On the Hepatine of the Liver, Its Relations to the Pathology of Diabetes Mellitus. Ailken
It has been universally recognized, as almost to have become a truism, that the advances which have been made in our knowledge of disease are for the most part dependent upon, or at least coincident with the gigantic strides which chemistry, physiology, and biology have taken within the last quarter of a century. In no case is this perhaps more evident than in that of those recent and brilliant discoveries which have been made by many of the most eminent physiologists of our day, in which those light on a disease, the nature and cause of which have baffled the ingenuity of medical men. During the two centuries which have passed since it was first distinctly recognized.

Before proceeding then to a short sketch of the pathology of diabetes mellitus, the disease I refer to, it will be well to review what have been partly traced the advances made in our knowledge of excretory physiology of late years, more particularly with reference to the experiments and discoveries of the distinguished French and English physiologists, M. Claude Bernard and Dr. Panco.
I am very pleased to present the old thing...
By the researches of various physiologists it has been satisfactorily determined that the processes of organic constituents of our food undergo certain chemical changes before being absorbed; - the starch being chiefly converted into dextrin and glycosidic sugar; whilst the sugar is partly decomposed into lactic acid and glycollic acid. After absorption, - which may be effected either by the lactation or by simple emulsion into the vessels, decomposition into lactic and ultimately into CO₂ takes place, - thus these compounds by a process of oxidation help to keep up the heat of the animal body.* Sugar has more indubitably been discovered to be a constant ingredient of the blood, partly no doubt owing to its small quantity, - probably also to a great extent to defective chemical analysis. But that it is a normal constituent of the blood taken from all parts of the system, so which up to a recent time has been included among the extraneous matter, has been satisfactorily shown by the careful analyses of Pay, Harvy, and others, not only of the blood but it would seem (the indeed in minute quantities) of the urine also as maintained first by Biot, and corroborated lately by Dr. Bence Jones.
That the sugar is in great part derived from the food is abundantly proved by the simple fact of its great increase after eating largely of carbohydrates or amylaceous articles, as shown by von Behring, who found that, while the blood of rabbits fed on barley contained as much as 0.382 per cent sugar, that of rabbits fed on oats only yielded 0.107 per cent, 48 hours after. After 24 hours observation the sugar rose to 0.045 per cent. But whilst the carbohydrates or amylaceous constituents of the food are undoubtedly the principal sources of this sugar, it has been satisfactorily proved to have other origins. It was the observation of the fact that sugar continued to be found by Diabetics even then confined to a strictly animal diet, that led to the well-known series of experiments by the illustrious physiologist Bernard, the brilliant results of which not only show his great skill in executing them, the impecunious he displayed in their interpretation, but also led to the establishment of what is well known as the theory of the glycogenic function of the liver.

It was in the year 1848 that Bernard, while examining the constitution of the blood proved to his no small surprise, that the blood of
the Portal vein is that of the system generally, in animals fed exclusively on animal substances, was destitute of sugar, that of the hepatic vein, Dr. Cava, in a little side of the heart contained it in abundance. Finding this that the hepatic tissue alone after death gave evidence of sugar, he drew the immediate inference that the liver possessed a sugar-forming function, that it stored the sugar into the blood, tended to undergo oxidation to administered to the uses of the animal body. Such at least was the theory found by Bernard at first, but like most of the great things, it was destined to undergo important modifications. At times it was the least of those from the hands of the originator. He at first held the opinion that the liver possessed the power of forming the sugar out of the glycogen or any other compound of the Portal blood, and clearly demonstrated the fact that after death (his experiments being all on blood first motion) the blood between the liver and the lungs contained sugar independent of the nature of the aliment, or of the processes of digestion. We need not go into the experiments by which he proved this. They have been repeated so conclusively so often that it would be superfluous to do more than state the fact. But the question
which of these substances could these sugars contain? Not necessarily from the aliment, as it is as abundant in the blood of omnivora and herbivora. His experiments showed that it might be found in the hepatic blood of animals which had been killed while feeding, or, when in a fasting state. He elucidated this subject then he performed some experiments of the following nature—

I. A dog was killed 2 hours after a full meal of meat and bones. The abdomen at once opened. On examination of the duodenum, there was no sugar found, but a large quantity in the leaves of the portal blood, as a less amount in that of the right chamber or the heart.

II. A dog was killed after fasting 3 days. There was nothing in stomach or intestines. No sugar was found, but distinct evidence of it in the blood of the portal vein and right side of the heart. The presence of sugar in the portal blood in both these experiments seems to have perplexed Burnet; yet a little, but his ingenious mind soon found a solution of the difficulty. He believed that the great cause of the portal circulation was the contraction of the abdominal partition going on...
During life, it is the consequence, as soon as the animal ceased to breathe, the pressure would be taken off the capillaries, so the result would be a reflux of blood from the liver into the portal vein. That this idea was correct he showed by the following experiment. A dog while actively digesting animal food was killed by section of the carotids. The abdomen was at once opened, and ligatures placed in the splenic, mesenteric, or portal veins, just at their entrance into the liver. The blood was collected and examined, no evidence of sugar could be found in the various branches of the portal vein, but when an aperture was made in it in the hepatic side of the ligature, the blood that flowed out was collected and found to contain sugar. Although these experiments proved that the production of sugar was independent of the elements of the food, yet they could scarcely be said to have given him a much greater insight into its true origin, but another of his experiments seemed to him to clinch what was still obscure.

Having proceeded exclusively in meat for some days he killed it suddenly, opened its abdomen, removed the ligature before the blood could possibly have time to coagulate. He then thoroughly washed out its tissues by injecting cold H2O into the portal vein.
This glycerine hepatica, an extract from the hepatic
cells by boiling, its precipitate by alcohol, is a
white, tasteless, amorphous mass, soluble in 1400
parts, the chemical formula: $\text{C}_n\text{H}_{2n+2}\text{O}_n$. 
Continuing to do so till the liver was exhausted, the residue
110 contained nothing of sugar, till more could be got from
the liver tissue cut up and boiled. Having thus deprived it
of all peptizable matter he left it for 24 hours
of dryness in vacuo and found a large quantity of soluble
sugar, which must have been formed subsequent to the
injection of the, out of some previously insoluble
macerated material. This showed him that that the
sugar was not directly formed by the liver tissue itself,
but that its formation was outside the vessels, and to
his discovery coincidently with Hensel and Payr, of a
substance which having properties intermediate between
those of dextrine and hydrated starch, being con-
vertible into sugar in the presence of any ferment
he found glycogen, but to which Payr afterwards
applied the name of hepaticose or the cambial substance
of the liver. Bernard then finding that this sub-
stance was so easily convertible into sugar,
that the process went on very actively at first,
was of course obliged to abandon the idea of the
combined action in the liver itself, to explain the
phenomena in some other way. He then proceeded
to the conclusion that the glycogen was formed out
of the solid tissue of the liver itself by a
process of sequestration, the resulting sugar in this case
being...
May more. Bernard imagines that this may be due to the secretion of the substance of the bile. He points out that this function of secreting the blood is not requiring an excretory duct. As there is any true relation, he asks, between these secretions? Can we admit, that the albuminous matter of the blood, on entering at the hepatic cells, undergoes disintegration — the agitated portion serving for the production of bile, the hydrogenorganic products of sugar? If so, the two functions would go on the same time, but experiment seems to prove that they rather alternate with one another, so that the secretion of the one seems to be at a minimum while that of the other is greatest. If we make a belching after we find that the bile is secreted in greatest quantity 4 hours after a meal, while sugar is most de
duced in from 3-4 hours, or while digestion is most active. But comparative physiology seems to give even stronger evidence. In the feline place we observe that, while intestinal digestion is going on, a farceinous liquid flows that the bile duct into the stomach, and continues to do so till it fills both the stomach and bile duct itself, giving rise to a considerable enlargement of the liver, 2.
being the hepatic cells, in which it is known that any
organic substance can be easily seen under the microscope.

Whereas this glycogen escaped from the cells into the
blood, the immediate result was the production of
sugar, which he had shown to be, like so constant an
ingredient of the blood between the liver and the lungs,
and in such a proportion that the further he
the liver sugar the less sugar will be found;
Bernard's own view as to the use of the sugar in
the animal economy evidently coincided (at least at
that time) with those of the eminent chemist
Kleibig. He supposed that after leaving the liver it
was gradually decomposed into lactose and then
finally into CO₂ to be given off by the lungs.
Thus done in part to keep up the heat of the
animal body. I believe that it is still an
accepted thing with many physiologists that
the part of the sugar in the blood may undergo
such a decomposition. If so, it must be a very
small quantity indeed, considering the unimportant
quantity of sugar normally in the blood that is in the
liver.

According to Bernard's idea at that time, the lungs
of the perfused sometimes opposed to one small
in the animal economy, the former destroying that
lysed tis is gradually absorbed from the stomach just as the absorption is about to end, a fluid bile flows into the small intestine and apparently until the next meal.

On the intestine there are evidently distinct and real arrangements for the tissue reactions, that form the sugar consisting of cells analogous to those of the liver in vertebrate man situated in the coats of the intestines.

* We are speaking of the tissue where sugar can travels to be indirectly formed in the liver.
amount in the blood produced by the latter.
But Bernard's theories as to the origin and destination
of the sugar at least were by no means lost altogether.
Seemann had from the very commencement of his
experiments pointed out that the albuminous con-
stituents of the food as well as the products
of the decomposition of the tissues, might by a
process of decomposition be converted into sugar.
A similar idea seems to be held by George Stein.
He thought it fully confirmed by the fact discovered
by Seemann, that a smaller amount of albuminates
exist in hepatic than in portal blood.* That the amylace
substance may, in some way, be formed from the nitrogenous
inside a element of the food, seems pretty evident from the
fact of its formation going on even in a purify animal's body.
Dr. Kennedy has shown that amylace cannot be extracted
from the meat upon which these animals are fed. Yet its
formation also goes on even in the last stage of
incubation. There cannot be the slightest doubt however
that the really great source of the amylace in the
animal is the fermentous constituent of the food, so
Bernard himself has shown that the amylace absent
from the muscular tissue of a fasting horse was restored
by a full meal. In fact the very much larger
proportion of sugar discoverable after death in the
The theory is rejected by the fact of sugar being found in the liver of a fetuses even as early as the 8th month, in a very rare case, in the animal Kingdom, as in the arteria hepatica. That the sugar in the liver of the foetus is not derived directly from the mother is proved by the fact that it is not to be found in the liver earlier than the 16th month. I have not the slightest doubt that the liver with its animals, for an long time as is compatible, and these observations do not alone would be found to contain abundance of sugar, after the others.

I may here mention another very lately put forward to the origin of the sugar, viz. that it is the result of changes undergone by fatty matter. Now and osmotic from them in the liver itself. (Wundt)

But the subjecting on the latter as the correct notion, I put forward a theory as to its being derived from the decomposition of the conjugated acid of the bile as absorbed from the intestines. Both views offer too highly improbable to have scarcely a shade of evidence in their favour.
from of herbivorous animals led to the idea that this waste,
formed from the aliment vein, was simply stored up there.
Hence Sanson published a paper in support of the
theory that the only real stock fermen was
vegetables, so that a part of them stored went to the
growth or maintenance of the animal tissues, whilst another
part was stored up in cells going to nourish such
herbivorous animals as fed on it. By these in turn
the plant is partly used up as the vital forces,
partly deposited in the tissues, more particularly
in the liver, so it is to the latter source alone that
one would trace all the sugar found in the blood of
animals, a supposition which of course appears
not only untenable but almost absurd when we
know that it is still to be found in the liver after
the animal has been fed for months.
Berard's original idea, it will be remembered,
was, that the mural in some way was formed out
of the gland itself. He did not think that the
sugar was directly deposited from the portal blood,
but rather imagined that this went to form the
fat which may be found so abundantly in most
of the sarcineous animals, a portion
of the sarcineous constituents of the portal blood.
that fat may be formed from compounds of the cadaverous group does not I think admit of doubt. Here the fat in the liver of these unfortunate green fish is to obtain the famous 'oil gras.' The formation of a true fat from honey by bees is another example both of these in evidences that stand to show in some way (probably indirectly) as we will go on see how the formation of emulsions, &c. may stand to the formation of lard.
point for this purpose. The same would be just as to state that the production of fat was occasioned with that of sugar, the production of the former ceasing, if that of the latter be materially large enough to function of the mouth; while fat is deficient in the home of diabetes, sugar is deficient in fatty liver. But that the liver processes the sugars of the perineum, if sugar into fat is by somem unspecified faculty procured, the proper to which sugar is applied in that organ being, as we shall see, probably very different. But not only have Bemard's theories as to the origin of anything been objected to, but it has also been yet a faculty known by Ciourou. The ly, Perry and others that, per force, ministrating as a prelude, to keep up the animal heat, by a constant process of oxidation, going on in the lungs, the amount of sugar found in the left side of the heart cannot be discovered to have undergone any appreciable diminution. The ly condition just agrees with Griesinger that the sugar to a certain extent disappears in the capillaries of the system generally; for he found somewhat less in the veins than in the corresponding arteries of a little. He goes so far as to think that it must furnish directly to the various tissues and organs some substance necessary either for their development, or repair of what they have lost. If so I think that it must be evident that it
Demand was indeed led to abandon the oxidation theory himself at a later period. By finding figures in the primary burn of the liver of a very early age, he also by noticing that the gas passed through the blood containing sugar had no more effect on destroying it than had CO₂, H₃, etc. The theory as it was then developed as to its uses is rather a strange one. Lave found that a substance capable of giving rise to sugar existed in the lungs and muscles of the fetus he imagined that two kinds of fermentation took place there, the one, a conversion of this fermenting substance (as he imagined it to be), into sugar, the other a heteroic fermentation at the expense of the sugar. The first alone, he thought went on in normal intestinal life, or the sugar is converted, he thinks, into the development of the tissues, starting to be formed about the 8th or 9th month. Accordingly, attempting to apply this theory to the adult, he states that the most important uses of the sugar are fulfilled in the lives of the organism when the albumen was material is being disintegrated to give rise to the
cannot be in the form of sugar that it is subservient to the nutrition, for the form of sugar termed inosite has been discovered in muscles, yet it could seem certain to be the product of the decomposition of albuminous substance.

As Pavy altogether denies that sugar can undergo direct oxidation in the animal body, he believes that from whole purposes it may be done, it will be executed by the lungs; for he knows of no process by which its destruction could be effected in any part of the circulatory system.

His statement at least coincides with his own experiments as to the small quantity of sugar normally in the blood, as with those of Bichat and Bruce, DNA at its constant presence in the urine. Like a great many other theories which have not stood the test of time, that of Liebig as to the destruction of sugar in the lungs, was rejected as true without any great evidence in its favor, strongly condemned as it appeared to be by the glycogenic theory, and the pronounced views of its supporters. Hence when the new thing was forced to follow, the other necessity fell with it.

Before proceeding to consider Pavy's discoveries, we must shortly attend to the experiments which Bovard preferred to elucidate the influence of the nervous system upon the glycogenic function. Like all other functions of the animal body, he naturally imagined that it
must in some way be under the control of the nervous system, so it was in prosecuting researches to this end that he accidentally discovered that, by obstructing a part of the flow of the blood near the origin of the Pneumogastric nerve, a temporary artificial Diabetes was created, the duration of which never exceeded a few days. So rapid indeed is the production of sugar in such a case, that it can according to the discoverer himself, be found in very solution except the urine in twenty minutes after the operation, but if the irritation be too great, or a powerful galvanic shock transmitted through the part, its production will soon cease. A similar explanation has been given of the fact, that sugar is so seldom found in the human liver after death, all means ofry it is supposed being exhausted by the decrease which comes the patient off. Even in the last stages of Diabetes sugar ceases to appear. Bernad's idea was at first that the stimuli was simply conveyed by the Pneumogastric nerves to the liver to control the glycoserific function, but he was soon obliged to abandon this simple explanation, for he found that other nerve lesions produced a similar result, e.g. irritation of the spinal cords even after section of the vagi. Having found too that the inhibition of C2 H4 CO the exciting energies sufficed to give rise to glycosuria, he found the thing so long genera accepted, that the normal stimulus, originating from
the action of the air on the terminal branches of the pulmonary
gastric as in the lungs, can convey by them to the medulla,
its influence propagated to the brain by the spinal and other
ganglia; being then a great reflex action with the
medulla as its center. This theory derives its chief support
from the fact that division of the cervical vagi arrests the
secretion of ptyalin, because, while irritation of the lower
part of the cut nerve produced no result, a temporary
diabetes is created by pinching the upper. If the cord be
divided too below the origin of the phrenic nerves, (or even
as a man divides it to preserve life,) irritation of the vagi
has no effect in producing diabetes.

This theory like the others prefixed, by its discovery was
by no means lost in its integrity. Hunter was the first to
differ from the views of the eminent French physiologists,
regarding a mechanic state of the animal very finely as only
symptoms of a disease, he pointed out, that the ptyalin might
arise in different ways. It might be due to an impediment
to its assimilation, or, of course accumulating in the blood,
the poison would necessarily escape by the anus. Or it
might originate in some change in the secreting organ, only
producing a more than usual activity in the discharge of
its function, or by an artificial imitation of the nerves
as by breathing imitating respiration, the object, however,stem-
nously to Byrom's idea that the normal stomach was sep-
Due to the more rapid flow of the blood, the non-assimilation in consequence of the free peritoneal elements.

The prolonged use of alcohol has been mentioned as one of the causes of cirrhosis of the liver.
plied by the air in the lungs. If such were the case, we would expect to find little variation in the amount of oxygen throughout the day. Such, however, is not the case. The produc-
tion of oxygen varies greatly, being at one time nearly dou-
ble, at another nearly one, without any corresponding
change in the respiratory processes. He therefore believes
that we will find the real origin of the stimulating in
the organ itself, as probably in the stimulating effect
exerted by the portal blood on the pancreas of the dog.
His experiments in support of this view, consists in
injection into the portal circulation of substances, which
we may fairly consider irritating, such as ether, C\textsubscript{6}H\textsubscript{12}O,
and the sugar ammonium. These invariably produced artificial
Diabetes. On the manner he explains the effect of the
food in producing sugar in the same, the portal blood being
then necessary in most stimulating. The absence of this
stimulus would explain the fact, he thinks, that the production
of sugar falls to a minimum in a fasting animal, on
the feed only on bulky matters, which being taken up
rapidly by the leucocytes can add nothing to the stimula-
ting quality of the portal blood. In the same way too
glycogen may result from the injection of other ate into
the deadened is an experiment conducted on himself
which he believes
conclusively his theory, viz., that being eaten largely
of a highly spiced asparagus salad he became diabetic.
A slow lingering death generally causes the disappearance of
sugar from the urine.

He may here mention some of the theories brought forward
in opposition to that of Bernard. Amongst others, Siggi,
reviving an old idea of Misteek's, thought it once noted
to consider the liver as an excreting organ like the kidneys,
as one repository of performing the important function attrib-
uted to it. He imagined that it might simply separate
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from the blood a bag of sugar in its tissues; the sugar passing
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or would return it, little by little, to the blood. As Mr.

Figari, admitted the fact of the liver, containing sugar,
death independent of the element, all that was meant
to dispose his theory was to show that hepatic
blood did not contain sugar in appreciable quantities
prolonged fasting, while it might reappear against
a small diet. This was easily done.
Continued as to his no small alarm, for several days. One strong argument against his theory, he disposed of with
ingeniousness, viz., the fact, already mentioned, that division of
the cerebral orophyseis the production of oroga, but not on
occasioning the same results below the lungs. But the
choice to exert to oroga in cases of open wound operations,
if a sensible state be induced, or the fact that the various
attacks of democracy disease often occurs the discharge of oroga
in diabetics in strongly condemning of his views, the
above expression produced by section of the cerebral orophyseis
is, in itself, sufficient explanation of the disappearance
of oroga from the lungs, while the less severe nature of the
other operation (section of oroga below lungs) neither producing
any serious consequence at the time, nor producing death by
orogaphy, readily explains why the production of oroga is
not checked, or at the utmost only slightly disturbed by.

But the fundamental facts of Berend's
thing, have never been subjected to any very
acute attack until very recently, when Dr. Pany
published in Guy's Hospital Reports, a paper to prove
that, so far from the brain possessing a汶ghence function,
the production of oroga is not a physiological process
but merely a chemical transformation, only taking place at
death, or under certain morbid conditions of the symptoms.
+ In his experiments, have been conducted very carefully.
A theory so easily refuted simply sound to strengthen its brought forward by Bessard.
The deductions derived from these appear to me very conclusive, I may be persuaded if I enter into them in some detail. It is not the correctness of Bernard's facts that Pavy objects to, but the deductions derived from these facts, or rather, the application of what may be termed pathological data to the explanation of a vital process. Pavy, along with Herer, will be remembered disclaiming that substances to which Bernard at the same time gave the name of glycogen, but which Pavy objecting to, termed as implying a theory in which he did not concur, called Hepatic or the "Amylze Substances." Pavy knew, like most other physiologists, had not only thoroughly believed in, but had even confirmed Bernard's theory. His experiments he had often repeated, and believed in, that the production of sugar was as much, if not more, a function of the liver, as that of bile, his first experiments were simply to ascertain what was the influence of any particular diet on the production of sugar. His careful experiments and analyses did much to elucidate this subject, as he found — that,

I. Change of analyses of Xerophytes fed exclusively on normal diet - the dogs being killed suddenly or the sense of once removed that gave

(a) Relative weight of liver substance to that of body - 3/12 to 1.
(b) Average proportion of amylze in the liver - 7.17 percent.

II. Under a vegetable diet - (a) Rel. weight of liver to body 7 to 1.
(b) Average proportion of amyl oid—17.83 per cent.

III. Undigested diet with sugar—

(a) Ratio of liver to body (male) 1 to 1.
(b) Average of amyl oid—14.85 per cent.

These facts, which he satisfied himself of again and again, showed him most conclusively that the starch in sugar contained in the aliment was used by the liver in the production of the amyl oid, so it was this fact which led him first of all to think it strange that the sugar should only be converted into amyl oid to be transformed into sugar again. It was in fact while conducting some experiments as to the changes which he believes are still slowly flowing from the liver to the lungs, that having catheterised the right side of the heart of a living rabbit, he found to his no little surprise, that he could scarcely get any of the characteristic sugar reaction he had been so accustomed to from the blood of the same part of the heart. This assured his suspicion, so he repeated his experiments, taking every precaution that experience could direct. Yet his analyses were conducted with the greatest care, a desire to be impartial, will be evident from the fact that the amount of sugar he discovered in the right ventricle in 3 cases was as little as 4/1000 the 4/1000 of a grain per cent.

If we may in reality look upon the nearest to the normal
be reflect for a moment on the fact which Harvey had previously shown, that sugar is to be found in every vein corresponding to an artery throughout the body in quantities, any differences in which would seem admirably, if not entirely, of detection, it must be evident, (even granting that any amount of sugar was passed from the liver into the blood), that if such sugar reached distribution to any appreciable extent in the lungs or in the expelling system generally, it ought as naturally to have been found in the urine, as in the infirm case. Indeed it seems strange to me that this should not have attracted Harvey himself. The discovery of sugar in the blood in those quantities proves at least that the liver was not storing out of the circulation the large amount that Bernard imagined, a doubt a black of the glycerine being in another way by discovering the fact so much relied on by its supporters that the blood of the hepatic vein is right side of heart differed in its composition from that in the system, in more particularly in the venous pulsae in animals fed solely on grain diet.

Dr. Panay had most distinctly disproved the passage of any material quantity of sugar into the blood during life, yet he was by no means still inclined to deny the glycerine function of the liver, so he therefore proceeded
as nearly as possible the normal condition of that organ.

It has been known for some time that the presence of an albuminous
substance in the amylloid passing by the fermentative process
into sugar is determined to try the effects on the liver itself.

He accordingly injected a pretty strong solution of found
examination of the liver after death, that no sugar, or at the
most a very trace was detectable in it, by the most
dilutest solutions, so that this was not owing to the
destruction of sugar by the albumin was proved by his
finding its quantity quite unaffected on his injecting
it some time after death. But this is not all;
it has also been shown that excessive cold or heat
applied to a liver immediately after death is also capa-
ble of checking the transformation of the amylloid. Pouring
hotthie an animal suddenly opened its abdomen and cut off
solid of liver which was thrown into a freezing mixture.

he found that the change of the amylloid was arrested, while
the part remaining in the body presented, of course the
usual reaction in a short time. But further, he found
that a boiling fluid was capable of restoring the same thing,
must likely by coagulating the materials capable of acting
as ferment, but in this case the liver must be cut up
into small pieces to enable the boiling 40 to get at it once.

Bernard had noticed that the livers of cold-blooded animals
as the frog contained sugar, or not, according to the tropic.
at death, but the explanation of it was that it depended on an
attention to the activity of the glycerine function, by
removing & diminishing the activity of the circulation.
A similar fact has been noticed in some of the
animals whose organs are cut below the origin of the
plaque vessels, so that the temperature falls rapidly, & if it be kept
in a cold place, the brain immediately after death contains
no sugar. This is due to the fall in the temperature
and diminishing the activity of the muscles, changes, second.
and partly produced by the loss of an animal mortality,
which is kept up by warmth & artificial respiration.
The brain at death will exhibit the usual reactions, unless
functions be taken to prevent the formation of sugar,
and all that is necessary for the change of anything into any
other living life is its passage into the brain, but that
the necessary goes on to any small extent during life
as now evident. Comparing the extent of its transforma-
tion, with the large quantities of it stored up in the
brain, we must see it over that the disproportion
is great as to make it pretty evident that it must
serve some other purpose in the animal economy, although
this has not yet been satisfactorily settled. A strong
proof of its being capable of conversion into other active
processes in the body, disclosed, that the injection of
a solution of \text{Na}_2\text{CO}_3, giving life into the portal vein
Thus in a time of 92 days it is evident that less than 1/3 pint of hepatic acid is equivalent to the production of 3 lbs. of sugar (as he had previously shown). If the whole of the hepatic acid had been converted into sugar, there would have been 130 gms. of it.

Perry explains the conversion of the hepatic acid into other substances as being probably effected by a process of the nature of catalysis.

If a mixture of hepatic acid sugar be placed in a desiccated atmosphere on one side of a piece of bladder, the hepatic acid does not pass into the latter to any very slight degree, while the sugar diffuses itself all over.

Perry indeed admits that by chemical agency there may be a slight change of sugar into lactic acid, but it is not to any appreciable extent, at least to chemical reagents.
base on entire disappearace off of the hepatic without any possibility of the whole of it having been converted into sugar, otherwise it would have been found abundantly both in the liver or blood. As for this process being the case, that the amount of sugar discernible is not more than we should have expected from the \( \text{C}_2 \text{H}_5 \text{OH} \) which is diminished provisos to the injection. The products into which the hepatic is converted have not yet been detected. 

One of the strongest objections to the generally accepted theory of the rapid passage of sugar into the blood seems to me to rest on a physical fact, viz., that the oxymel, far from being an easily diffusible substance like sugar, only with difficulty passeth the animal membranes. Consider what would be the result if large quantities of sugar were being constantly found in the hepatic cells or pressing into the blood going with the Pan to that no destruction of the liver takes place, eth, in the lungs anywhere in the body. with Dr. Beal, that no higher quantity than 5 per cent. (according to others 3 per cent) can exist in the blood without giving rise to glycosuria. Why the result would be that the normal quantity of sugar, 1 in the urine would be so augmented that everyone would be diabetic even on an
animal diet, when according to the experiments of Lepel the blood of the hepatic vein contains as much as 5.21 per cent. of sugar, after a pernicious diet as much as 11.28 per cent.

It must be recollected, too, that the small quantities of sugar found in the right side of the heart by cold stream during life, have not all come directly from the liver.

It contains also that which has been sent from the body to the arteries, returned by the veins without distinct diminution in quantity, except that small amount we now know to be drawn from the renal arteries by the kidneys.

Having now so I think, most sufficiently long on the subject, and having given up the idea of a physiological function in the liver, I will pass on to consider what modifying effects on the production of sugar may arise from various physical and vital causes.

In a physiological state it seems undoubted that the acceleration goes on this the liver in such a manner as to cause but little disturbance of, or escape of the hepatic, or portal, which would generally be found to be very low if sugar was easily dissolvable, we constantly find that certain circumstances are capable of exciting a reaction in this normal and quiet state.
Another proof that the escape of amylase is due to a physical cause in the last cases is found in the fact that if the liver be made desensitized by the injection of a quantity of 110 after death, a similar escape of amylase is the result.

According to the glycosuric theory, we could expect less instead of more sugar under these circumstances, as it seems to result from the abnormal condition into which the liver is put as regards its metabolism.
one of these is the congestion produced in the brain by any cause either acting on the flow of blood to, or hindering the exit of the same from the brain. Under such cir-
cumstances (e.g.) as muscular exertion with obstruction to
the breathing, the circulation tends the brain becomes con-
grated, and an escape of amylloid takes place into the
blood, either by the pressure of the blood on the hepatic
cells, or by the violent action of the abdominal muscles,
from the obstruction of the breathing, on the organ itself.
Such an escape of amylloid is consequent glycerized, has
been noticed in pleurisy, intercostal, & coma, & is not
easily explicable on the above mentioned theory. In a
similar way we may explain the effect of section of the
external carotid by the use of &c. &c. in both of which we
find the two circumstances favourable to the escape of
amylloid— the obstruction to breathing, & the long continu-
ance, after violent muscular exertion.
That the blood in the normal state must exert some
effect in retaining the amylloid in its proper condition,
was ingeniously proved by the effect of ligature of
the portal vein. When this was done it has been found
that the urine, throughout the system generally was
greatly increased—a fact which seems at least to
depose the idea of Blaschke, that the stimulus for the
production of urine probably arises in the portal circulation.
By far the most important modifying agent in respect to the amount of attraction in the sugars produced is certainly the nervous system. Bernard's experiments had long proved this. But instead of considering the medulla as the regulator of the production of sugars, Panék is inclined to think that it rather supplies the force necessary to keep within very moderate bounds the chemical tendency of the complex to pass into sugar. In correspondence with this thing he would explain the effects produced by Bernard's famous experiment of puncturing the medulla, as produced not by an excitation but by an actual loss of nervous power, with its consequences of escape of complex into the blood.

How is this force transmitted to the brain we ask?

The division of the vagi or cord and diaphragm does not invariably result, if it does, is probably due to other causes than the loss of any supposed nervous influence transmitted by them. It must then depend then on some other channel, as accordingly Panék finds that if the whole heart be cut off or artificial respiration kept up for a kind a paralysing state of the mind will result. The only other nerve channel open to it is the sympathetic, but he was unable to find that section of the cervical cord of the sympathetic had no effect. Removal of the superior cervical ganglion however had to also the division of the vague filaments coming from the sub thyroidic ganglion.
I should indeed seem inclined to believe that the efferent branches of the sympathetic centers, which arise in the thalamus opticus, must pass downward toward the extremities of the cord, ending at the roots of the sympathetic to supply the vessels. Then the fibers of the 4th ventricle, which follow an enlargement of the vessels, escape the fibres, but if the anti column of the cord is cut, the influence does not descend to modulate the vessels.
to the intestinal canal are cause Diabetes. But that this glycerin
and results entirely from the stoppage of the nervous influence
is not yet distinctly proved. For the injection of carbonic
acid into the circulation previous to the division of the
sympathetic nerves prevents any Diabetes. *

Whether this may turn out to be the correct one it
is evident that as yet no decided opinion can be given
with regard to the real agency of the nervous system.
Before proceeding further we must give a summary of the
views arrived at by Parry.

I. It has, I think, proved, that during life at least, the
liver contains only a trace of sugar, but a large amount of glycogen.

II. The glycogen is largely converted by respiration into acid.

According to the old theory then we have the conversion of glycogen
into glycerin, glycerin back to sugar, again.

III. No appreciable difference, discernable in the blood in any
part of the system during life.

IV. In a physiological state the less digestible portions of the
food prevent its escape into the blood in any quantity.

After death, I think, from various disturbing causes during life a
conversion of glycogen into sugar takes place, this from
its digestibility at once escapes into the blood.

The experiments upon which these conclusions are founded
have been conducted with no particular device of avoiding
error, that they appear to me to be quite different in
themselves to do away with the old thing. They have however been
suggested by Mr. Huxley, and the paper, as it stands accordingly,
confounded with the objections.

Having first satisfied themselves that sugar is to be found in
the blood of dogs and even exclusively on meat, they proceeded
to test the reasons for the denial of the glycerin of the urine.
They found that the solution obtained from a vein of the live
blood of the dog on most safely plunged into a
fuming mixture after the animal had been killed by
shaking confined sugar, as did also the fleshes dissolved
from cheese of the live plunged into acidulated boiling
water. The quantity in either case was small, so great precautions
were taken to get a clear filtrate in order that any even the
slightest reaction might be seen. How Perry himself
at any time daring that a laws of reaction may under
these circumstances beget. In fact it is evident that
the blood of the live, both portal and hepatic, must contain
sugar, as it does so naturally even the the animal be fed
on an animal diet. I am not a little doubtful too
as to whether the plunging of the frozen slices of meat into
acridulated solution as the lay did before testing,
might not have a very opposite effect to what we
imagine it by increasing the probability of finding no sugar.
I am inclined to think that the action of a boiling
solution on the frozen slices would be to raise the
In Parry's own experiments he had cut the liver into small bits, rapidly mixed them about in the freezing mixture. When he'd frozen the pieces one season, cut them with a knife, and then reduced to pulp in a mortar, a faint yellowish color of acolloid was then found; but only a trace of aube. He had found that the rabbit was better than the dog for this purpose on account both of its abdominal wall and its liver being thinner. He had employed dogs in his experiments.
important to gradually allow time to pass, rather than obtaining the production of sugar, for Paré had pointed out, how necessary it is to expose every part to the action of the body the injuring solution. Hence, if we wish to prevent the formation of sugar, it was not seen to have been sufficiently attended to by Harley.

In another experiment in which a powerful dog had been killed by section of the mediastinal aorta, after 42 hours' starvation, blood was collected from the:

(a) the Vena Portae
(b) right side of heart
(c) from a portion cut off liver
(d) from aorta to inferior vena cava.

It is not denied that each of these bloods contained a trace of sugar, but it was said, unqualified evidence of it was not got in that from the liver, just which came to the notice to confirm than oppose Paré’s observations. It is evident that the digesting so many anterior veins of the collecting of blood from the various sources mentioned must have taken some time, so consequently, the very results follow from it that we could expect if Paré’s observations, as to the rapidity of change of the hepatica and passage of sugar into the blood of death, be correct. If the glycerinic theory on the other hand had been true, we would have expected...
The three days of starvation to which the animal was subjected before being killed must not have had much effect on the amount of glycerine, for Bunsen found an amount as 0.93 per cent of sugar in the brain of a dog which had been starved 14 days, 101 days after 12 to 15 days complete abstinence of food he has found very slight traces of sugar in the brains of dogs.
to have found nearly as much sugar in the hepatic vein, and of inferior quality to the liver, from the fact that no long was glycogen was converted into being transformed into sugar according to the old theory, no long would we expect in account of its great disintegrability to have found it in the blood of the system generally. The fact too that the blood in the right side of the heart was doubtful which Harvey applies as a proof of the correctness of the Bernad's idea, seems to me to be exactly opposed to it, for the example of the 'it had turned after death to become converted into sugar a piece into the blood in the liver itself, so as to be detectable in notable quantity there, could not have possibly reached the right side of the heart, especially if the portal vessels had been ligatured, as it flows there in great quantity posterior to the liver, also on account of most of it having escaped into the abdomen when most of its liver was cut off.

Thus experiments to this, the only ones known of as yet having been published to disprove the correctness of Parry's experiments, do not compute them, and in the smallest degree, as seem add support to the original glycogenic theory.

But while his observations have been attacked, they have on the other hand also been confirmed by Dr. M. Russell, but he seems to think that the
and destruction of the amniotic is very different from what
Perry imagines. He points out strongly the fact previously
observed that the fibroins of albumin of the portal blood
soon to be used up in some way by the liver. It seems to
destroy that coincidently with this process of desintegration,
the liver, in the case of the desintegrated compound, may be
injected into the non-nitrogenous fraction, which consists
of normally escaping as sugars, enters into the hepatic
portal blood as a nitrogenous constituent of its protoplasm,
partly he thinks as a substance resembling globulin in
some respects, in others, albuminoids.

If we examine the tissues of the foetus after the 8th
and 9th months of the placentas of many animals or
any before them, by Bernhard, we will find them regu-
larly loaded with a substance closely resembling the
amniotic of the liver. What this substance in the por-
tal tissues is gradually converted into the highly
nitrogenous principles of muscle, there can be little
doubt. Mr. Wm. Renouf is the first of opinion that
the liver may be quite able to do for the adult,
while the tissues in general, do for the foetus. Dr. Wilks
the Dr. derived from the desintegration fibroins
being that it cannot altogether escape from the
bile - with the hepatic. To support this theory he attemptes to show that in proportion to the amount of plasma which disappears, the quantity of B. in the bile increases; but that the colonies or corpuscles of the bile in its passage, tho' no longer greatly augmented, at the same time it seems to contain a new agitated compound resembling somewhat casein. During active digestion at least the hepatic blood contains a much lesser quantity of this than arterial; the latter in it, turns more than the portal. Along with this we find a great increase in the colonies or corpuscles of fat being known to physiologists. The great is this increase that the formation or reconstitution of colonies or corpuscles has been considered by some as one of the most important functions of the liver. Although it is hard to find that the idea of the liver being a blood forming organ is not one yet it still seems to me very doubtful. Hypothesis that a substance in all respects resembling albumen should take to itself within the liver, be derived from the metamorphosis of albuminous compound, & become thus converted either into a material resembling a colloidal blood cell or casein. Upon this much more relations between hepatic is fats to the part of the
formation of the latter being so much increased by the ingestion of large quantities of starch or sugar, the ultimate destination of the latter will, I think, more likely be found to have some connection with the production of fat. The rapid absorption of fat in diabetic patients, in whom the starch is sugar, or converted into sugar, or in which the amyloid passes out of the system as a useless material after its conversion into sugar, seems to me to bear strongly on the point in question, but the subject is one the unraveling of which will require the skill and ingenuity of the ablest physiologists.

Having thus reviewed the present state of our knowledge of the so-called glyogenic excess, I pass on to a short sketch of the pathology of a disease which ought not only to be interesting to us on account of its frequency, so often disastrous results, but also on account of its connection with those very physiological subjects in which I have been engaged in reviewing.

Diabetes — the name first given by Antonius to indicate that class of diseases in which there was an excessive excretion of urine, must necessarily have included many besides the one with which we have at present to deal. In fact, without entering
About 1844 Mr. Be the offered what then appeared to be a rather ingenious chemical explanation of the cause of the disease in question. It had long been known that sugar is destroyed in the presence of an alkali. Consequently, it was thought, if the sugar introduced into the circulation does not find the affinity suitable for its destruction, it will accumulate there to be excreted in the urine. Hence the proper method of treatment according to this theory would be the administration of alkalis.
To a history of this disease we may briefly state that it was not till 1872 that sugar was discovered in the urine by an acquaintance of Dr. With his 2 more than a century a half elapsed before this was known to be identical with grape sugar. Indeed, the close of the 18th century—in accordance with the physiological notions of his time, which attribute to the gastric juice the power of changing according to the nature of the food it had to digest—being alike with an animal acid with a vegetable diet—was divided to an alteration in the digestive processes, due to the fact that from he imagined the gastric juice had acquired changing vegetable element into sugar. Hence arose the plan of treatment which has come down to us in his name. Such a view of course was founded on many erroneous physiological ideas, but the true cause of it was not very obscure.

Let me here observe that one important point in reference to this disease has not yet been so strongly pointed out as it ought to have been, viz., that glycosuria, like albuminuria, is merely a symptom consisting in an increase of the normal constituent of the urine to such an extent as, if persistent, to give rise to any formidable, if ultimately, usually fatal results.
A previous affection has been noticed in several
cases of other complaints accompanied by a new
flow of urine, and also by, from my case, the abscess
noted in the kidneys of a rabbit, into whose veins sugar
had been injected.

I am inclined to think that the state of the
vein will depend upon whether it has been damaged
by a slow and gradual decline, for while the
abscess in the first case has been found large,
engaged with blood and charged with sugar, if the
abscess or gradually with the patient, progressively
atrophy or sugar will be found.
The third very salient feature is that the bodies of patients who have died of this disease shows the absence of the appearance of the kidneys, a circumstance commonly in accordance with the increased size they have to perform nothing more. Others have occasionally noticed a thickened vascular state of the kidneys which we cannot evade in considering that it is usually called by such labels of disease as "doubled work." It has indeed been written by Fitscher that the tissue is more homogeneous, firmer than usual, as also darker in color, but grains on the centurio maintains that that organ is in no way altered and that he has not been able to detect any microscopic changes in it.

I think them it must be evident that we cannot ascribe the disease to any organic structural alteration of the blood substance of that it ought to be ascribed to some alteration in its functional activity as understood Berners' idea. He imagined that there was an exaggeration of the functional activity of the lungs, leading to a production of pegan in excess of its power of destruction, or that the exaggeration of congestion then may be due either to an increase in volume of the pegan itself, or perhaps to an increase in the quantity of pegan contained in its tissue.
This view is supported by the fact that the spectrum never altogether vanishes, though it is very weak. The guilt is made exclusively animal.
The cause too he believed might be either in the
bone itself, or in what organ or in the nervous
system. If the glycemic thing, then the infection as
being founded on a P. motion, condition of the liver, its
expiration fell to the ground. Another idea was that
the formation of sugar in the liver might indeed remain
the same, but that there was some impediment of
effect to its normal destruction. But as this situation
is now been known to take place, this thing falls
to the ground also.

Let us see therefore what explanation of the phenomena
of this disease may be offered in accordance with the
theory of the formation of amyloid substance in the
liver of the views of Parry. If the liver, from any
reason was incapable of producing action of assimilating
the sugar derived from the food of their skin in an
active state of food, it must necessarily be that the systemas
would be undoubtly in these great quantities, as a
numerous ingredient of the blood, to be excreted by the
lungs. We have at present no proof of what the assimilating
function of the effect seen in a healthy state is not independent
we know will from the principle of fact, that common
but, such as acting too long, a quantity of asphagnos
(Stanley) or from, or in fact of any parallel phenomena
which may cause an increase of sugar to such an
It sometimes happens that in this ground class there may be impurities in the first of the patient from his assuming the foot of his table and sowing poisonous articles. It used to be thought that more urine was passed than could be accounted for by the fluids they took; but M. Proust found that when the patients were separated, strictly watched, as much 140 grams as they chose to drink, no more urine was passed than could be thus accounted for.

The smallest quantity of sugar sometimes seems to act in diabetics, producing an increased empty stomach, as Proct observed.
extent as to give rise to a temporary diabetes. On some occasions it is evident that no more sugar escapes by the urine than may be accounted for as taken in the food, but there is a second class in which this want of assimilation persists, the organ in combination with something more, for in this case we can find more sugar than is actually taken in the food, so in a third class of cases again it appears that the pancreatic element may be taken up to a certain extent, unless that ordinarily so small one, without producing glycosuria.

It is evident however that this defect in the assimilating power will not explain all cases, for we often find that the sugar continues to be passed in some amount even when all such fermentary articles are strictly excluded. The amyloid itself, if it is true, may be formed from albuminous substances, but we have scarcely any reason to believe that albuminous matter may be decomposed into glucose or even as the video. It is thought to maintain in the blood. So such a case we may believe that the amyloid passes into sugar from some fermentative action of the function of the liver. Experiments indeed have shown that such a congestion as may be caused by imperfect circulation, or obstruction to the flow of blood from the liver, may cause in increased amount of amyloid into the blood, so that many diseases causing embarrassment to the breathing
Their according to me. According to Payr & Wiedenm. because it is a chronic inflammation leading to the formation of cavities. Probably both causes.

Out of 4 Diabetic patients I have examined, this was the only cause assignable in two.
of obstruction to the circulation sets in a similar manner.

But in the last stages of Diabetes this may be a direct state of the lungs, this is not generally the case at first. I am inclined to believe that this disease state is some sort of the Diabetes, resulting from an altered state of the blood, deeply affecting the processes of nutrition. It is the way that I think we may at least in part satisfactorily account for the rapid progressive ascension of lossy weight in such patients, from the underlying microporous quantities of animal food.

But the real causes giving rise to this disease still remain without a clue to their solution, for all this we have imagined it to be traceable to cats in many instances, we are still in ignorance as to how this acts. It has been said to be an hereditary disease, or the demon in some cases to be true, or again it may not have occurred in quite a few people. A temporary Diabetes has been proved experimentally in at least one case in which the cause of a horse on the right by poaching pure butter to it. On one case it might be due to rupture of the blood cells or escape of unliquid into the blood. It is an objection often dependent on certain special lesions, which in my opinion may give the following cases.

(2) A little girl was brought into one of the London Hospitals with fracture of the case of the skull. She died...
Another idea was that it might be related to some
any influence on the circulation that the liver, and
which, the obstruction to breathing such energy
products might cause.
few symptoms of an examination, the urine in the bladder was
very pungent. There was an effusion into the floor of
the abdomen in this case, to which I am inclined
to attribute it. On another case, that of a medical
practitioner who had an attack of opthalmia followed by tonic
palsy of the left side, Diabetes showed itself in 5 weeks.
So rapidly indeed is it connected with cerebral
lesion that Dr. Marshel endeavours to show, that such lesions
so frequently the consequence, so not the cause
of Diabetes, thinking it quite possible that if the
disease might give rise to hemi- or paraplegia just
as it does to a stroke of fever. On the case of
a female who had been Diabetic for 7 years, whose
left eye, having been a central attack, he found a deep
final atresia between the back part of the eye
optic thelomas and the corpora quadrigemina, which he
was inclined to ascribe to the Diabetes. I think how
how that this idea is by no means supported by the
actual facts of cases brought forward. In the mem-
randum, in such a long standing Diabetes, might be
only a coincidence.

But there are some evidences that the presence of sugar
in the blood causes considerable alteration in the nutritive processes. It is a well-known physiological
fact that the normal relationship between
The blood to the tissues is one of the great aids in maintaining the circulation. The presence of a large quantity of sugar in the blood probably modifies this relationship in normal cases, and may render the blood unfit for the healthy discharge of its functions. In these cases many of these structural and functional disorders are common among diabetics. Thus it is, that we may account for these conditions, found by the breaking of living tissue, so common in the latter stages of diabetes, or else for the production of cataract, in many instances, as with this disorder. Brief experiments indeed seem to prove that the latter is very intimately connected with the presence of sugar in the blood. Dr. Mitchell ob.

...
As a similar circumstance ascribes the occurrence of
large, dry necroses to an gangrene which contin-
ues.
...the more general and extended effects of which will may of times be described.

No doubt there may be more to account for the rapid diminution of vitality produced than the mere loss of a valuable ingredient of the food or the presence of oxygen in the blood; but we cannot precisely explain why one patient should get so much worse than another, even though not allowing so much oxygen to escape by the urine. Indeed the it is evident that we are not yet able to fathom the true causes of this disease, it should be our earnest effort to gain a correct knowledge of the physiology of the subject, remembering that without such knowledge we will strive in vain to elucidate its true pathology.

It is only when these recognised symptoms go hand in hand, that we can hope to make progress or see the day when the pathology of such diseases as Diabetes will be clear to us. Othen but not till then, can we expect to adopt treatments at present directed to the alleviation of symptoms, become really efficacious in retaining young men in restoring to health those of our fellow creatures who suffer under this painful malady.