THE LUMLEIAN LECTURES ON THE DIGESTIVE FERMENTS, AND THE PREPARATION AND USE OF ARTIFI- CIALLY DIGESTED FOOD.

Delivered before the Royal College of Physicians.

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LECTURE II.

PEPSIN AND TRYPSIN—DIGESTION OF PROTEIDS.

VARIOUS kinds of albuminous or proteid substances are used by mankind as food. The most important of these are muscular flesh, the casein of milk, and egg-albumen from the animal kingdom—and gluten, albumen, and legumin from the vegetable kingdom.

Proteids are attacked by the digestive ferments at two points in the alimentary canal, by pepsin in the stomach and by trypsin in the small intestine. Between these two acts of digestion there is a complete break in the duodenum, owing to the abrupt change of reaction from acid to alkaline which occurs at that point.

Gastric digestion is, in all creatures, an essentially acid digestion; but the most varied opinions have been entertained as to the nature of the acid. It has been supposed in turn to be hydrochloric acid, lactic acid, acid phosphate of lime, butyric acid, and even acetic acid. Much of this confusion has arisen from not distinguishing between the acid of pure gastric juice as secreted into an empty stomach, and the acid of the gastric contents during the digestion of a meal. A good deal of light has been thrown on this subject by the recent researches of C. Richet.* This observer found himself in exceptionally advantageous circumstances for the study of the gastric juice. He had under observation a young man on whom Verneuil had successfully performed the operation of gastrostomy for the relief of impermeable stricture of the oesophagus, the result of swallowing inadvertently a quantity of caustic potash. The complete occlusion of the oesophagus enabled Richet to obtain and examine the gastric juice in a pure state, uncontaminated with saliva. All food had to be administered through the fistulous opening left after recovery, and the observer could at any moment—as in the famous case of Alexis St. Martin—withdraw portions of the gastric contents for examination. Richet also took advantage of the new method of separating the various organic and mineral acids from one another, made public by Berthelot in 1872.†

Berthelot had found, on shaking up an aqueous solution of any acid with ether and then allowed the two fluids to separate, that a part of the acid passed into the ether, and that the remainder clung to the water, and that their ratio between these two parts was a constant quantity. He called this ratio the *coefficient of partage*, and found that its value was a fixed characteristic for each particular acid. Solutions of the mineral acids were found to yield nothing, or almost nothing, to ether when agitated with it; but organic acids were found to pass into the ether in considerable, though very variable, quantities—the proportion varying in a constant ratio according to the nature of the acid.

Testing pure gastric juice, uncontaminated with food or saliva, by this method, Richet found that almost all the acid was retained by the water, and that only a small proportion—about one in twenty-two—passed into the ether. This showed that the acid of pure gastric juice was almost entirely a mineral acid, with only a minute admixture of organic acid. The organic acid (tested by the same method) exhibited a coefficient of partage closely corresponding with that of sarcocollactic acid. The nature of the mineral acid was determined by a method similar to that employed by C. Schmidt, and yielded the same result—namely, undoubted evidence that the mineral acid of pure gastric juice was hydrochloric acid. But Richet found that this mineral acid did not behave in the presence of salts of the organic acids quite in the same way as free hydrochloric acid does. The observations of Berthelot

had shown that when free hydrochloric acid is added to a solution of acetate of soda, or other similar organic salt, the mineral acid attaches the base entirely to itself and throws the whole of the organic acid free into solution—so that the mixture, when tested by the method of coefficient of partage, behaves exactly like an unmixed solution of the organic acid. When pure gastric juice was put to this test, it was found that, although it liberated the organic acid largely, it did not do so to the same extent, by a good deal, as if the mineral acid contained in it had been entirely free. It behaved, rather, as hydrochloric acid does when united with a feeble organic base, such as leucin or peptone; and, on the ground of what appear to be very careful experiments, Richet came to the conclusion that this feeble base was probably leucin, derived from the gastric mucus, and that the acid of pure uncontaminated gastric juice was hydrochloric acid in loose combination with leucin.

Richet next proceeded to examine the free acid actually existing in the stomach during the digestion of a meal in his patient with gastric fistula. He found, as might have been expected, that this differed from the acid of pure unmixed gastric juice—in this respect, namely, that it contained a very much larger proportion of organic acids, in comparison to the mineral acid, than pure gastric juice. It was evident that the mineral acid had to a large extent seized upon the bases of the acetates, malates, lactates, butyrates, and other organic salts always present in the food, and had set free their organic acids. The real work of digestion then, so far as the acid constituent is concerned therein, is largely performed by various organic acids thus set free from the articles of food which are undergoing digestion.

Richet found that the acidity of the contents of the stomach during digestion, although it varied through considerable limits, had a marked tendency to maintain the normal average. If acid or alkali were added to the digesting mass, the mean was presently restored automatically—the stomach in the former case ceasing to secrete acid, and in the latter case secreting an increased quantity of acid.

The Effect of Gastric Juice on the Salivary and Pancreatic Ferments.—The observations of Berthelot on the power of a mineral acid to set free the acids of organic salts and to take their place with the bases—and the further observations of Richet, showing that the acids actually free in the gastric contents during digestion were organic acids, have led to the re-examination of a point of some importance—namely, as to whether the salivary, and more especially the pancreatic ferments, were or were not destroyed by the acid contents of the stomach. The matter has a practical interest in this way. If the gastric acid destroys these ferments, it is evidently useless to administer pancreatic preparations by the mouth during digestion, because they would be rendered inert by the acid contents of the stomach. On the other hand, if they are not destroyed in passing through the stomach, but merely lie dormant and recover their activity in the alkaline medium of the small intestine, then we can administer pancreatic preparations during digestion with every prospect of their passing uninjured through the pylorus and proving useful in assisting digestion in the small intestine.

A series of experiments bearing on this question were submitted by T. Defresne to the Académie de Médecine and the Académie des Sciences towards the close of last year, and have attracted some attention. On the ground of these experiments, Defresne arrived at the following conclusions; namely, that saliva continued its action on starch in the stomach without interruption; that the pancreatic ferments in like manner preserved their activity in the presence of the gastric acid; that the acids of the chyme, being organic acids, did not really destroy these ferments, but merely reduced them to a state of temporary inertness, so that, when the acidity of the chyme was neutralised in the duodenum, they recovered their powers and exhibited undiminished activity both on starch and on proteids.

As the question had a direct bearing on the medicinal administration of pancreatic preparations, and indirectly on the administration of malt-diatase and malt-extract, I thought it desirable to repeat some of Defresne's experiments and to put the question raised by these experiments to the test in other ways.

One of Defresne's (apparently) most convincing experiments was the following, which I give nearly in the words of the abstract of the paper published in the Proceedings of the Académie de Médecine for Nov. 4th, 1879. When 20 grammes of dilute hydrochloric acid, having twice the acidity of the normal chyme, are mixed with 20 grammes of egg-albumen, what follows? The acidity of the medium is no longer due to free hydrochloric acid, but to the lactic and phosphoric acids of the white-of-egg which have been set free. In presence of these acids, pancreatic may be digested for two hours in the warm chamber with impunity. And if, at the end of this period, the acidity of the mixture be neutralised, digestion is accelerated and the pancreatic peptonises 38 times its weight of albumen.

* *Du Suc Gastric*, by Ch. Richet. Paris: 1878.

† *Ann. de Chimie et de Physique*, 4e série, tome xxvi, p. 395.

I repeated this experiment in the following manner: 40 grammes of chopped boiled white of egg were mixed with 40 cubic centimeters of dilute hydrochloric acid of the strength of 4 per 1000. This mixture was subjected to a preliminary digestion of two hours in the warm chamber at 40° Cent. (104° Fahr.) The object of this preliminary digestion was to allow the hydrochloric acid a sufficient time to seize on the bases, and to set free the organic acids of the white of egg. At the end of this time, 5 cubic centimeters of an active extract of pancreas were added to the mixture. A second experiment was arranged in exactly the same way, except that filtered saliva was substituted for extract of pancreas. The mixtures were kept in the warm chamber for a further period of one hour, and were then filtered and carefully neutralised. On testing the neutralised filtrates, I obtained approximately the same results as Defresne. The diastatic and proteolytic ferments of the pancreatic extract were found active, but not so active by a good deal as if the extract had been diluted to the same extent with simple water. In the second experiment with the filtered saliva, the ptyalin had preserved its activity quite unimpaired.

These experiments, however, involve a fallacy which vitiates the deductions intended to be drawn from them. White of egg has a highly alkaline reaction, and although the acid used in the experiment possessed double the strength of the normal gastric juice, it was found that the mixtures, at the end of the two hours' preliminary digestion, had only a comparatively feeble acidity—in fact, only one-seventh of the normal acidity of the gastric contents. It has long been known that the salivary and pancreatic ferments are able to resist a feeble acidity, but the question really at issue is: Can these ferments resist the average acidity of the contents of the stomach, when, moreover, this acidity is rendered still more destructive to them by the presence of pepsin?

I tested the question in this way. A distinction is drawn, and rightly, between acidity due to free hydrochloric acid, and a similar degree of acidity due to an organic acid. Now, lactic acid is a typical organic acid, and it is also an acid which is often, if not always, present in the contents of the stomach during digestion. I prepared a solution of lactic acid corresponding in saturating power to the normal gastric acid (2 per 1,000 HCl.) To 50 cubic centimeters of this dilute lactic acid, I added 5 cubic centimeters of a solution of pepsin and 5 cubic centimeters of an active extract of pancreas. I prepared a second similar experiment, but substituted filtered saliva for pancreatic extract. The mixtures were then placed in the warm chamber for one hour. At the end of this period the solutions were exactly neutralised and tested. They were both found to be absolutely inert. Not a vestige of amylolytic nor of proteolytic power had escaped destruction.

I had an opportunity of trying the same question in a still more satisfactory way. While I was examining the throat of a patient suffering from an ailment which did not affect his general health, a portion of the contents of the stomach was ejected, and fortunately caught in a clean vessel. This was immediately filtered, and about 10 cubic centimeters of clear acid solution were obtained. The period of digestion was three hours after breakfast. One half of this was devoted to testing its saturating power. It was found to possess an acidity very nearly corresponding with that of normal chyme. To the remaining portion five drops of extract of pancreas and five drops of filtered saliva were added, and the mixture was placed in the warm chamber for one hour. At the end of this time it was exactly neutralised, and divided into two equal portions. One portion was tested with a drop of starch-mucilage, and found to be absolutely devoid of amylolytic power. The other portion was added to an equal volume of milk rendered slightly alkaline with bicarbonate of soda, and was then placed in the warm chamber. Not the slightest digestive action was produced on the milk in twelve hours.

I may mention that in the above experiments I used milk as the test of proteolytic activity. I had become thoroughly familiar with the behaviour of milk with pancreatic preparations during a long course of observations, and was therefore able to detect the slightest signs of pancreatic action.

With this evidence before me, I am unable to accept the conclusions of Defresne and others in Paris, who allege that saliva and pancreatic preparations can resist the normal acidity of the stomach in full digestion; and who recommend the administration by the mouth of pancreatic preparations during the period of chymification. I will in my next lecture point out the time and the method in which these preparations may, I believe, be administered by the mouth with sure prospect of success.

Digestive Proteolysis.—The changes undergone by albuminoid substances in digestion are still very imperfectly understood. It is however known that the chief end-product of the transformation is peptone. It is also known that between any native proteid—egg-

albumen, muscle-fibrine, casein, or legumin—and the end-product peptone there are intermediate grades and by-products, which have hitherto proved difficult to define and isolate. The constitution of the proteid molecule is still unknown to chemists. That it is a highly complex aggregation is certain; and it can scarcely be doubted that the way to a better knowledge of its constitution lies in a persevering study of the action on it of the digestive ferments. It has been already seen that in the case of starch the action of diastase furnished the key to the constitution of the starch molecule; and, similarly, it is not unreasonable to expect that the mystery of the proteid molecule will be finally solved by a study of the action on it of pepsin and trypsin. Attention has hitherto been too exclusively directed to peptic digestion, which is complicated by the interaction of an acid. Pancreatic digestion is, in this respect, a simpler process—inasmuch as it requires the interference neither of an acid nor an alkali, but is a reaction, pure and simple, between the ferment and the proteid. This, however, is a question of the future.

Characters of Peptones.—The end-product peptone has been fairly isolated and its characteristics defined. If the filtered product of a pancreatic digestion of egg-albumen be evaporated to dryness in a watch-glass at a temperature of 104° Fahr. (40° C.), there remains a glassy straw-coloured residue resembling dried gum. With the point of a penknife this can be chipped off in shining scales, which may be easily reduced to a fine whitish powder—this is nearly pure peptone. This substance is extremely soluble in water; and its solutions, even when highly concentrated by evaporation, betray no jellying and no viscosity, but continue diffuent almost to the moment of desiccation; only just before drying up do they assume a slightly syrupy consistence. When the latter point is approached, the solution deposits beautiful white crystalline sheaves of tyrosin and spheres of leucin. From the constancy with which these crystalline bodies make their appearance in pancreatic digestion, it may be inferred that they constitute an essential portion of the final products of the transformation.

The reactions of peptone are mostly of a negative character. Its solutions give no precipitation with nitric acid, nor with boiling, nor with ferrocyanide of potassium and acetic acid. The behaviour of peptone with alcohol is peculiar. When a strong peptone solution is dropped into absolute alcohol, the peptone is precipitated as a white sediment, but it is not truly coagulated into an insoluble modification, as all the other proteids are; for when the alcohol is removed, the deposit is found to have preserved its solubility in water—even after prolonged contact with the alcohol. Solutions of peptone are precipitated by those metallic salts which throw down other proteids, also by tannin when the solutions are neutral. When the solutions are rendered alkaline, the cupro-potassic test (Fehling's solution), added in very small quantity, produces a rose-red coloration, whereas other proteids produce a violet tint. Physiologically, by far the most important reactions of peptone are its extreme solubility in water and its diffusibility through organic membranes. With regard to the latter point, contradictory statements have been made by different investigators. Otto Funke rated the diffusibility of peptone through the membrane of the small intestine higher than that of common salt. On the other hand, von Wittich concluded that peptones did not pass through parchment-paper more rapidly than unaltered albumen. My own observations support the view that peptone is incomparably more diffusible through parchment-paper than the native proteids. In the case of milk, the effect of digestion is very marked in regard to its behaviour in the dialyser. When milk was dialysed for 48 hours into twice its volume of water, not a trace of proteid matter could be detected in the diffusate; but when milk had been previously digested for a couple of hours with pancreatic extract, an abundant reaction with tannin and Fehling's solution was obtained after dialysing it for eight hours.

My results with egg-albumen were equally striking. I prepared a solution by agitating white of egg with nine times its bulk of water, and straining the product through muslin. When this solution was dialysed into twice its volume of water for 32 hours it yielded absolutely no reaction with tannin nor with the cupro-potassic test. But when the same solution was previously digested, either with pepsin and acid or with pancreatic extract, and then dialysed, it gave in five hours a slight but distinct reaction, both with tannin and with Fehling's solution, and in sixteen hours a most abundant reaction.

The theoretical views held by physiologists in regard to the intimate nature of the transformation undergone by proteids in the presence of pepsin and trypsin are still unsettled, but recent opinions converge towards the idea that the process is, in the main, one of progressive deduplication with hydration, similar in type to the transformation of starch by diastase. This view receives a positive support from the recent analyses of Henninger. By operating on highly purified albumen,

fibrin, and casein, Henninger* succeeded in obtaining peptones in a state of great purity. An analysis of peptones so obtained indicated that they contained less carbon and nitrogen, and proportionally more hydrogen, than their original proteids. The differences were, it is true, small, but they pointed distinctly in the direction of the conclusion that there was a fixation of the elements of water by the proteid, in the course of its transformation into peptone.

Henninger also believes that he has succeeded in reversing the process, and in reproducing an albuminous substance from peptone by operating on it with dehydrating agencies. He found that when fibrin-peptone was heated with anhydrous acetic acid at 80° C. (176° Fahr.), or was maintained for an hour at the temperature of 160° to 180° C. (320° to 356° Fahr.), it yielded a body which agreed closely in its reactions with syntonin.

The intermediate products which are generated in the course of proteid digestion, and stand between the original proteid and the end-product peptone, are very imperfectly understood. The laborious researches of Meissner and Kühne have shown that several such intermediate bodies are produced, but these have not yet been adequately isolated and defined.

[To be continued.]

ABSTRACT REPORT OF LECTURES

ON THE

COMPARATIVE ANATOMY OF MAN.

Delivered at the Royal College of Surgeons of England.

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LECTURE III.—THE RACES OF AMERICA.

THE natural history of the population of the great American continent, as it existed before the changes wrought by the European conquest which followed the adventurous voyage of Columbus, offers an interesting but difficult problem to the anthropologist. Do all these various tribes, of which one thousand seven hundred are enumerated by Keane—and these must be a small portion of those formerly existing—extending from the Polar Sea to Cape Horn, through such various climates, and inhabiting regions so diverse in their physical characters, belong, as many writers have averred, to one primary division of the human species; or are they capable of being divided into groups having as strongly pronounced distinctive characters as are to be found among the inhabitants of the Old World, as has been stated by others? Again, if we find difficulty in dividing them into well-marked groups, do we find such actual differences of character as to lead to the belief that they are all of common origin; or have we reason to think that they are the result of the mingling together, in various proportions in different districts, of two or more distinct sources of population? Furthermore, inquiry will naturally be directed to their relations with other people. Whether we consider them as one or as several people, we shall have to ask, With which of the races of other parts of the world are they most nearly allied?

The views till lately held as to the peopling of America, though perhaps under various modifications and disguises, may be grouped under two heads. 1. The inhabitants of that continent were a distinct autochthonous or indigenous people, created in the country in which they were found, and therefore not related to those of any other land. This is the theory of the polygenistic school, but is probably not held by many scientific men of the present day. 2. The monogenists mostly believe that they are descended from the Asiatic people, who in comparatively recent times passed into America by way of Behring's Straits, and then spread gradually over the whole continent as far as Cape Horn; and that their nearest allies must, therefore, be looked for in the north-eastern regions of Asia. It has also been thought by those who have held the same general views, that, at all events, a partial peopling of the American continent may have occurred from southern Asia by way of the Polynesian Islands, or from North Africa across the Atlantic. The discovery of the great antiquity of the human race in America, as

well as in the Old World, has caused a considerable modification of these theories. The proof of a very considerable antiquity rests upon the high and independent state of civilisation which had been attained by the Mexicans and Peruvians at the time of the Spanish conquest, and the evidence that that civilisation had been preceded by several other stages of cultivation following in succession through a great stretch of time; but the antiquity of the quasi-historical period thus brought out is evidently thrown into the shade by the evidence now accumulating from various parts of the United States, Central America, and the Pampas, that man existed in those countries, and existed under much the same conditions of life, using precisely similar weapons and tools as in Europe, during the pleistocene or quaternary geological period, and perhaps even farther back in time. As in Europe his works are found associated with the remains of *Elephas primogenius* and other extinct mammals, so in America are they found in contemporary deposits with *Elephas Columbi*. If the deductions commonly made from these discoveries be accepted, and the fact admitted that men lived both in Europe and America before the surface of the earth had assumed its present geological conformation, the data from which the problem of the peopling of America is to be solved are altogether changed. Recent palæontological investigations, especially those carried on with great success in the neighbourhood of the Rocky Mountains, show that an immense number of forms of terrestrial animals, that were commonly supposed to be peculiar to the Old World, are abundant in the New. Indeed, many such, as horses, rhinoceroses, camels, etc., are more numerous in species and varieties in the latter, and therefore the means of land-communication between the two must have been very different from what it is now. Taking all the circumstances into consideration, it is quite as likely that Asiatic men may have been derived from America as the reverse, or both may have had their source from a common centre in some region of the earth now covered with sea.

However this may be, the population of America has been for an immense period practically isolated from the rest of the world, except at the extreme north. Such visits as those of the early Norsemen to the coasts of Greenland, Labrador, and Nova Scotia, or the possible accidental stranding of a canoe containing survivors of a voyage across the Pacific or the Atlantic, can have had no appreciable effect upon the characteristics of the people.

The evidence derived from the study of the physical characters of the Americans shows that there is, considering the vast extent of the country they inhabit and the great differences of climate and other surrounding conditions, a remarkable similarity in essential characters, with at the same time much diversity in detail and in other characters which perhaps are not of so much primary importance as has been often thought. The construction of the numerous American languages, of which as many as twelve thousand have been distinguished, is said to point to unity of origin, as, though widely different in many respects, they are all, or nearly all, constructed on the same general grammatical principle—that called *polysynthesis*—which differs from the languages of any of the Old World nations. The mental characteristics of all the different American tribes have much that is in common; and the very different stages of culture to which they had attained at the time of the conquest, as that of the Incas and Aztecs and the hunting and fishing tribes of the north and south, which has been quoted as evidence of diversity of race, were not greater than those between different nations of Europe, as Gauls and Germans and Greeks and Romans in the time of Julius Cæsar. Yet all those were Aryans; and, in treating the Americans as one race, it is not intended that they are more closely allied than the different Aryan peoples of Europe and Asia.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—There have been considerable alterations in the mode of conducting the primary examinations in anatomy and physiology for the diploma of membership of the College. On the 2nd instant, 173 candidates presented themselves for examination, who were required to answer in writing two distinct papers on anatomy and physiology respectively, instead of one as heretofore on the combined subjects. The time allowed for the anatomical examination was from 1 to 3 P.M. After an interval of an hour, they assembled again from 4 to 6 o'clock, to answer a series of questions in physiology with the same conditions. At the oral examination, instead of proceeding to three tables for an examination of ten minutes at each, they were taken at two tables for fifteen minutes each; one in anatomy, on well-dissected and recent subjects, and three preparations from the museum; at the other, they were examined in physiology. The examiners in anatomy were, at one table, Messrs. Durham and Bellamy; at another, Messrs. Pick and Rivington; in physiology, Messrs. Power and Lowne, and Messrs. Marrant Baker and McCarthy. Mr. Christopher Heath is the Chairman of the Board.

* A. Henninger, *De la Nature et du Rôle Physiologique des Peptones*. Paris: 1878.