 institution of dramma of the muriatic acid. With what object his universal remedy was given I was unable to discover. The clerk, he imagined it might act by improving the general state of the patient, or possibly enable it to throw off the disease. Arsen is one of that class of substances such as arsenic, quinine, etc., 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 osmic diathesis, perhaps, or by the use of vegetable or mineral acids, is but adding fuel to the fire unless the
act on the Hahnemannian principle "Similar simileus curavit." 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 men 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. Theoretic 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 persistence 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 instance 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. And if not, and if the multitude 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 is our trust and expectation that they will one day spread over every department of medicine.

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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 wiser 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 defended, better 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 consider,
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 whilst 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 mutantur in illis."

James Lumsdaine Pryden.

Edinburgh
March 31, 1853.