XLIX.—*On the Chemistry of Digestion.*

[A Discourse delivered to the Fellows of the Chemical Society.]

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By the chemical phenomena of digestion, we mean those chemical changes which food undergoes in the stomach and intestines, the object of which is to transform it into certain soluble substances on the one hand, and into emulsions on the other; for under those conditions only, can the food taken be absorbed into the blood-vessels and lacteals, and thereby effect the purpose of nutrition. If from some circumstance connected with the nature of the ingesta, or a vitiated state of the gastric and intestinal secretions, the metamorphosis in question does not take place, what has been eaten will be voided, more or less unaltered,—a fact of importance in a medical point of view.

My attention has been directed for many years to the subject of the present discourse, and I avail myself, with pleasure, of this opportunity of recording the valuable aid of my former assistant, Dr. Frederick Dupré, in a considerable portion of these inquiries.

The stomach, during the period of fasting, contains a small quantity of mucus, exhibiting a slight, though decided, alkaline reaction; this can be easily ascertained by testing the few drops of the rosy and frothy fluid obtained from the stomach of a dog having a gastric fistula, or external opening in that organ. As soon as solid food is taken, the stomach secretes in abundance a strongly acid fluid, the gastric juice, and the process of digestion commences. The action of the gastric juice on the contents of the stomach is generally considered as due to its acid constituent, and to a substance called *pepsin*, which it contains in very small quantity. It should be remembered, however, that every one of the constituents of gastric juice must have a share in its action on food; just in the same way as certain therapeutical agents, such as mineral waters, are possessed of medicinal properties, partly on account of a special substance they contain, and partly from the united influence of the whole of their constituents. Owing to this circumstance,

it is important when experimenting on gastric juice, to use, as far as possible, the secretion obtained from an animal, such as the dog, and avoid conducting the inquiry with a digestive fluid prepared artificially by mixing together a dilute acid and pepsin. I invariably used in my researches the gastric juice of four dogs, extracted from each animal through a gastric fistula with which it had been provided. The secretion was excited with hard-boiled cartilage, or soft bones. By this means I obtained, from two dogs, about a gallon of gastric juice; and a much larger amount could have been extracted within the same time, had it been required.

In order to determine the composition of pure gastric juice, it would be necessary to excite its secretion by means of hard substances, perfectly insoluble in that fluid: unfortunately, under those circumstances, as for instance, when dogs are made to swallow pebbles, the quantity of gastric juice secreted is but very small, and barely sufficient for a chemical inquiry. It must be remembered that hard animal tissues, such as cartilage, or even bone, are rapidly acted upon by gastric juice, so much so, that the fluid obtained from the stomach after the ingestion of these substances cannot be regarded as the pure secretion.

The acidity of gastric juice may be considered as one of its characteristic features. It is remarkable that chemists and physiologists do not yet agree as to the nature of this free acid, although, from the investigations of Bidder and Schmidt, Dr. Prout's opinion on the subject now prevails, and the acid substance is believed to be hydrochloric acid; the experiment which Bidder and Schmidt undertook in order to resolve the question, was as follows:—

“About 100 grammes of gastric juice were used, to which nitric acid and nitrate of silver were added; the amount of chloride of silver obtained was determined, which yielded the weight of the whole of the hydrochloric acid present. After the excess of nitrate of silver had been removed from the gastric juice by precipitation with hydrochloric acid, the fluid was evaporated to dryness, carefully incinerated, and the weight of the bases determined; the quantity of hydrochloric acid necessary to neutralize these bases was then calculated.” By so doing, Messrs. Bidder and Schmidt obtained, on the one hand, the weight of the whole of the hydrochloric present in gastric juice, and on the other, the weight of the hydrochloric acid necessary to neutralize the bases; and as they found that the total amount of hydrochloric acid present was

greater than was necessary to neutralize the bases, they concluded that gastric juice contained some free hydrochloric acid. In order to decide whether there was any free acid in gastric juice besides hydrochloric acid, these enquirers determined the acidity of gastric juice with an alkaline normal solution, and they found the amount of the base necessary for the neutralization of this free acid to be exactly, or nearly equivalent to the quantity of free hydrochloric present, which had been ascertained in the first part of the experiment; they therefore concluded that the whole of the free acid of gastric juice is hydrochloric acid.

Notwithstanding the apparent correctness of this method of investigation, the gastric juice of a dog on which I have experimented, has appeared to me, for the following reason, to contain more or less of another acid besides hydrochloric acid. I happened to place some gastric juice in Graham's dialyser, which was made to float on distilled water. After a time, the secretion contained in the dialyser had lost certain of its immediate principles, which had passed into the distilled water. At first the acid gastric juice gave an abundant precipitate with nitrate of silver, but the bulk of the precipitate gradually diminished, the hydrochloric acid passing into the distilled water; and, finally, after coagulating the albumin by heat, and filtering, the addition of the reagent failed to give even a trace of a precipitate, thereby showing that the hydrochloric acid had entirely found its way through the membrane. On testing the fluid in the dialyser at that period of the experiment, it exhibited a distinctly acid reaction; consequently the gastric juice was still acid, although it did not contain a trace of hydrochloric acid, showing that another acid was present besides the hydrochloric acid.

The acidity of gastric juice, according to Bidder and Schmidt, ranges from 0.1708 to 0.3353 % of hydrochloric acid. I have had frequent opportunities of testing the degree of acidity of this secretion, and have found it to correspond to between 0.085 and 0.303 % of hydrochloric acid; these numbers, being rather lower than those of Bidder and Schmidt. While enquiring into the acidity of gastric juice, I observed that the degree of this re-action varied according to the period after the ingestion of food, at which the fluid was collected. The first quantity removed from the stomach was the most abundant, but the least acid; gradually less and less of the secretion could be obtained, but it became more and more acid; while the last quantities

of the gastric juice which were extracted exhibited the maximum degree of acidity. The following is a table showing the quantities of gastric juice extracted from a dog bearing a gastric fistula, at different periods after the animal was fed, and also the degree of acidity of the fluid, expressed as potash, necessary to neutralize 100 CC. of the secretion. In four experiments the acidity invariably increased, so much so that the degree of acidity was considerably greater towards the close of each experiment than it was at the beginning.

Acidity of Gastric Juice.

The *time* is counted just after the dog took his meal, consisting of boiled wind-pipe. The *acidity* is expressed in grammes of potash necessary to neutralize 100 CC. of gastric juice. The experiments were made in middle of March, 1860.

No. I.

Time after food taken.	Quantity.	Acidity.
30 minutes	2oz.	0·065
40 ^m later	1oz.	0·113

No. II.

30 minutes	lost.	
30 ^m later	2oz. 2dr.	0·130
10 ^m later	7dr.	0·156
10 ^m later	6dr.	0·169
10 ^m later	5dr.	0·195

No. III.

30 minutes	7dr.	0·208
30 ^m later	1oz. 6dr.	0·227
30 ^m later	1oz.	0·273
30 ^m later	3dr.	0·377
30 ^m later ...	1oz. 5dr.	0·390

No. IV.

39 minutes	2oz. 6dr.	0·180
10 ^m later	1oz. 3dr.	0·190
17 ^m later	2oz. $\frac{1}{2}$ dr.	0·235
15 ^m later	1oz. 4dr.	0·250
8 ^m later	5dr.	not determined.

This gradual increase of the acidity of gastric juice must be due, partly to the first quantities which are secreted being diluted and neutralized by the slightly alkaline mucus contained in the fasting stomach; but more especially, I believe, because the fluid secreted towards the end of digestion, is really more acid than that secreted at the beginning. This last hypothesis appears probable, if it be remembered that the mucus of the stomach, during the period of fasting, is but slightly alkaline, and exists therein but in small quantity. Whatever be the cause of the fact, the gradually increasing acidity of gastric juice, after food has been taken, appears established, and must serve some important purpose in connection with the process of digestion, one of these objects being obviously to add to the power of the stomach of digesting those pieces of food which have not been properly masticated. The outside of each morsel of animal food, which has been masticated, will not require for its digestion the action of strong gastric juice; but the inside of the morsel, especially in the case of animals, which is not so well trituated with the teeth, will require for its digestion the action of a more powerful or more acid gastric juice.

If we consider the average acidity of gastric juice to be due to the presence of 0.253 % of hydrochloric acid; and, if it be admitted, with Bidder and Schmidt, that an adult man, weighing about ten stone, secretes in twenty-four hours about 6400 grammes of gastric juice, then no less than about sixteen grammes (247 grns.) of free hydrochloric acid will be extracted from a human adult's blood, and returned into it in twenty-four hours. This acid must result from the decomposition of chloride of sodium, as was suggested by Prout* in 1834; but he adds "What becomes of the soda from which the muriatic acid has been disunited?" He proceeds to state, as his belief, that the largest part of this soda is probably directed to the liver, and passes off in the bile. We are now aware that such is not the case, and Dr. Bence Jones, by his researches on the acidity of the urine during the period of digestion and fasting, has solved this interesting question.† Blood is always alkaline; it must be so for the maintenance of health.‡ There is, however, in the blood a constant tendency to the forma-

* Chemistry, &c., of Digestion, 1834, p. 500.

† Phil. Trans. 1849.

‡ Dr. Pavy has observed that, after phosphoric acid has been injected into the circulation, the urinary secretion contains sugar.

tion of acid; but, before the blood can turn acid, the excess of this substance is eliminated by the secretions; consequently acids are constantly being secreted from the blood, sometimes in the perspiration, sometimes in the urine, sometimes by the stomach. When the secretion of acid in the urine is active, that of the stomach is quiescent, and *vice versâ*; during the secretion of gastric juice, the acidity of the urine is greatly diminished. At the time when digestion is at its height, the acidity of the urine is at its minimum. These are the interesting results of Dr. Bence Jones' inquiries. We may therefore surmise that, during digestion, the chloride of sodium of the blood yields hydrochloric acid to the gastric juice, while the soda is immediately taken up by the acid, which, during fasting would have been excreted with the urine, but which remains in the circulation while digestion is going on.

If chloride of sodium be the source of the principal constituent of the gastric juice—*hydrochloric acid*—this salt must be one of the most important immediate principles of the blood; and we can understand, why, when animals are for a time comparatively deprived of chloride of sodium in their food, they eliminate none of this salt in their excrementitious secretions; and, consequently, in such cases, the same hydrochloric acid serves over and over again for the gastric secretion, while all the other constituents of the body are undergoing the normal process of waste. This is one of those admirable provisions of nature which have fitted animal life to be preserved under so many different circumstances.

The main object of the gastric digestion is the transformation of albuminous food into a substance which Lehmann has called *peptone*, and the conversion of neutral fats into fatty acids. Albumin, fibrin, casein, gelatin, and chondrin are modified in the stomach, and assume new characters, obviously in great measure with a view to their more ready absorption into the blood. Under the influence of the gastric juice, albuminous or protein-compounds lose their coagulability by heat and mineral acids, and likewise their property of forming insoluble combinations with most metallic salts. Lehmann has been unable to discover any difference between the quantities of nitrogen, carbon, oxygen, and sulphur contained in the peptone and in the substance from which it was derived. As to cartilage and gelatigenous bodies, they are converted in the stomach into substances which, according to Lehmann, correspond perfectly in their physical, and in most of their chemical properties to the peptones of the protein-bodies. We

gather from the observations of this chemist, that, in his opinion, the various peptones derived from protein and gelatin compounds are sufficiently analogous to be considered as one and the same body. Peptones must be looked upon as modifications of albumin, fibrin, casein, gelatin, and chondrin, approximating to albumin of blood; indeed they are partly assimilated compounds.

Although I have no reason whatever to disbelieve Lehmann's views regarding the analogy existing between the chemical characters of peptones, still they do not appear to agree altogether in their physical properties; and this point is one of much interest. Some peptones, or perhaps only one kind of peptone, acts on polarised light, rotating the plane of polarisation to the left, while others appear to exhibit no such property.

I observed, in the spring of 1860, that gastric juice acts on polarised light; and for the following twelve months I diligently inquired into the various circumstances connected with this phenomenon. Shortly after my results had been communicated to this Society, I found in Henle and Meissner's "Bericht über die Vortschritte der Anatomie und Physiologie," for 1859, that Hoppe had already observed this same optical property of the gastric fluid; and I willingly give up to him the priority of the discovery; at the same time it should be understood that Hoppe merely detected the bare fact, and only expressed an opinion on its cause, based on one experiment. He believed this phenomenon to be due to a substance secreted in the gastric juice, while I have shown that it is owing to a product of the digestion of animal food, or a *peptone*.

There are two different animal tissues, which, when submitted to the action of gastric juice, in or out of the body, yield polarising peptone—these are cartilage and the mucous tissue of boiled intestines, which can be easily separated from the muscular tissue. I could obtain none, or no appreciable quantity of this substance, from pure coagulated albumin or coagulated casein, when digested in gastric juice out of the body. My experiments on the digestion of meat out of the body, have failed to give me any clear results, although dogs fed exclusively on cooked beef-steaks for a week, invariably yielded a gastric fluid which acted on polarised light. We can be sure that the constituent of gastric juice which thus rotates the plane of polarisation of light, is a *peptone* and not a *substance secreted*; for if, after keeping a dog fasting for thirty

hours or longer, and then washing out his stomach thoroughly with water, the animal be made to swallow silicious pebbles, the small quantity of gastric juice secreted has no power of rotating the polarised ray. The result of this experiment is at variance with that obtained by Hoppe, who, after allowing an animal to fast, excited the gastric secretion with a glass rod, without however, taking the precaution of washing the stomach, and found that the fluid acted on polarised light. After exciting the secretion with fragments of bone, I obtained a gastric fluid which exerted but a very slight influence on polarised light, showing only seven divisions to the left in Soleil's saccharometer, while when the secretion was excited by cartilage, the rotation was from thirty to forty divisions, obviously from the digestion of the cartilage; and moreover, gastric juice, mixed with cartilage or with the internal tissue of boiled tripe, and exposed in a water-bath to a temperature equal to that of the body, acquires, after a short time, a power of deviating the plane of polarisation, which may be twice as great as that it possessed before the commencement of the artificial digestion.

After many experiments as to the best method of extracting from the gastric fluid the peptone under consideration, I succeeded in preparing it in a comparatively pure state, and then found it to be quite similar in its chemical properties to Lehmann's peptone. Four experiments were made with the dry substance in order to determine its rotatory power in Soleil's saccharometer. Solutions of the peptone in twenty-five cubic centimetres of water yielded for 1° , or division of the instrument, 0.020, 0.023, 0.027, 0.029 grammes: average 0.024 grm. Therefore, when gastric juice is examined in the saccharometer, for every degree of rotation to the left, the fluid contains 0.024 grm. of polarising peptone, or a proportion closely approximating to that, in twenty-five cubic centimetres.

Besides its office of transforming meat and allied articles of food into soluble substances, the stomach is possessed of another power no less important for the purposes of nutrition. I have discovered that it has the property of converting neutral fats, containing stearin, margarin, and butyrin, into their corresponding fatty acids; this fact, simple as it appears, is the key to the explanation of the digestion of fats. The fats of food are constantly neutral, they are not acidified by the process of cooking,

although heated even for a length of time in contact with the acid juice of flesh, and as fatty acids are found in the stomach, it must be owing to a phenomenon of gastric digestion. If a dog bearing a gastric fistula be made to eat butter, the fluid extracted through the fistula a quarter of an hour or twenty minutes later, or even less, will smell strongly of butyric acid. The fat of beef or mutton, after having remained for a certain time in the stomach, yields to alcohol, although not to water, an acid reaction. When the food taken contains but little fat, the whole of it, perhaps, is acidified during the gastric digestion; in those cases where much fat is ingested, I believe a part of it escapes from the stomach, without having undergone any change. With respect to the olein of food, I had concluded in a paper I communicated to the Royal Society, in 1858, that this substance is not acidified in the stomach, but I do not wish to be too positive regarding this statement.

The importance of the transformation of neutral fats into fatty acids in the stomach will be readily understood, if we take into consideration the action of bile upon these substances, the characteristic physiological property of that secretion being its power of converting fatty acids into an emulsion, while, with regard to neutral fats, it exhibits no such influence: consequently fats undergo in the stomach a certain transformation, by which means the bile becomes capable of acting upon them, and transforming them into an emulsion.

I must now beg to make a few observations on the phenomenon of fatty emulsions.

When neutral fats or fatty acids in a fused condition are agitated with water, no emulsion is formed, but large globules are seen to pervade the fluid; on standing they immediately run into each other, and rise to the surface, the aqueous fluid remaining perfectly clear. When fused *neutral fats* are agitated with a solution of neutral tribasic phosphate of soda, I have observed the same phenomenon to take place as with pure water, but when fused *fatty acids* are treated with a solution of phosphate of soda, an emulsion is formed, or in other words, the globules of fat lose the property of running into each other; they remain separate, the fluid assuming a milky appearance: consequently phosphate of soda does not act equally on neutral and on fatty acids. This subject appearing to me of great interest, I have given it much attention,

and I have found that the emulsion produced by acting on fatty acids with phosphate of soda is invariably accompanied by the formation of a certain quantity of soap; and a fact worthy of note is that the formation of soap persists, although, from the neutral phosphate becoming transformed into an acid phosphate, the emulsion is suspended in an acid fluid.

Emulsions of fat are also produced when bile and fused fatty acids are agitated together, or when pancreatic juice is shaken with both neutral or acid fats. This state of emulsion or of minute division of fats is indispensable for their absorption in the blood; an inquiry into the real nature of an emulsion would be therefore an object of much importance. Is it not something more than a mere mechanical division of fats into very small globules? I believe there are strong grounds for the assumption that there can be no emulsion without a chemical action, which may be conceived to take place in the following way:—When fused fatty acids are shaken in a test-tube with phosphate of soda or bile, the fat is instantly divided by a mechanical process into very minute globules, just as would happen if the fat was agitated with water; but at that moment each of these very small fatty particles becomes surrounded with a layer of soap, from the surface of the globule being saponified by the phosphate of soda or bile. From this circumstance the globules of fat lose their property of running into each other, and acquire a slight increase of specific gravity, which however is not sufficient to prevent them from rising slowly in the mother-liquor, and finally occupying the upper part of the liquid. Thus it is that the fluid is milky, and that the emulsion takes a much longer time to rise to the surface than pure oil would. The chemical analysis of the emulsion bears out this view, for I have found it to consist invariably of free fatty acid and soap.

This theory may have been already proposed without my knowledge; its adoption will assist in explaining the absorption of fats: for in this case, when in the form of an emulsion, they can no longer be in direct contact with the intestines, a layer of soap intervening between the fat and the membrane. Soaps may be conceived to pass through a membrane, whilst fat is known to be incapable of so doing, consequently we may imagine fats to be absorbed under the form of complex globules, the inside of which is free fat, and the outside soap.

Let us now return to the action of bile upon fats. After I had observed the property of phosphate of soda of emulsifying fatty acid, and not neutral fats, it struck me that bile might be possessed of a similar power, which I found to be the case; and, after giving this important subject all the attention it deserved, the results of my enquiries were communicated to the Royal Society in 1858. Shortly afterwards I was informed that bile had already been observed by Lenz, of Dorpat, to possess the above-mentioned property; and, by referring to his valuable Dissertation "On the Digestion of Fats," I found that he was the first who discovered, so far back as 1850, that bile emulsified fatty acids, but not neutral fats; he also noticed that the emulsion was attended with the formation of soap, and I readily avail myself of this opportunity of acknowledging the fact.

I cannot find that Lenz conducted his experiments with other fats than oil. I employed the solid fats of meat, which are those usually taken into the stomach; my attention was especially directed to the quantitative analysis of the emulsion, in order to determine the proportions of soap and fatty acids it contained; and finally I discovered this remarkable and interesting fact, that if the mother-liquor in which the emulsion is suspended be filtered from the emulsified fat, it is capable, notwithstanding its strongly acid reaction, of forming more soap and emulsifying more fatty acid, although before filtration the saponification had been entirely arrested; the filtrate from this second operation is likewise capable of effecting a further saponification and emulsion, but the action is less and less powerful; in one series of experiments, the proportions of fatty acids saponified were 20.5 %, 12.7 %, and 3.8 % of those experimented on.

The importance of the change which neutral fats undergo in the stomach will now be readily understood; for it is indispensable to their subsequent emulsion in the intestines by the bile, under which form they are absorbed. I do not wish, however, to attribute to bile exclusively the power of digesting fats: for I fully believe that a portion of the fats taken into the stomach is not acidified, and, consequently, must escape the action of the bile; in this case the pancreatic juice effects the required emulsion. It is remarkable that in both cases the fats are absorbed in great measure under the form of emulsified fatty acids; for it is now generally admitted that the pancreatic juice has the power of acidifying neutral fats, as was discovered by Prof. Bernard.

This absorption of fatty acids explains a fact I observed, with Mr. Verdeil, while at work in Messrs. Wurtz and Verdeil's laboratory at Paris, in 1851—namely, that blood contains free fatty acids.

The alimentary canal is so perfectly adapted to the functions of digestion, that notwithstanding the great variety of food taken, and the amount of nourishment ingested, which is frequently much greater than that strictly required for the maintenance of the body, only a very small proportion of food passes off in the evacuations in the healthy state; they may be said to contain no element of food soluble in water, for they merely yield to water a small quantity of an albuminous substance possessed of the characters of the albumin of the pancreatic juice, which in all probability it is. Under the microscope, we find in the alvine dejections, a few fragments of muscular tissue, from the meat taken, and the hairs of wheat ingested with bread; a few cells and fibres are all that remains of vegetable food. None of the fats of food are found therein in the free state, but the evacuations contain small quantities of phosphate of soda, soda soaps, and a larger proportion of earthy phosphates and earthy soaps.

The principal object of the alvine evacuation is obviously to rid the body of certain parts of the intestinal secretions, which, after having served their purpose in effecting the digestion of food, are not fit to return into the blood. It is very difficult to trace the connection of these excreted substances with the various intestinal secretions; in this respect, we must at present rest satisfied with probabilities. Among these various substances there is one of great interest, I have called *excretin* [$C_{78}H_{78}O_2S$]. This substance, which has been fully described elsewhere,* crystallises from its alcoholic or ethereal solution, exhibiting beautiful silky crystals, which are acicular four-sided prisms. In its properties it closely resembles *cholesterin*, being soluble in hot alcohol and ether, sparingly soluble in cold alcohol, insoluble in water, and not saponifiable; like *cholesterin*, it dissolves in small quantity in the bile. It has also some physiological connection with *cholesterin*, as I have found the excreta of very young children to contain no *excretin*, but *cholesterin*, whilst it is the reverse in the case of young people and adults. On this account, I believe *excretin* to be a constituent of the bile.

* Phil. Trans., 1854, ii, 265.