ON THE

PHYSIOLOGY OF DIABETIC SUGAR

IN

THE ANIMAL ECONOMY.

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&c. &c.

SINCE Professor Bernard, rather more than ten years ago, announced that the liver possessed a sugar-forming function, no subject in physiology has received a more careful examination than that of glucogenesis. In Germany, France, America, as well as in these islands, a multitude of investigators have toiled in this newly-opened gold-field of science, and have brought to light many important facts.

The aspect of the question is now, however, undergoing a change, for recent observations show that there is reason to doubt the truth of Bernard's discovery, which for a time seemed supported by such unequivocal evidence that it had been received as an established physiological fact.

It is proposed in the following paper to endeavour to give a simple, and, at the same time, faithful account of the history and present condition of our knowledge of the origin of sugar, and the changes it is liable to, in the animal economy.

It may be urged by some that details are here entered upon of a too elementary nature, and that facts are cited, and experiments enumerated, which are no longer new to the scientific world. To such it must be answered that this communication is not intended for the perusal of those who have kept pace with the progress of physiological investigation on this subject, but rather of those whose multifarious professional occupations prevent them from searching out for themselves from the immense mass of material which has, during the last few years, accumulated upon this subject, what is substantially true and what is incorrect. Starting then with the simplest facts, it shall be my aim to indicate what accurate information we have on this important subject, and to show, without entering into controversy, how far the careful observation of independent inquirers has yet reached in establishing new truths with reference to sugar in the animal economy.

Some readers will, perhaps, not deem it superfluous if, before entering more directly upon the subject, a few remarks are premised upon the varieties of sugar met with in the organic structures, and the most convenient tests for the detection of sugar in organic solutions.

In the vegetable kingdom several kinds of sugar exist; of these, grape-sugar is, so far as elementary analysis is concerned, identical with diabetic sugar. In animals two varieties only are found—*diabetic sugar and sugar of milk.*

The latter, known also as *lactine*, *lactose*, *salt of milk*, is an essential ingredient in the milk of all mammalia, but is not met with in any other secretion; it readily undergoes change into lactic acid, and, either in the digestive process by passing through the liver, or by the action of dilute acids, is transformed into diabetic sugar.

Diabetic sugar, equally well-known as *glucose*, *grape-sugar*, *sugar of urine*, *liver sugar(?)*, *sugar of starch*, *fruit sugar*, is found to exist normally in the animal economy, and in certain morbid conditions makes its appearance in considerable quantities in some excretions. Every one knows that the most striking feature of the formidable disease, diabetes, is the existence of a large quantity of this sugar in the urine; and the same material has been found in the serum of blisters, the sweat, the pericardial serum, &c., of diabetic patients.

The attention of physiological chemists has of late years been so much directed to the "sugar question," that, as a natural result, a considerable variety of tests has been devised for the detection of saccharine matter in organic solutions. For the benefit of any one wishing to try the various merits of each test alluded to, reference is made to the publication, in which it will be found more fully described. The liquor potassæ test of Moore[a]; the chloride of tin test of Maumené[b]; Boettgers[c] subnitrate of bismuth test, and Loewenthal's test-solution formed with protochloride of iron, may each and all have especial advantages, but by much the greater number of test solutions selected by chemists for the ready detection of glucose belong to the class known as *cupro-potassic tests.*

[a] Lancet, p. 751. September, 1844.

[b] Archives Générales de Médécine, vol. xxii., p. 494. 1850.

[c] Zeitschrift der k. k. Gesellschaft der Aerzte zu Wien, September 20, 1858; and Journal de Physiologie, vol. ii., p. 145.

To this category belong Trommer's, Kletzinsky's[a], Capezzuoli's[b], Donaldson's[c], Barreswils[d], Fehlings[d], &c., of which, as they will be constantly referred to in the following pages, the two latter may be spoken of at greater length. Besides these, the all important test by fermentation, and the beautiful method of optical analysis devised by M. Biot, and depending upon the action of a liquid containing sugar upon polarized light, deserve special notice.

The test solutions of Barreswil and Fehling are very similar to each other, and are for ordinary purposes the most ready and convenient mode of detecting the presence of diabetic sugar; they have the great merit of not only indicating its presence, but, by a little care, of showing with considerable accuracy the amount of glucose contained in a given quantity of a saccharine solution. Certain precautions, however, are necessary in the use of these test solutions, for, if kept for a considerable period, these liquids undergo a change which causes them alone to yield a precipitate on boiling; it is well, therefore, occasionally to test whichever is employed by boiling it, and so prove that it has not undergone the peculiar change which, causing itself on being boiled alone to yield a copper oxide, would occasion the mistake of supposing sugar to exist in a solution where it was not really present. When the fluid to be tested contains blood, albumen, colouring matter, or any organic constituent of the body, which might interfere with the action of the copper test, such materials are best got rid of by mixing the fluid with animal charcoal, and filtering. Animal charcoal is unquestionably a better means for effecting this object than either acetic acid, or crystallized sulphate of soda, all albuminoid matters, colouring matter of the blood, uric acid, &c., being completely retained on the filter by its aid, and the clear liquid thus obtained being equally suited for either the cupro-potassic or optical tests. Although these test solutions are to be regarded as very valuable, giving indications in general very accurate and delicate, especially when combined with the use of animal charcoal, yet it must be remembered that this reaction does not give an absolute certainty of the existence of sugar; glycerine, tannin, cellulose, chloroform, &c., may pro-

[a] Dublin Quarterly Journal of Medical Science, p. 93. August, 1855.

[b] Journal de Chimie Médicale, p. 359. 1844.

[c] Traité de Chimie Anat. et Physiol., par Ch. Robin et F. Verdeil, vol. ii., p. 570; and Journal de Chimie Médicale, p. 641. 1851.

[d] Leçons de Physiologie Experimentale, par M. Claude Bernard, troisième leçon, p. 49. Cours des Semestre d'Hiver, 1854–5.

duce various degrees of a reaction similar to glucose. Hence the necessity of not relying solely on any cupro-potassic test.

Barreswil's Solution.

	Grammes.	Grains.
Cream of tartar, ...	50 =	771·7
Carbonate of soda, ...	40 =	617·36
Sulphate of copper, ...	30 =	463·02
Potassa cum calce, ...	40 =	617·36

Distilled water, enough to make the whole when dissolved measure one litre (1·76 imp. pint.).

One hundred cubic centimetres (28 fluid drachms) of this solution are exactly discoloured by one gramme (15·434 grains) of glucose.

Fehling's Solution.

	Grammes.	Grains.
Sulphate of copper, ...	40 =	617·36
Concentrated solution of tartrate of potass, ...	160 =	2469·44
Ley of soda, of specific gravity 1012,	560 =	8643·04

Distilled water, enough to make the whole measure one litre (1·76 imp. pint).

Ten cubic centimetres (2·8 fluid drachms) of this liquid are precipitated completely by 11·5 cubic centimetres (3·2 fluid drachms) of a solution containing 5 per cent. of glucose.

If either of these reagents be added to a solution containing diabetic sugar in sufficient quantity to produce a decided blue coloration, and the solution be then boiled, the liquid loses its transparency, passes through different shades of green, yellow, &c., and finally deposits a reddish precipitate of protoxide of copper. According, however, as either the sugar or the re-agent predominates, every intermediate shade of colour, green, yellow, red, &c., may result, but it is the reduction of the metallic oxide, not the precise tinge of colour, which is the important character.

Fermentation Test.—This test, which, as every student knows, acts by causing sugar to undergo vinous fermentation, whereby it is converted into alcohol and carbonic acid, is attended with more certainty than any other. As each equivalent of sugar gives rise to the formation of two equivalents of alcohol, four of carbonic acid, and two of water, it is possible, by estimating the amount of carbonic acid formed, to make use of this as a quantitative as well as a qualitative test for sugar. It is true that it requires a longer time for its reaction to take place than the others, but, on the other hand, it is not interfered with by the presence of those colouring matters, &c., which must be got rid of before the employment of the cupro-potassic reagents.

It is unnecessary to dwell upon the details of this method[a] of detecting the presence of sugar, which are to be found in every hand-book on this subject; but it should not be forgotten that this test does not yield such *infallible indications* as some physiologists would have us believe. Although we are told that the property of fermenting characterizes sugar, inasmuch as sugar is defined as a substance which undergoes alcoholic fermentation, yet it has been recently shown by a chemist of rapidly rising reputation, M. Berthelot[b], that glycerine, mannite, dulcine, sorbine (substances having many properties of importance in common with sugars, yet not considered identical with them) are also capable of undergoing alcoholic fermentation in the presence of yeast. The yeast used in these experiments should be well washed, so as to be carefully freed from traces of sugar or fecula, and, to avoid error, a comparative experiment should be made with pure water in a tube similar to, and in like circumstances with that in which the liquid being tested is placed.

The method of optical analysis of solutions containing sugar gives evidence of extreme delicacy, for polarized light makes known differences in sugars when chemical analysis fails to detect any. The sugar of fruits causes a deviation of the plane of polarization to the left, while diabetic sugar causes a deviation to the right. The sugar known to exist in the fluid of the allantois, causes polarized light to deviate to the left like cane-sugar, yet has the other properties of glucose: it ferments easily, turns brown with potash, and reduces the salts of copper.

Although it has been long known (since in 1677 Thomas Willis first indicated the fact) that in certain morbid conditions the urine and other secretions contain sugar, it is only in comparatively recent days that the normal existence of this substance in the animal economy has been pointed out. Since the investigations of Professor Bernard, presently to be

[a] The directions given by F. W. Pavy, M. B., in his paper on Saccharine Matter, &c., Guy's Hospital Reports, vol. viii., p. 321, in reference to this method, are clear, simple, and practical.

[b] M. Berthelot, sur la Fermentation Alcoolique, Annales de Chimie et de Physique, 3e Serie. 1857.

detailed, have drawn much attention to the subject, diabetic sugar has been more carefully sought for in the healthy secretions, and has been found existing normally, or at least upon slight disturbances of health, where it was not formerly at all supposed to exist.

Furthermore, it has been discovered that injuries and excitations of parts and organs not hitherto looked upon as immediately connected with diabetes, may give rise to this complaint in a more or less permanent form. To the mind of the scientific physician nothing is more pleasing or more full of practical importance than the study of those conditions where, so to speak, health and disease meet,—where the normal state approaches to, and slight deviations from the normal state give rise to, symptoms which, when exaggerated, constitute formidable disease. Here it is his province to search for the beginnings of disease,—to seek for the early commencement of maladies at first remediable, but at a later period hopeless. Hence the necessity of looking carefully to the presence of sugar in the excretions of health, and hence the value of the experiments which show under what various circumstances the diabetic condition may exist.

Independently of the supposed sugar-forming function of the liver, glucose is found in the blood of animals fed on amylaceous diet; and, according to the experiments of Berard and others on animals fed on meat, sugar formed, as he conceives, during the digestive process enters the animal organism through the absorbents and thoracic duct. It is true that the existence of sugar in the fluid contained in the thoracic duct of a meat-fed animal may be accounted for by some as being derived from the lymphatics of the liver; but Berard has proved the existence of sugar in the lacteals of the mesentery before joining with those coming from the liver. The analysis of Bernard himself and Lehmann prove that the blood may contain sugar even during perfect health; and if the quantity amount to anything considerable, the kidneys, more promptly than any other glands, undertake its elimination. We are told—but unfortunately these facts are not supported by the corroborative testimony of all observers,—that the urine contains sugar during fœtal[a] life; that in old age also the urine becomes saccharine; and that in women[b] nursing, or during the later stages of pregnancy, a

[a] Compare Dr. W. D. Moore on the Existence of Sugar in the Urine of the Fœtus, No. 39 of this Journal, August, 1855; and Bernard, Leçons de Physiologie Exper., p. 393. 1855.

[b] Compare the statements of Th. Kirsten of Leipzig, Schmidt's Jahrbuch, vol. xcvi., p. 185; H. Blot, Gaz. Hebd., vol. iii., p. 41, 1856; and E. Wiederhold and Leconte, Schmidt's Jahrbücher, vol. xcvii., p. 14.

notable amount of sugar is to be found in the urine. Professor Brücke, indeed, goes further with reference to the existence of sugar normally in the renal secretion. He says, that up to the present time sugar has been sought for in the urine as the symptom of a grave malady. Now, on the contrary, this principle is found to form an element of normal urine. He has published a memoir, in which he has announced the discovery that the presence of sugar is constant in the urine of man in the healthy state[a].

Dr. Hammond[b] has found sugar in his own urine after living for six days exclusively upon starch; but it can hardly be said that this is a normal presence of sugar, nor yet is it the result of disease, although it must be admitted that one could not determine whether the saccharine urine may be the result of the starch diet simply, or of the dyspepsia which resulted from six days of such diet. That disordered digestion is not unfrequently followed by transient diabetes, is well known. So full of interest do these cases of transient diabetes seem, that I cannot refrain from giving Dr. Harley's account of his observations made upon himself, which are both instructive and amusing:—

"About five years ago," he says, "at a time when I was much occupied in studying the physiology of diabetes, I regularly tested my urine twice a day, and on one occasion I found it to contain a small quantity of sugar. On the day in question I had partaken freely of asparagus salad, and, thinking that this might perhaps be the cause of the presence of sugar, I determined to try the effects of a greater quantity. The following day, the sugar having entirely disappeared from the urine, I again partook of the same salad both in the morning and afternoon. In the evening, on testing the urine, I found very distinct indications of sugar. As the observation was to me one of great interest, I determined to make some further experiments on the subject, in order to discover how many hours this state of saccharine urine would continue. During two days I ate large quantities of the asparagus salad, taking care to have it made as stimulating as possible with vinegar and pepper. The result was far beyond my expectations; for, instead of the sugar disappearing from the urine in a few hours after I had ceased partaking of the diet in question, it continued to be secreted during several days, until I at last became very much alarmed lest the disease had been permanently induced. On the evening of the fourth day the sugar had almost entirely disappeared; but on the fifth it returned in increased quantity,

[a] Brücke, Journal de Physiologie, vol. ii., p. 338. 1859.
[b] Transactions of the American Medical Association, 1857.

so much so, that a drop falling on the boot left a distinct white spot. I could not account for the recurrence of the disease, as I had been particularly careful in my diet during the two previous days. I have mentioned," continues Dr. Harley, "this experiment, because it appears to me that if a flow of saccharine urine be induced in a healthy person—as I consider myself to be—by disordering the digestion and over-exciting the liver, it is very probable that a cause, insignificant in itself, but operating upon a predisposed constitution, might tend to produce the disease"[a].

Sugar in the urine has been found after eating cheese and other substances of difficult digestion. It is worthy of remark that Dr. Jesson, of Dorpat, has rendered horses diabetic by feeding them with hay damaged by moisture. The writer of this Paper has found sugar in abundance in the urine of brewers' horses fed upon "the grains" in the brewery to which they belonged. M. Reynoso has observed sugar in the urine as a result of the internal administration of lead, arsenic, and sulphate of quina; and Leconte, after giving dogs nitrate of uranium, found them diabetic.

Physiological experiment has shown that in animals the diabetic condition may be created by injuring or exciting organs, which might at first seem to be but remotely related to each other. Of these experiments, perhaps the most remarkable is that of Bernard, whereby a puncture made in the middle line of the floor of the fourth ventricle is followed by a flow of saccharine urine.

For the performance of this experiment, it is necessary to perforate the occipital bone with an instrument suited for the purpose, a little posterior to or below its tubercle. The cavity of the cranium having been entered, the animal being now fixed in an exceedingly steady position, the instrument is to be pushed onwards in a direction downwards and slightly forwards, until the basilar bone meets its point; it is then carefully withdrawn in the same direction in which it entered. In this operation the cranium, the cerebellum, and the medulla oblongata are successively pierced; when successfully performed upon a healthy and vigorous animal, the urine is found in a short time after to be strongly impregnated with saccharine matter. The presence of sugar may be detected in an hour, or an hour and a half after the puncture has been made, and may last for a period varying from some hours to some days

[a] Harley on the Physiology of Saccharine Urine, British and Foreign Medico-Chirurgical Review, p. 199. July, 1857.

The precise space on the floor of the fourth ventricle where the puncture must be made, in order to produce artificial diabetes, is exceedingly limited; according to Bernard[a], when the puncture is made in the middle line of the floor of the fourth ventricle, exactly in the centre of the space comprised between the origins of the acoustic and pneumogastric nerves, there is an increase of both the hepatic and renal secretions at the same time; if the puncture be a little higher up, there is very often merely an augmentation of the quantity of urine (polyuria without diabetes); if a little below the point indicated, the passage of sugar alone is observed, the urine continuing scanty (diabetes without polyuria).

The mode of producing glucosuria in an animal poisoned with *curara* is, Bernard conceives, explicable by the action of this poison upon the nervous system. Curara is a substance used by the savages of South America to poison their arrows, and has the remarkable property of completely annihilating the functions of the cerebro-spinal nervous system. Although in the present state of our knowledge upon this subject, it may be difficult to give an unhesitating assent to Bernard's explanation of the fact, yet the experiment upon which the fact is based is of a nature so striking that it is given in Bernard's own words:—" We introduced under the skin of the back of a large dog, at the commencement of the digestion, a certain quantity of curara in solution; at the end of twelve minutes the effect of this substance was manifest, and respiration was arrested; artificial respiration was then practised for two hours and a-half, with precaution, and only stopping for half a minute now and then; during this time the circulation continued perfectly right; the blood was black in the veins, in the arteries, arterial red; but it became black everywhere when insufflation ceased. During all this time there was abundant secretion of tears and saliva. A wound, which had been made some days previously, in order to collect the pancreatic fluid, and which was beginning to cicatrize, gave exit to an abundant serosity. The urine was examined, on different occasions, without sugar being found there; after two hours and a half it was proved to be present in large quantities. The proportion of the urine was increased, and the muscular contractility was much exaggerated; violent contractions resulted from touching a muscle with the point of a bistoury."

Artificial diabetes may be produced by other means than giving rise to lesions of the nervous system, either by mecha-

[a] Leçons de Physiologie Experimentale, p. 339. 1855.

nical injury or the action of poisons directly affecting the nervous centres; it may arise from injury or irritation of the liver. Persons have been known to become diabetic from contusions in the region of the liver; and a case has been cited in which an individual who had received a kick from a horse in the right hypochondrium, had, in consequence, saccharine urine, a symptom which disappeared when he recovered from the contusion. Some of the most valuable results which have been obtained in this direction, we owe to Dr. George Harley, of University College. So long ago as during the summer of 1853, he communicated to the Société de Biologie of Paris, the discovery of a new mode of producing diabetes artificially in animals, by means of stimulants introduced into the portal circulation. He has since repeated and extended his experiments, which have been confirmed and somewhat modified by Bernard. Alcohol, ether, chloroform, methylated spirit, or ammonia injected into the portal vein, give rise to the secretion of saccharine urine. Into the portal vein of a good-sized dog in full digestion, Harley injected fifteen drops of liquor ammoniæ, diluted with forty cubic centimetres of water. In twenty-four hours afterwards, on the animal being killed, his bladder was found enormously distended with urine, which not only reduced the copper in the liquid of Barreswil, but fermented most rapidly. It is not necessary that these stimulants should be introduced directly into the circulation by injection into the vena porta to excite diabetes; the same effect is known to result from the injection of stimulants into the intestine simply, and from this experiment we can readily understand how diabetes mellitus may be produced by the abuse of alcoholic drinks in persons predisposed to the disease.

Another mode of causing artificial diabetes has been pointed out by M. Reynoso, which consists in disturbing the function of the lungs by causing an animal to breathe irritating or stimulating vapours; thus temporary glucosuria is consequent upon the prolonged inhalation of ether or chloroform. In order, however, to induce a flow of saccharine urine, the inhalation must be kept up for a considerable time; and in testing the urine in this, as in other experiments where chloroform is used, it must be remembered that this substance causes the reduction of the metallic oxide in the cupro-potassic solutions; and that, consequently, it is the test by fermentation upon which the experimenter must rely. It must be enough at the present time to state that the repetition of the experiments here given as to the methods of inducing artificial diabetes, by many independent and careful investigators, leaves little or no doubt as to the truth of the facts; but the theories which have been broached, and the hypotheses which have been founded upon these experiments, are as numerous as the individual observers. An analysis of such theoretic views would be out of place.

Let us now consider the question, Does the sugar which is found in certain conditions in the excretions, in various organs, in the blood, &c., come into the animal organization from without? or are there organs in the animal body which can fabricate sugar, no matter what may be the nature of the aliment supplied?

It is not my intention to answer this question, but merely to bring forward what may be regarded as truthful evidence *pro* and *con*. In truth, Bernard's announcement—that nature, not being willing to intrust the animal creation to an alimentation often depending upon accidental circumstances, had placed within the bodies of animals an organ, the liver, which is capable of making sugar from blood—has, since it was first promulgated in 1848, up to the present time, given rise to constant discussion, which seems far from being yet terminated. It has been said already that Bernard's doctrine seemed based upon such unequivocal evidence, the so-called sugar-forming function of the liver has been received and recorded in many of the best hand-books of physiology as an established fact. The acceptation of it, however, was not universal. In 1855, in the "Comptes Rendus" of the Parisian Academy of Sciences, Bernard replies to an attack of M. Figuier, who denied that animals possessed the power of forming sugar, and referred that found in the liver of carnivorous animals to an external source. M. Sanson[a] has upon the same subject ventured to differ from the learned academician, and so lately as last year states his conviction (based upon experimental proof) that there is but one source of sugar in the animal economy, and that this source is external; and he conceives that carnivorous animals find in the tissues of the vegetable feeders upon which they live the dextrine which is the primitive material from which is formed the sugar necessary for the performance of their functions.

The objections urged against Bernard's views have been made the subject of special investigation by the French Academy; and although the commissioners conceived that M. Figuier[b] had based his arguments on grounds that were unten-

[a] De l'Origine du Sucre dans l'Economie Animale, Journal de Physiologie, vol. i. 1858.

[b] Comptes Rendus de l'Académie des Sciences, Juin, 1855.

able, and M. Sanson failed to make good his statement: the question, nevertheless, cannot be regarded as settled, nor can it be said that unanimity of opinion prevails with regard to its details.

Among the researches which cast doubt upon the sugar-forming power of the liver, those of Dr. Pavy[a] unquestionably stand foremost, and are entitled to the fullest consideration. In his communication in Guy's Hospital Reports of last year he tells us that, from a consideration of all the facts brought forward, which in every respect, to the fullest extent, corroborate each other, and which stand uncontroverted by any single result he has yet encountered—he thinks we are unavoidably led to deny to the liver that sugar-forming function, with which, in recent days, it has been endowed by physiologists. In whatever manner subsequent discoveries may solve the difficult problems connected with this question; whether or not it shall hereafter be clearly shown that Bernard was in error in supposing that the tissue of the liver is actually endowed with the power of producing sugar: it must never be forgotten how much is due to the genius of this great experimental inquirer; how many new facts his spirit of physiological research has elicited; how many truths are now to be regarded as permanent scientific acquisitions, which, but for him, would still lie hidden. The vigour of his intellect, the zeal of his pursuit of scientific knowledge, his indefatigable earnestness, his accuracy of observation, have opened so vast a field of inquiry, and have afforded such abundant material for investigation, that to him in justice must be attributed such acquisitions to knowledge as have been evolved from the intellectual fermentation excited by the novelty of his ideas and the originality of his experiments. In fact, to read his own words and follow his own reasonings upon his "Nouvelle Fonction du Foie"[b], points out the necessity of putting in no other language than his own the details of his researches, with such clearness and simplicity are they given.

In the year 1843 the following facts became for Professor Bernard an object of physiological investigation. The strange affection known as diabetes mellitus is characterized by the appearance of a superabundance of sugar in the organism, to such a degree that the blood is surcharged with it; all the tissues are impregnated, and the urine especially contains it,

[a] The alleged Sugar-forming Function of the Liver: Guy's Hospital Reports, 1858.

[b] Nouvelle Fonction du Foie considéré comme Organe Producteur de Matière Sucrée chez l'Homme et les Animaux: Paris, 1853.

sometimes in enormous quantities. Yet, constantly in such cases, and particularly when the disease is intense, the quantity of sugar expelled by the diabetic patient is quite above that which could be furnished by the feculent or saccharine substances which compose his diet, and the presence of saccharine matter in the blood and its expulsion by the urine are never completely arrested, even at a time when there is absolute suppression of saccharine or feculent aliment.

It was after an attentive examination of these circumstances, observed in diabetic patients, and which are known to all physicians, "that," says Bernard, "I was led to think that there might be in the animal organism phenomena still unknown to chemists and physiologists, capable of giving birth to sugar from other sources than substances containing fecula." Thus led to engage in a series of experiments, Bernard was at first surprised at the unexpected results which he obtained. An adult dog, in vigorous health, was fed during seven days exclusively on meat, of which he ate *à discretion;* at the end of this time he was sacrificed by pithing, while the digestive process was going on. The blood of the hepatic veins was collected in order to search therein for saccharine matter, and great was the surprise of the experimenter when he proved, very readily, and in a manner admitting of no doubt, that there existed a considerable quantity of sugar in the blood, which was going out of the liver of a dog, which, by the fact of his exclusively meat-diet, had been deprived of sugar during seven days. This result was too unexpected and too important to be accepted without scruple. Repetition of the experiment was the only way of removing doubts, and this was done with similar results, and has been done since with like result, by the most skilful physiological experimenters in the New and in the Old World.

No doubt whatever now exists as to the fact that in animals fed exclusively upon meat for a period even of many weeks, when killed promptly by section of the medulla oblongata, no sugar is found in the blood *entering* the liver by the vena porta, while sugar does exist in the blood *leaving* the liver by the hepatic veins; but this fact has been variously explained by different investigators. M. Figuier has at least the merit of showing that further researches were required regarding the *new function* of Bernard, and the latter consequently engaged in new experimentation, which gave another aspect to glucogenesis. He submitted to careful washing the vessels of the liver of a healthy dog, which had been for some time fed on meat exclusively, and was killed by cutting the medulla oblongata. This was done by passing a stream of water through the liver, entering by the portal, and having exit by the hepatic veins, after traversing the organ. The washing was prolonged until the liquid discharged from the hepatic veins was no longer discoloured by blood, and did not give any evidence of containing either sugar or albumen. This object was accomplished in forty minutes, and then a small portion of the liver examined in the ordinary way was proved to be wholly free from sugar. Twenty-four hours later the fluid dribbling from the liver was found rich in sugar. From this experiment, Bernard concluded that the sugar is formed in the liver at the expense of a particular material by a kind of fermentation; in short, he came to the conclusion, that in the liver of an animal just killed there exists sugar, easily soluble and capable of being washed out of the hepatic tissue; but that there likewise exists in the liver-structure a less soluble material, which remains behind after washing, yet is easily convertible into sugar by the action of some ferment already formed in the liver. Advancing step by step, Bernard found that this material, which was slightly soluble in water, proved insoluble in alcohol, and he struck out the following mode of showing its presence:—The fresh and yet warm liver of a recently killed animal was cut into slices, washed, and then pressed through a hair sieve. The pulp thus obtained was treated with alcohol, until all sugar was removed, and then dried. This pulverized mass, if mixed with water at the ordinary temperature, and let stand for a time, gave evidence of sugar; but, if similarly treated with hot water, and allowed to stand for even a longer time, no trace of sugar made its appearance. Bernard was thus led to surmise that there existed in the liver a substance analogous to amylum, and this substance, he and Hensen, about the same time, succeeded in obtaining in the pure state. Bernard named it glucogenic substance. Since its discovery it has received a multitude of names, each author conceiving that his own name possessed peculiar merits. It has been called by Hensen, *sugar-forming substance;* by Nape, *amylum;* by Schiff, *liver-starch;* by Pavy, *hepatine;* by others, *glucogene* or *amyloid substance.* If I may venture to offer an opinion upon the subject, I should suggest that the last name be that generally adopted, for, although resembling starch, it is not identical with it. Moreover, in naming a newly discovered substance, probably of high import in the economy, it is not well to involve in that name any theory with regard to its use or function; and, further, it appears from the researches of microscopists of high repute, that a material allied to, if not identical with that in question, is not confined to one organ, the liver, nor one function, that of making glucose; hence the necessity for a name embracing a wide generalization. M. Sanson[a] still insists, and his assertion receives some support from the report of M. Poggiale[b], that "glucogenic matter is met with in all the tissues of herbivorous animals." Bernard, who had already pointed out the presence of a sort of "animal fecula or glucogenic matter" in the muscles and lungs of the fœtus[c], has recently shown that it exists at a particular period in the placenta, and has even given a drawing of the microscopic appearance of the filiform papilla from the amnion of the calf, showing the cells filled with "amylaceous matter;" while M. Rouget[d], in a communication of great value, the first part of which only has as yet been made public, expresses the hope that in the subsequent part of his work he will be able to show that the presence of "amyloid substances," as a constituent part of the elements of normal tissues, is not limited to one single order of animals, nor to a single organ, the liver, among vertebrata, but is common to the elements of many organs; sometimes only during certain periods of their development; sometimes all through life, and plays a most important part in the definitive constitution of the tissues of a great number of the vertebrata.

Whatever name may be given to this substance, whether glucogene or amyloid matter, when obtained from the liver in the pure state, it is a whitish, tasteless, inodorous, neutral, non-crystalline powder, insoluble in alcohol and acetic acids, but soluble in water. It gives with iodine a reaction resembling dextrine, sometimes resulting in a blue, sometimes a dark chestnut brown colour. It does not reduce the copper of the cupro-potassic liquid, nor does it ferment in presence of yeast; but if boiled with dilute mineral acids, or placed in contact with diastase, saliva, blood, pancreatic juice, it is quickly transformed into sugar, which both ferments and reduces Barreswil's solution. Its properties give it a place between starch and dextrine. Pelouze, by the action of fuming nitric acid, has transformed it into xyloidin, and gives for it the formula C_{12}, H_{12}, O_{12}. Injected into the veins of living animals, it is rapidly converted into sugar; and, being eliminated by the

[a] Journal de la Physiologie, &c., p. 104. Janvier, 1859.

[b] Rapport de l'Académie de Médécine sur le Formation de la Matière Glycogene, Journal de la Physiologie, p. 549. 1858.

[c] Sur une nouvelle Fonction du Placenta, Journal de la Physiologie, &c., p. 31. 1859.

[d] Des Substances Amyloides, de leur Role dans la Constitution des Tissus des Animaux: same Journal, p. 85.

kidneys in this condition, gives rise for a time to strongly marked diabetes: and herein there is a prominent point of difference between amyloid substance and the material which it so closely resembles, dextrine,—for the latter remains in the blood for a long time unchanged. Alkalies interfere with and arrest the transformation of this substance into sugar when in contact with saliva, blood, &c.,—a property which will subsequently be seen to be of much practical importance; for by its help the change of this substance into sugar can be promptly arrested by injecting a strong solution of potash through the liver soon after death.

It is of consequence to know what may be the readiest and best means of obtaining the amyloid substance of the liver. Bernard[a] has indicated, in his first memoir upon the subject, the following proceeding for the extraction of "glucogenic matter:"—The liver is to be divided into very thin slices, and immediately placed in boiling water, in order that the glucogenic matter may be prevented from undergoing change into glucose. The pieces of liver are next bruised in a mortar, and then boiled for about an hour, in a quantity of water sufficient to bathe the mass. This is expressed, and the expressed liquid filtered. The liquid thus obtained—which is of an opaline tint—is mixed with four or five times its volume of absolute alcohol, and there is immediately formed an abundant flaky precipitate, of a yellowish-white colour, which is collected upon a filter, and washed several times with alcohol. There is thus obtained an impure "glucogene," containing azotized matter. Its aqueous solution is coloured by iodine, but does not reduce the cupro-potassic solution, nor ferment in contact with yeast. To free it from the foreign matter which it contains, it is to be boiled for half an hour with a very concentrated solution of caustic potash, and, a little water being added, it is to be filtered. The solution must now be again precipitated by the addition of four or five volumes of alcohol. The deposit, again collected upon a filter, is submitted to repeated washing with alcohol, to remove the potash. The substance thus prepared contains a little carbonate of potash, which is not soluble in alcohol; it is, therefore, indispensable to redissolve the whole in water, saturate the carbonate of potash with acetic acid, and

[a] Gazette Médicale, March 28, 1857. It is but justice to state that Hensen, if not prior to, at least independently of Bernard, isolated the glucogenic substance of the liver: in December, 1856, he exhibited this substance before the Naturwissenschaftliche Gesellschaft at Wurzburg; and on the 1st of April, 1857, in Virchow and Hoppe's Pathological Institution. But the French physiologist has the advantage of having first published an account of it, and the manner in which it is to be obtained.

a third time precipitate with alcohol. The acetate of potash remains dissolved in the liquid; the "glucogene," then separated by filtration, is perfectly pure.

Such was the first procedure of M. Claude Bernard. Wishing, however, to shorten the process, as well as to use less energetic agents, he imagined a much more simple means of separating the "glucogenic matter." It consists in pouring a great quantity of crystallizable acetic acid upon a very concentrated and filtered decoction of the organ that one wishes to examine. At once a whitish precipitate separates, which is "glucogenic matter," for the albumenoid substances are soluble in acetic acid. When the organ examined contains no glucogene, acetic acid gives rise to no appreciable precipitate. This procedure possesses incontestable advantages; it readily, and in the space of a few minutes, discovers whether or not glucogenic substance is contained in any given tissue or organ. The acetic acid does not destroy the albumenoid substances, nor expose the experimenter to the risk of forming himself the very substance he seeks for. In this manner is obtained from the liver, in sufficient quantity for chemical examination and physiological experiment, amyloid substance of animal origin, closely similar to, if not exactly identical with, the amyloid substances thus designated by Virchow, and met with by him and others —Meckel among the number—in the parietes of the ventricles of the brain, in the prostate gland, in the degenerated walls of the small arteries of the spleen and intestine, in the liver, kidneys, and lymphatic glands; now also known to exist in the epithelial formation of the fœtus,—not only in the epithelia of its respiratory and digestive passages, but even in that of the skin and its appendages.

It may be, that some may say it is premature to speak of this material as of animal *origin*, yet it seems certain, that an amyloid substance, having reactions analogous to and being nearly allied with cellulose, starch, and dextrine, is met with widely diffused through the animal organization; that this substance[a], having a particular constitution and special characters, establishes a sort of transition between nitrogenous and non-nitrogenous compounds; between the proximate principles of the animal and those of the vegetable tissues; and, finally, that it may be as justly regarded as having a truly animal origin as the fats and oils of the animal economy.

Yet it must be admitted, that both M. Figuier, and later, M. Sanson, have adduced some important experiments tending

[a] M. Rouget, des Substances Amyloides, *op. cit.*, p. 89.

to prove that the glucose or the amyloid substance, from the transformation of which the glucose of the animal economy results, is of external origin. It is, no doubt, quite possible, that as the kidney is endowed with the power of laying hold of and eliminating from the blood at each round of the circulation, with inconceivable promptitude, the urea which exists in the blood in barely recognisable quantity, so the liver may be able to lay hold of and store up within itself the amyloid matters, which, in the case of carnivorous animals, can only be introduced into the circulation in the minutest quantities, through the medium of the amyloid substance known sometimes to exist in the tissues of the herbivora.

Without entering into the controversy as to whether it be the special attribute of the liver to form this substance, or to appropriate it when introduced into the system from without, it may be stated to be no longer a matter of doubt, that the hepatic organ during health contains a large quantity of it within its secreting cells. Knowing this, and remembering that extreme facility with which the amyloid substance of the liver is changed into sugar in the presence of blood, the question arises, Does this transformation occur in health and during life, while the circulating blood permeates the structure of the liver? or, is the sugar found in the blood of the hepatic veins in the *primary* experiment of Bernard, the result of post-mortem change? The amyloid substance of the liver being immediately after death transformed into sugar by contact with the blood, a transformation controlled, if not entirely prevented, by the presiding agency of the nervous system during life. The latter view is that taken by Dr. Pavy, and very ably advocated by him in his papers in Guy's Hospital Reports of last year. Deficient in many respects as I feel this communication to be, when I consider the vast amount of labour which has of late years been bestowed upon the subject of which it treats; scanty as is the selection made from the abundant supplies of the literature of the subject, yet it would be indeed incomplete were I to pass over the researches of Pavy in silence. They are of a nature curiously interesting and instructive, and exhibit in their author not merely the patient spirit of inquiry after truth, but the all-important quality in a scientific investigator, that of readiness to resign a theory which had been at one time adopted, as soon as new facts are discovered, at first sight unimportant but which observation shows to be inconsistent with the theory in question. Not to be led astray by foregone conclusions; not to be blinded by an hypothesis based upon even apparently sufficient data; nor too closely wedded to a theory from which it may become almost painful, if not impossible, to be disunited, are principles often with difficulty carried into practice.

I have myself verified most of the conclusions arrived at by Dr. Pavy in his paper "On the alleged Sugar-forming Function of the Liver," in Guy's Hospital Reports, 1858, and have repeated his experiments with various modifications. While, therefore, I offer my testimony as corroborative of the results which he has obtained, I feel it right, in giving a resumé of his researches, to lay before the reader his own account of the experiments which most strongly support the position which he maintains.

It had been the conviction of Pavy, as of Bernard, whose pupil he had been, that sugar was being constantly poured into the general circulation from the hepatic veins, and he was engaged in prosecuting inquiries into the destruction of the sugar thus formed in the animal economy. This destruction he fancied took place in the lungs, and while engaged in some investigations relative to this subject he found it necessary to abstract blood direct from the right side of the heart of a living animal, by introducing a catheter through the right jugular vein into the ventricle. To his surprise he found the blood thus obtained scarcely at all impregnated with saccharine matter; so unexpected was this result, and so much at variance with the views which he at that time held, that he confesses that he was inclined to the opinion that the blood could not have been fairly drawn from the ventricle, or that perhaps it was accidentally derived from the blood of the descending cava, not yet freely mixed with that coming from the liver. These suppositions he was by degrees obliged to set aside, as he found, from a great number of observations, that blood thus obtained yields the merest trace of sugar under an ordinary and natural condition during life; the reaction of Barreswil's solution with it being so slight as sometimes to be overlooked altogether. In repeating this experiment, I have arrived at results quite in accordance with those of Pavy. If the blood be dexterously withdrawn from the right side of the heart, which is best managed by introducing through the jugular vein a small silver catheter fitted to a pipette, the bulb of which is capable of containing about an ounce, and which has a piece of vulcanized Indian rubber tubing so fixed to it that the blood can be sucked in by the action of the mouth; and if, at the same time, the animal be prevented from making any convulsive movements, scarcely a trace of sugar will be discovered in the serum. But if an animal under precisely similar circumstances, so far as regards diet, be killed by pithing, and, ten minutes after death, an ounce of blood be collected from the right side of the heart and the large veins leading to it by the aid of a catheter introduced after opening the thorax, the serum of this blood will be found rich in sugar.

From a consideration of these and like facts, Pavy was led to believe that the blood issuing from the liver was, during life, either entirely free from sugar or very nearly so; and, further, it occurred to him that the liver might also, during health and life, be free from saccharine matter. This supposition, he admits, so strong was his conviction of the truth of the glucogenic function of the liver, he regarded as in the highest degree improbable. Nevertheless, he determined to investigate further, and, being aware of the presence in the liver of the amyloid substance already spoken of, and knowing the readiness with which this substance is transformed into sugar when in contact with blood and at an elevated temperature, he saw the necessity of adopting some means of arresting this transformation without at the same time destroying the principles concerned.

This transformation may be retarded or entirely prevented by cold or by the presence of an alkali or acid. We have, therefore, within our reach two modes of immediately after death preventing the amyloid substance of the liver from being converted into sugar, as it otherwise will be, owing to the moderately elevated temperature of the animal body and the contact of the blood. These methods consist in, either with all possible expedition reducing the liver to a very low temperature, or injecting into its vessels an alkaline (300 grains of potash in three ounces of water), or an acid solution (300 grains of citric acid in three ounces of water)[a].

The following are the primary experiments of Pavy. A healthy dog, which had been for some time kept under observation and fed upon tripe, but not fed on the day of the experiment, was killed by pithing. The abdomen was instantly opened by free longitudinal and tranverse incisions, and 300 grains of potash in three ounces of water injected through the portal vein towards the liver. The injection was allowed to penetrate only a portion of the liver, a part of it having been firmly held by an assistant to secure it from contact with the alkali. The syringe being removed, and the portal vein ligatured, the non-injected portion was separated from the other before the grasp of the assistant was loosened. The injected

[a] The quantities here given are only sufficient for partial injections of the liver. Dr. Pavy prefers the latter, as it acts less unpleasantly on the hands. To obtain the liquid for testing, it is necessary to heat with sulphate of soda, filter, and neutralize. Barreswil's solution can then be used.

part, which was rendered pale and soft, was treated in the following manner, to test for sugar:—A piece, being placed in a mortar, was triturated to a pulp. A sufficient quantity of strong sulphuric acid was cautiously added to neutralize the alkali, and leave a slight acid reaction; by which a solid mass was procured, that yielded a clearish fluid on squeezing in a piece of flannel. This fluid was collected, and rendered alkaline with potash, so as to enable the copper test to be applied. It was found that boiling with the Barreswil solution produced no precipitate of suboxide of copper. The non-injected part, treated with the sulphate of soda according to Bernard's method, gave a most abundant reduction of the copper solution. But in order to render the experiment complete, and show that the treatment to which the injected portion of the liver was submitted had not destroyed the sugar, a piece of that which had not been injected was now pounded in a mortar, with a sufficient quantity of a strong solution of potash to thoroughly saturate it, and allowed thus to remain for about five minutes. It was then treated in the same manner as the injected portion, and, on boiling with the Barreswil solution, gave as strong a reaction as that which had been simply heated with the sulphate of soda. After the injection had been effected, the chest was opened, and the contents of the right ventricle removed. The blood presented a perfectly natural appearance, for the capillaries of the liver appear to give way instead of allowing the solution of potash to pass. On examining the blood according to the usual process, the colour of the Barreswil solution remained unchanged under the influence of even prolonged ebullition.

In performing this experiment, everything depends upon the rapidity with which the injection is effected after the life of the animal has been destroyed. The transformation of the amyloid substance of the liver into sugar takes place so speedily after death, that, unless the greatest promptitude is exercised, an unsuccessful result is obtained.

The same observations are applicable to the use of cold as a means of arresting the post-mortem production of sugar, and of displaying the condition of the liver natural to life.

If a dog be suddenly killed by destruction of the medulla oblongata, the abdomen at once opened, and a piece of the liver cut off and plunged into a mixture of ice and salt, the post-mortem formation of sugar will be prevented. It is necessary to have recourse to certain precautions, in consequence of the extreme facility with which the sugar is formed after death. The freezing mixture of ice and salt should be ready before-hand, and so far liquefied, that the portion of liver experimented upon may be plunged into it and cooled as quickly as possible. A healthy dog, which had been for some time past kept upon animal diet, and had been fed at 10½ in the morning, was suddenly sacrificed by pithing at 4 P.M. The abdomen was instantly opened, and a piece of the liver cut off and thrown into the freezing mixture. The other portion of the liver, after remaining in the animal some minutes, was removed and submitted to a quantitative analysis. The amount of sugar indicated was 2·96 per cent. The frozen liver was also submitted to analysis; sections through the centre, which remained still soft, contained within a fraction of half a grain per cent. of sugar. The edges and moderately thick outside parings were treated so as to yield a highly concentrated spirituous extract. In this the saccharine impregnation was so inappreciable as to be unsusceptible of quantitative determination.

"The only just inference," says Dr. Pavy, "that I can see to be drawn from these experiments is, that the liver does not enjoy the special functional import that has in recent times been bestowed upon it by physiologists. Such a statement is not incompatible with the result of previous experiments. The conclusions upon which our former notions were based were drawn from results obtainable after death. But it now becomes apparent that we are no longer justified in regarding these results as indicating the condition that belongs actually to life. It is not that Bernard's observations were incorrectly recorded, or his experiments inaccurate, but that hypotheses were based upon them which a more extended examination of the subject has shown to have been founded upon insufficient data."

While admiring the acuteness with which Dr. Pavy has pursued the track which observation of minute results first led him to enter upon, it is a great pleasure to be able to testify to the accuracy of his observations. To bear witness to the truth of the investigations of others, or raise one's voice against the errors that others may propagate, is a duty as agreeable on the one part as it is invidious on the other. It will be believed, therefore, that it is with real gratification that I, in corroboration of the truth of Dr. Pavy's experiment, give my support, feeble though it be, to the views which he has propounded.

Known facts seem to lead almost irresistibly to the following conclusions:—That the liver exercises a special function in forming a substance, which happens to be with extreme facility, by a process allied to fermentation, convertible into sugar. The material in question (amyloid substance of the liver) is always present in the hepatic tissue in the healthy state. During life and health it seems able to resist transformation into sugar. With the destruction of life, and, as a consequence of certain injuries and diseased states, this power of resistance diminishes, or ceases to exist, and saccharine matter appears in the structure of the liver and in the blood; while, under normal circumstances, the blood circulates through the liver, and escapes charged with, at most, an exceedingly minute amount of sugar.

It has been already observed that the introduction into the circulating fluid of the amyloid substance of the liver is accompanied by the immediate transformation of this material into sugar,—a statement which may be easily verified by injecting some of it into the jugular vein of a living animal, when it at once gives rise to the diabetic condition. In like manner, if any cause—such as a blow over the region of the liver, violent convulsive movements, strugglings during operation, or during the administration of chloroform—so to speak, dislodges from the liver some of its amyloid substance, this material, thus entering the circulation, is changed into sugar; and more or less transient diabetes is the result.

While the glucogenic theory of Bernard was still undisputed, the question of what became of the sugar, which the liver was supposed to be constantly forming, was discussed with much earnestness. This question, of course, loses much of its importance in the present state of our knowledge. Nevertheless, the researches of Pavy[a] himself, as well as the experiments of Limpert and Falck[b], should not be overlooked by those wishing to search into the history of the subject before us. The latter authors have shown that every variety of sugar, when introduced into the blood in moderately large quantity, is in part thrown out by the kidneys. Of cane sugar the most is thus got rid of; of milk sugar, a smaller quantity; and of grape sugar, still less;—the last remaining almost entirely in the body when but a moderate quantity is introduced into the blood.

It is not intended in the present communication to enter into a discussion as to the pathology or treatment of diabetes. Before its pathology can be satisfactorily investigated, the physiology of the subject must be placed upon a firm basis. It is to be hoped that much has been done in this direction; and it is certain that of late years many pathological facts of much importance have been established which, but for physiology, would still remain undiscovered. Andral's pathological facts

[a] On the Normal Destruction of Sugar in the Animal Economy: Guy's Hospital Reports, 1855.

[b] Virchow's Archives, 1856; and Schmidt's Jahrbücher, vol. xc., p. 274.

regarding the production of sugar in the animal economy illustrate in a striking manner some of the views lately adopted by physiologists. The remarkable case which he cites, in which a diabetic patient limited to an exclusively meat diet, and at the time using no amylaceous food whatever, produced more than 20 ounces of sugar daily, would at least seem to show that this material may be abundantly produced in the living organism from nitrogenous compounds.

The observations of the same author on the post-mortem appearances of the liver, in five cases in which he had an opportunity of examining it in diabetic patients; Erichsen's remarks on *surgical* diabetes met with as a result of injury of the head; the coincidence of inflammatory and gangrenous affections of the skin (anthrax, &c.) with mellituria; and the connexion shown to exist between cerebral disease and diabetes: all indicate pathological conditions requiring to be carefully scrutinized before the obscurity which hangs over the diabetic condition can be satisfactorily cleared away.

Admitting that up to the present time science has done comparatively little towards materially bettering the condition of the diabetic patient, or arriving at any definite conclusions regarding the nature of this strange complaint, yet it is most pleasing to see the combined efforts of the chemist, the microscopist, the pathologist, and physiologist, all tending in the same direction, all with one object; nor does it appear unreasonable to hope that the period is not far distant when they will be rewarded by being able to grapple successfully with this formidable malady.

Since the foregoing communication was placed in the hands of the printer, I have received the last number of the "Journal de la Physiologie de l'Homme et des Animaux," containing the conclusion of M. Rouget's admirablé paper already alluded to, and one by C. Bernard on "Glucogenic Matter considered as a condition of development of certain tissues in the Fœtus." These communications will be perused with much interest by those engaged in studying the subject treated of in the foregoing pages. Professor Bernard conceives that in animals, as well as in vegetables, the glucogenic and amylaceous matters seem to be present as a constituent principle of the protoplasma, from the bosom of which the organic evolution is accomplished. He finds that all the epithelial membranes, whether of the cutaneous or mucous surfaces, contain, during a certain period of fœtal life, glucogenic matter, under divers forms. At no period of the organic evolution has he been able to find it in the nervous or osseous tissues. In embryos of sheep and oxen, 15 to 20 centimetres in length, the muscular fibre appears under the form of a tube containing nuclei, and an interspersed granular substance, which is nothing else than glucogenic matter.

Glandular tissue, like that of the nervous and osseous system, does not contain this material, the liver alone, among glandular organs, being an exception.

M. Rouget speaks of amyloid substances as being found in the tissues of vegetables under two principal forms: 1st, contained in a cell, as *amorphous* or *granular starch;* 2nd, in the condition of cell membrane, or intercellular substance—*cellulose.* These have their analogous conditions in the tissues of animals, that variety of amorphous starch met with in the cells of the roots of the dahlia, inula, &c., corresponding to the amylaceous plasma (*zoamyline*), contained in the elements of the tissues of the embryo in the cells of certain epithelium (as of the uterus, vagina, tongue); and, above all, in the cells of the hepatic parenchyma in the adult; while animal cellulose is more abundantly found in the lower regions of the animal kingdom.

Zoamyline is, then, the newest name given to that variety of amyloid substance found by Sanson in the muscles, by Bernard in the tissues of the fœtus and the placenta, and now known to every one to be abundant in the liver, and to exist widely diffused throughout the organic structures.