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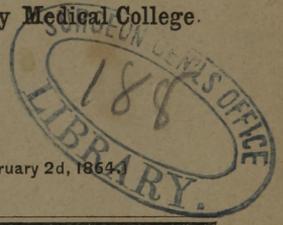
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Howard Townsend

GLYCOGENIC FUNCTION OF THE LIVER.

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BY HOWARD TOWNSEND, M. D.,

Professor of Physiology and Materia Medica, Albany Medical College.

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[Read before the New York State Medical Society, Albany, February 2d, 1864.]



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That the liver secretes bile has been long known, but that it performs in the animal economy another important function which is the production of a sugar, has only been known since the year 1848, when M. Claude Bernard, Prof. of Physiology in the College of France, demonstrated to his class this function, which he denominated the Glycogenic Function of the Liver.

Both Magendie and Prof. R. Thompson showed long since that when large quantities of saccharine or amylaceous matters were employed as food, the general mass of the blood is found to contain an appreciable portion of sugar, but M. Bernard has by his experiments proven that a sugar nearly allied to glucose is a constant constituent of the blood drawn from the hepatic vein, ascending cava, right auricle, and pulmonary artery of all animals, whether they may have been fed upon amylaceous or saccharine substances or upon food entirely destitute of these principles. In fact, that the liver can actually generate sugar from other than amylaceous compounds, which fact Bernard demonstrated by obtaining sugar from the substance of the liver, even of animals which he had fed for a long period on animal food alone, and this discovery of Bernard's was afterwards verified in the Giessen Laboratory (Liebig's). The blood in the hepatic vein of these animals was found to contain sugar, though none could be detected in the portal vein, proving that it had been elaborated in the liver.

In herbivorous animals whose food contains a large supply of amylaceous and saccharine matter, the liver does not thus furnish any very large amount of this sugar, but on the contrary a portion of the saccharine constituents of the portal blood seems to be converted, in its passage through the liver, into fatty matter.

In carnivorous animals, though, which have already a supply of fat in their food but no sugar, the transforming process would seem to be of a different kind, sugar being produced *de novo*, although it

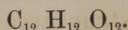
has not yet been determined from what element of the blood it is elaborated.

There is a strong probability that the production of this liver sugar takes place at the expense of the protein compounds, and that it is the chief means through which the products of the disintegration of muscular and other albuminous tissues are made available for the maintenance of animal heat by means of the combustive process.

Of the character of the sugar thus produced in the liver little is yet definitely known, but it would appear far to surpass even glucose in the readiness with which it is carried off by the respiratory process, for according to Bernard, twelve grammes may be injected into the blood with no more effect upon the urine than is produced by 2.5 grammes of glucose, or of 0.5 of cane sugar.

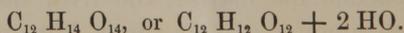
The word Glycogene, which gives the name to this function of the liver, is derived from two Greek words, *γλυκνς*, *sweet*; *γενεσις*, *generation*. The glycogene which is elaborated by the liver, is the first formation in the hepatic tissue, which secondly becomes converted into liver sugar by a process of catalysis.

This glycogenic matter is regarded as intermediate in its nature and properties between hydrated starch and dextrine, according to Pelouze its ultimate composition is:

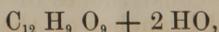


If this glycogene be mingled with human saliva, at a temperature of 100° F., the mixture will be found to reduce the salts of copper just as glucose will, proving that the glycogene has been converted into sugar by a catalytic process, just as vegetable starch would be changed under like circumstances.

Glucose is the term now commonly employed in chemistry for grape, fruit, starch and honey sugar, a variety of sugar occurring naturally in many vegetable juices. It differs from cane sugar in being much less soluble in water, and also less disposed to crystallize, and if it be injected into the blood vessels it does not pass off to an equal extent by the kidneys. Its chemical composition is:



Cane sugar, *Sucrose*, the chemical formula of which is:



is chiefly obtained from the sugar cane. If it be injected in any considerable amount into the general circulation, it is neither assimilated nor is it removed by the combustive process; but

like soluble salts when thus introduced, it is removed by the kidneys, being speedily detected in the urine.

Of grape sugar it would require a much larger quantity to be injected into the general circulation before a trace of it could be detected in the urine.

Magendie gives the following as the proportions in which different sugars require to be injected into the jugular vein before they can be detected in the urine :

Cane sugar	1
Sugar of milk	5
Glucose	50
Liver sugar	240

Fifty times as much glucose as cane sugar must be injected before it can be detected in the urine, and nearly five times more of liver sugar than of glucose before it can be detected. Hence it is obvious that this liver sugar is applicable to some purpose within the system, not requiring to be cast out as a foreign substance.

Though much has been established by physiologists as regards the function of the liver, there yet remain many points to be determined, and before we can have any accurate knowledge of its phenomena, we must have a more accurate and positive knowledge of its histology or minute structure. The parenchyma of the liver consists of an aggregation of little granules one fourth to one half of a line in diameter, which granules are called *acini* or *lobules*. Though not very distinctly marked in the human liver, they are clearly so in the liver of the hog, forming little polygons, each independent of its neighbor, and presenting a very distinct outline.

Each lobule or acinus of the liver represents in its structure a miniature of the whole organ, therefore describing one, gives an idea of the histology of the whole gland.

In each acinus or lobule we find :

1. A mass of hepatic cells.
2. The terminal ramifications of the venæ portæ and the hepatic veins.
3. The biliary apparatus consisting of the radicles of the hepatic duct, and the terminal branches of the hepatic artery.

The cells found in the liver which constitute its proper secreting substance are irregularly polyhedral from $\frac{1}{20000}$ to $\frac{1}{10000}$ of an

inch in diameter, having soft granular contents, some minute oil globules and a nucleus.

Minute branches of the *venæ portæ* (interlobular veins), are found in the spaces between the lobules or acini forming a vascular network covering the entire surface of the lobules excepting their bases, these send off branches which penetrate into the lobule, from which plexus the intralobular vein has its origin, which intralobular vein is a rootlet of the hepatic vein.

The hepatic cells fill up the meshes of the capillary plexus of the lobule, and in their aggregate whole constitute an epithelial network, which is intermingled with the web of capillary vessels. These elements of the liver probably constitute its glycogenic apparatus.

The hepatic duct enters the liver at its transverse fissure along with the hepatic artery and portal vein, accompanying these vessels to the lobules. In its course it gives off many arborescent branches, from which arise capillary tubes entering the substance of the lobule; these tubes are lined by a single epithelial layer made up of small cells, but the mode of origin of the radicles of the hepatic duct is still very obscure. The hepatic artery accompanies the hepatic ducts to the lobules, supplies them with very numerous branches, and finally terminates in the capillary plexus of the portal vein.

This biliary plexus was first described and figured by Kiernan and since by Beale. This apparatus of the biliary ducts and the hepatic artery constitute a tubular gland. The liver, therefore, may be considered as made up of two glands intimately intermingled. One, the blood gland, which is concerned in the secretion of sugar, and the other, the tubular gland, in the secretion of bile.

Though, as we thus see, we have much yet to learn of the histology of the liver, of its minute structure, before we can have a very precise knowledge of its physiology. Still we now know something tangible as regards its function, for we have lately learned through the investigations of Bernard, that this large gland plays a more important part in the functions of the economy than merely secreting bile, which is the elaboration of liver sugar, which during health is a constant process. Glucose is the term used for this liver sugar, yet it is not strictly correct, for though liver sugar closely resembles glucose, it is not identical. It is a sugar of animal origin common to all species of

animals yet known, and may be distinguished from all other sugars by the readiness of its decomposition in the blood. It has its origin in the tissue of the liver most probably in one of the group of cells which we have been considering, though it is a secondary product produced by the transformation of glycogene which is found anteriorly to the liver sugar, and which is easily converted into this sugar by any of the animal ferments, like those contained in the blood, or the ptyalin which is found in the saliva, by all of which glycogene is converted into sugar by a catalytic process similar to that which would transform starch under like conditions.

This sugar is absorbed by the blood from the tissue of the liver, and disappears soon after entering the general circulation, ordinarily not to be found in the lung tissue.

The precise nature of the changes which it undergoes after entering the vascular system is not known, but according to Lehman and Robin, it becomes at first converted into lactic acid ($C_6 H_6 O_6$), which decomposes the alkaline carbonates of the blood, setting free their carbonic acid and forming with the bases lactates of soda and potassa, and thus aiding very materially in the respiratory process, and the evolution of animal heat.

Whilst speaking of the Glycogenic function of the liver thus in detail, we must, if it be but a mere allusion, notice the work lately published in London by Dr. Pavy of Guy's Hospital, on Diabetes, who having followed Bernard's course at the college of France, and at first enthusiastically adopted his views, now in this new work combats the views of Bernard denying that the liver in a normal state can secrete sugar, considering the phenomena the result of a *post mortem* change, or owing to some embarrassment in the hepatic circulation. He acknowledges that glycogene is developed in the hepatic cells, he designates it "amyloid substance," but the sugar he thinks can only be found after death, he gives notes of some experiments of blood "drawn from the right ventricle during life, containing scarcely a trace of sugar; whilst after the subsequent destruction of life, the blood which flowed from an incision into the right heart gave indication of a copious saccharine impregnation." Pavy considers that "Bernard's observations are not incorrectly recorded, or his experiments inexact; but that fallacious inferences, as shown by more extended investigation, have been drawn from these

experiments and their results." One more quotation is all that we will make from Dr. Pavy's interesting, but by no means conclusive work. He writes :

"Although I can not attempt to offer an explanation of why the amyloid substance escapes as it does transformation into sugar during life, whilst the effect takes place with such rapidity after death, yet the fact remains the same."

This certainly seems a trivial mode of endeavoring to refute M. Bernard's thoroughly scientific investigations, and logical deductions. Yet Dr. Pavy has a quasi supporter in one of the ablest physiologists of the Faculty of Medicine at Paris, Longet, who in speaking of these views of Pavy, says, "they seem to merit consideration," and when speaking of Bernard, says, "without mistaking the importance of the results obtained by Claude Bernard, we cannot accept the interpretation that this skilful experimenter has given to those facts with which he has enriched the science."—[Longet, *Traité de Physiologie*, vol. 1, fascicule 3, page 935).

This theory of the Glycogenic function of the liver, as established by Bernard, is now so well known, so generally received, that it seems almost necessary to apologise for occupying the time of the society, in minutely describing it, but we have been tempted thus to do, because of a successful effort in exhibiting this liver sugar from the human liver in an experiment lately performed before the class at the Albany Medical College, which was very satisfactory for, as all who have investigated the subject of the glycogenic function of the liver, too well know, it is exceedingly rare to be able to detect it in the *human* liver, while it is the common sequence of an examination of the liver of animals, not but what it is produced in the human liver just as it is in the liver of animals, but in our investigations with the human liver, we very rarely have the opportunity to experiment upon one in a healthy condition. Consequently sugar is rarely found in the human liver. To quote Bernard's own words on this point, he says: "As to the presence of sugar in the *liver of man*, it is evident that in the *greatest* number of cases where it has been sought after, *it was impossible to detect it.*"—[*Leçons de Physiologie*, page 182]. And in the same work, he says: "During severe maladies, particularly acute ones, the nutritive functions are seriously impaired, the function of the liver ceases, the liver *producing no more sugar.*"

I may be permitted to add that, though a witness of many of Bernard's experiments made at the College of France, it was never there my good fortune to see sugar extracted from the *human* liver.

Previously to performing the experiment before the society, of exhibiting the sugar from the human liver, I will give a brief account of the case which affords us this demonstration.

Not long since, a terrible affray occurred in a bar-room of one of the prominent hotels of our city, between two desperate characters, which resulted in the death of one of the combatants; he being shot through the heart by a ball from a pistol in the hand of his opponent.

The man, who died almost instantaneously, was, in his physique, like a Hercules; some 35 years old, and a magnificent specimen of robust health and strength, and as with most of his fraternity—coming from a class commonly called “roughs”—he drank deeply, and intoxication was one of the exciting causes of this fatal quarrel.

The autopsy was performed some twelve hours after his death, when a portion of the liver was taken (which, by the way, gave a very strong odor of alcohol), and having been broken into a pul-taceous mass, and thoroughly washed in order to remove all the blood possible, was boiled so as to coagulate the albumen and concentrate the liver juice; then the mass was thrown upon a filter and the fluid filtering through was again filtered through animal charcoal, when it came forth a clear opaline fluid, pure liver juice. This juice, boiled in a test tube with some of the *cupro-potassique* test, gave the characteristic reddish-fawn color proving that it contained sugar. Had there been no sugar in the liver juice, the blue color of the test would have remained unchanged, as it did when applied to juice extracted from the lung of the same man. Such was the result of the experiment before the class in the lecture on physiology, as had been the result when the experiment was conducted by Prof. George F. Barker, in the laboratory of the college.

We used Kletzinski's cupro-potassique test, the formula for which is as follows: 2 parts saturated solution of sulphate of copper, 3 parts of glycerine, 4 solid caustic potash.

If this be dropped into a solution containing sugar, the deutoxide of copper is robbed of one of its equivalents of oxygen by the sugar because of the strong affinity of sugar for oxygen,

and the copper is thrown down as the red protoxide; whereas, if there be no sugar, the sulphate of copper remains unchanged, a deutoxide, retaining its blue color.

We obtained a like result with Trommer's test and the other commoner ones, but Kletzinski's is so delicate that it is unnecessary to resort to any other.

NOTE.—The experiment was performed before the society with the same satisfactory result which had been obtained in the experiments at the college. The sugar of the liver juice de-oxidising the deut-oxide of the sulphate of copper, throwing down the red prot-oxide of copper, whilst the copper test remained unchanged, when dropped into the fluid pressed out of the lung tissue, proving that it—the lung juice—contained no sugar.

