THE LUMLEIAN LECTURES

ON THE DIGESTIVE FERMENTS, AND THE PREPARATION AND USE OF ARTIFICIALLY DIGESTED FOOD.

Delivered before the Royal College of Physicians.

By WILLIAM ROBERTS, M.D., F.R.C.P., F.R.S.,
Physician to the Manchester Royal Infirmary; Professor of Clinical Medicine
to the Owens College.

LECTURE II.*

PEPSIN AND TRYPSIN—DIGESTION OF PROTEIDS.

Comparison of the Action of Pepsin and Trypsin.—The action of pepsin and trypsin, although similar in the main results, is certainly not identical. There is a markedly larger production of leucin and tyrosin in tryptic than in peptic digestion. Moreover, the action of the two ferments on different proteids appears to vary both in character and in energy. Milk is much more readily digested by pancreatic extract than by artificial gastric juice; but in the case of egg-albumen the advantage lies decidedly with the gastric juice. The study of the digestion of egg-albumen by the two methods yielded some interesting results. I employed for this purpose a dilution of egg-albumen with water, in the proportion of one in ten. This remains uncoagulated after being boiled in the water-bath, and furnishes a favourable medium for studying the digestion of albumen—much more favourable than the chopped boiled white-of-egg usually employed. It permits the ferment to be at once brought into uniform and intimate contact with the particles of the albumen, thus obviating the irregularity and want of constancy which necessarily attend the operation of a solvent acting on solid pieces of variable size, which can only be attacked progressively from their surfaces. In the raw state, this solution is digested with extreme slowness by artificial gastric juice; and pancreatic extract is nearly inert on it; but after being boiled it is attacked with energy by both the gastric and the pancreatic ferments.† When the boiled solution was treated, in the warm chamber, with pepsin and hydrochloric acid the transformation of the albumen went on rapidly and without interruption to its close. In the earlier periods of the action, the mixture gave a dense precipitate with nitric acid and with ferrocyanide of potassium, but this precipitation became progressively less and less pronounced, until, at the end of two or three hours, these reagents only produced a slight haze. The albumen was now completely digested, or at least as nearly so as could be reached, for this remnant of a reaction persisted even after a further digestion of twenty-four hours.

When the same solution was treated with pancreatic extract, the progress of events was different. For an hour or two (the time varying with the quantity of extract added) there was no apparent change; but at the end of this time the mixture lost its diffuent condition, and became converted into a gelatinous mass, exactly resembling a thin starch jelly. By-and-bye the gelatinous matter broke up into little masses, which floated in a transparent liquid. At this point, the action seemed to be arrested. The floating masses of jelly remained almost undiminished in quantity after twenty-four and even forty-eight hours. When the mixture was filtered, the liquid portions came through perfectly transparent, and the jelly-like matter was left in the filter. The filtrate was found to be a rich and very pure solution of peptone, uncontaminated with any undigested or half-digested albumen. The jelly-like matter was found to be insoluble in water, hot or cold, but it dissolved readily in acids, and was rapidly digested by pepsin and hydrochloric acid. If a large amount of pancreatic extract were used, a considerable proportion of the jelly-like matter was slowly dissolved; but the main result was always the same, the pancreatic ferment was only able to convert a part of the albumen into peptone, whereas the gastric ferment converted the entire quantity, with the exception of an insignificant residuum.‡

* Concluded from page 577 of last number.

† In cooking this solution it is advisable to use the water-bath, for otherwise some of the albumen coagulates and cakes on the bottom of the vessel, and the liquid froths up in an inconvenient manner.

‡ Most observers have noticed the occurrence of this indigestible residuum (named "Dyspeptone" by Meissner) in the artificial gastric digestion of proteids. I have noticed the same in the digestion of milk by pancreatic extract.

In the case of milk, the relation of the two ferments is reversed. Tryptic digestion of milk is rapid, and leaves only a very slight residue, whereas peptic digestion is slow, and leaves a large residue. I have some further observations to make on the digestion of milk by pancreatic extract, but it will be more convenient to take up the subject when I come to speak of the use of this ferment for the preparation of artificially digested food.

Peptogens.—I may here advert to a singular view advanced by Schiff in regard to the production and secretion of pepsin and trypsin. Schiff found that when an insoluble aliment, such as white of egg (or fibrin, or meat which had been deprived of its soluble portions), was introduced into the stomach of a fasting animal no pepsin was secreted, and the albumen remained undigested; but if with the albumen certain soluble aliments were introduced into the stomach, then pepsin was produced, and digestion immediately began. To these substances, which had the power of provoking the formation and secretion of pepsin, Schiff gave the name of "peptogens". Among the most effective peptogens were found to be solutions of dextrine, extract of meat (or soup), infusion of green peas, bread (which contains dextrine), gelatin, and peptones. On the other hand, solutions of grape-sugar, soluble starch, fat-emulsion, or gum, had no peptogenic effect; and milk and coffee had not much. Schiff further found that peptogenic substances were just as effective when they were injected into the blood, or into the cellular tissue, or introduced as enemata into the rectum, as when they were introduced directly into the stomach. On the other hand, when peptogens were injected into the small intestine their influence was not observed; their effect seemed to be annulled by some action of the mesenteric glands, or by some change induced in them in their passage along the thoracic duct. On the ground of these experiments—and they were numerous and oft-repeated and gave constant and decisive results—he concluded that the absorption into the blood of these soluble aliments was a necessary preliminary of proteid digestion, that no pepsin or trypsin was secreted unless these substances existed beforehand in the blood. The first act, according to Schiff, of gastric digestion was the absorption from the constituents of a meal of these soluble peptogens by the veins of the stomach. On this followed immediately the secretion of pepsin, and the commencement of digestion proper.*

These views and experiments of Schiff have not been allowed to pass without challenge, but they have not yet been overturned. If they should be substantiated, they will give, curiously enough, a scientific sanction to the prevailing custom of commencing dinner with soup.

THE MILK-CURDLING FERMENT.

You all know that one of the most striking properties of gastric juice is to curdle milk. This property is utilised on a large scale in the industrial art of making cheese. Rennet, which has been used for that purpose from remote antiquity, is simply an infusion of the fourth stomach of the calf in brine. The curdling of casein by rennet does not depend upon the acid of the gastric juice, for it takes place when the milk is neutral or even faintly alkaline. It has until lately been believed that this property was an inherent attribute of pepsin, but this opinion is no longer tenable. Brücke succeeded, by a process which I need not particularise, in producing pepsin which had an energetic action on proteids, but which did not possess, except in the feeblest degree, the power of curdling milk. Mr. Benger also found that an extract of pig's stomach in saturated brine, while it possessed energetic action as a milk-curdler, had comparatively only feeble proteolytic powers. We must therefore regard the agent in gastric juice which curdles milk as a distinct substance from pepsin.

In the course of my experiments on pancreatic extract, I made the unexpected observation that the pancreas also contained an agent capable of curdling milk. I found this property in the pancreas of the pig, the sheep, the calf, the ox, and the fowl. In whatever way the extract of the gland was made, whatever solvent was used, this property of curdling milk was present in it; but the brine-extract exceeded all others in curdling capacity. If a few drops of extract of pancreas be added to some warm milk in a test-tube, the milk becomes a solid coagulum in a few minutes. Some minutes later, the whey begins to separate from the curd. In short, the action resembles exactly that of calf's rennet; and, so far as I know, you could make cheese with pancreatic rennet as perfectly as you can with gastric rennet. There is, however, not an absolute identity of the two agents. I said just now that gastric rennet produced curdling in neutral and even in faintly alkaline milk; but if the alkali exceed a very small proportion, ordinary rennet does not curdle milk. I found that an alkalescence, exceeding that produced by one grain of bicarbonate of soda to an ounce of milk, altogether prevented the milk from being curdled by gastric rennet. But this is not

* See Schiff's *Leçons sur la Physiologie de la Digestion*, vol. ii, p. 200, et seq. Paris: 1867.

so with pancreatic rennet. You may add two, three, or four grains of bicarbonate of soda to each ounce of milk, and still the pancreatic rennet will induce curdling with undiminished energy. Milk is likewise curdled by pancreatic extract, when quite neutral, and even when very faintly acid. Indeed, it appeared to me that a very faintly acid milk curdled more actively with pancreatic extract than neutral milk, but not so actively as alkaline milk.

That the curdling agent of the stomach and pancreas is a true ferment, and not some inorganic chemical agent, seems to be proved by the fact that boiling, or even heating to 160° F. (70° C.) instantly destroys its power. I found, moreover, that, like other soluble ferments, it is precipitated, but not truly coagulated, by alcohol; for it recovers its solubility and activity when the alcohol is removed, even after a contact of several weeks.

The curdling ferment of the pancreas is a distinct body from trypsin, as the following experiments show. 1. Some brine-extract of pancreas (which was known to possess proteolytic energy) was acidulated with hydrochloric acid in the proportion of 1 per 1000, and then placed in the warm chamber at a temperature of 104° F. (40° C.) for a period of three hours. It was then carefully neutralised with bicarbonate of soda. When thus treated, the extract was found to have lost its proteolytic power, but its curdling action on milk was almost as energetic as ever. 2. A portion of the same brine-extract of pancreas was filtered under vacuum pressure through porous earthenware. The filtered product was found to possess an undiminished faculty of curdling milk, but it had almost no power of dissolving the curds. The curdling ferment had evidently traversed the earthenware freely, but only traces of trypsin had passed through.

What is the real function of the curdling ferment? Seeing its striking reaction with milk, one's first idea is that it must have something to do with the digestion of casein. But a little consideration shows that this idea is altogether improbable. Although all mammalia start life on a milk-diet, milk does not form a part of the normal diet of any adult creature except man. Nor can its universal presence in the mammalian digestive organs be regarded as a vestigial phenomenon—a "memory" of the suckling phase of their existence—for the same curdling property is found in the stomach and pancreas of the fowl, which never at any period of its life fed on milk. Moreover, it may be doubted whether the ferment in question is the actual agent which curdles milk on its passage into the stomach; for the acid of the gastric juice, which also curdles milk, would probably be beforehand with it, inasmuch as its action is a good deal more prompt than that of the ferment. In the pancreatic digestion of milk, the occurrence of curdling has appeared to me to be a distinct hindrance to the process. Has this ferment any true digestive functions? I think this is quite open to doubt. Its action on milk is apparently akin to that of the fibrin-ferment on blood, and it may likewise have some kindred purpose, but what that purpose may be I am unable to conjecture.

EMULSIVE FERMENT: DIGESTION OF FATS.

The digestive change undergone by fatty matters in the small intestine consists mainly in their reduction into a state of emulsion, or division into infinitely minute particles. In addition to this purely physical change, a small portion undergoes a chemical change whereby the glycerine and fatty acids are dissociated. The fatty acids thus liberated then combine with the alkaline bases of the bile and pancreatic juice, and form soaps. The main or principal change is undoubtedly an emulsifying process, and nearly all the fat taken up by the lacteals is simply in a state of emulsion, and not of saponification. It is, however, quite certain that both these processes do take place in the small intestine, though in very unequal degrees. The only question in connection with the digestion of fat which I propose to examine is: Whether these changes are produced by the operation of a soluble ferment, or by some other and different agencies? In his latest utterances on this subject, Bernard* insisted that the digestion of fat, like the digestion of starch and proteids, consisted in the action of a soluble ferment, which he named *Ferment Emulsif*. This ferment, he alleged, first emulsified and then saponified fats. In the intestine, the change scarcely went beyond emulsion—in this condition fat was found in the contents of the lacteals. Saponification took place almost exclusively further on, and, later, in the blood. It is certainly established that the pancreatic juice exercises a marked influence on the digestion of fats; and it is in the pancreas, according to Bernard, that the emulsive ferment is to be found. Bernard demonstrated that healthy pancreatic juice has quite a special faculty of emulsifying fats. Pancreatic tissue has also the same property. If a portion of fresh pancreas be rubbed up with fatty matter and water, you get an emulsion which is fairly persistent. I have not

had an opportunity of examining the behaviour of pancreatic juice with fatty matter, and cannot therefore speak of its properties; but it is singular if, as alleged, the effect of pancreatic juice and pancreatic tissue on fat be due to the presence of a soluble ferment, that the extracts of pancreas possess none of the same power. I have made extracts of pancreas in various ways—with simple water, with chloroform-water, with dilute spirit, with solutions of boric acid, of borax, and of both combined, with glycerine and water, with brine, and with solution of salicylic acid and of salicylate of soda; and yet I could not satisfy myself that any of these extracts possessed any special power of emulsifying fats, nor of liberating the fatty acids and inducing saponification. Paschutin* states that the emulsive ferment of the pancreas can be extracted by a solution of bicarbonate of soda. An extract of pancreas, made by myself with a two per cent. solution of bicarbonate of soda, was indeed found to have a very marked emulsifying power; but it had the same power, even in an enhanced degree, after being boiled, which showed that its emulsifying properties could not depend on the presence of a soluble ferment.

I was equally unsuccessful in my attempts to verify the alleged power of extracts of pancreas, and of crushed pancreatic tissue, to liberate the fatty acids. When fresh pancreas, finely triturated with sand, was digested with milk in the warm chamber, I could not obtain satisfactory evidence of the development of free acid from the decomposition of the fat of the milk by a soluble ferment. The pancreas itself yields a slightly acid solution when infused in water, and a mixture of milk and pancreatic tissue always showed a slight acid reaction; but when this primary acidity was neutralised, no further production of acid took place until such a time had elapsed as was sufficient to permit the development of organised ferments and the origination of the lactic fermentation. If the development of organised ferments were prevented by the addition of antiseptics—such as chloroform or a combination of boric acid and borax—a mixture of milk and crushed pancreas remained neutral for several days. The same results followed when I operated on emulsions made with crushed pancreas and lard or olive oil. In my numerous observations on the digestion of milk with various pancreatic extracts, I never could detect the production of an acid reaction, unless organised ferments were permitted to intervene.

I obtained similar negative results with almond emulsion. Bernard attributed the formation of an emulsion when almonds (or other oily seeds) were rubbed up with water, to the presence in the seeds of a soluble ferment. But I found, to my surprise, that almonds which had been boiled for seven hours still produced a perfect emulsion. As all known soluble ferments are destroyed by boiling, this result seems irreconcilable with Bernard's view. I also found that almond emulsion, kept in the warm chamber for six or eight hours at a temperature of 100° Fahr. (38° C.), showed not the slightest evidence of an increase of its original faintly acid reaction. It appeared to be more probable that the fatty matter in the almond existed in the seed in the condition of a solid emulsion; and that the formation of a fluid emulsion by trituration with water was due simply to the liberation of the minutely divided oil-particles, rather than to the intervention of a soluble ferment.

It is with considerable hesitation that I venture to place myself in even apparent contradiction with so great an observer as was Claude Bernard; and I by no means pretend that these observations traverse the main conclusions for which he contended as to the digestive transformations of fat in plants and animals. The views which Bernard developed on the digestive process are based on inductions so wide, and observations so multiplied, that I feel satisfied that their substantial accuracy will be ultimately established in regard to fat, as they have already been established in regard to starch and cane-sugar.

Some observations made by Brücke promise to throw a fresh light on the digestion of fat. Brücke found that oils and fats which contained an admixture of free fatty acids—in other words, which were more or less rancid—were emulsified by a slight agitation with a weak solution of carbonate of soda. J. Gad extended these observations, and showed that even simple contact of a rancid oil with the alkaline solution was sufficient to effect a mechanical division of the oily matter. I have repeated these observations, and the results are certainly remarkable. The different behaviour of two specimens of the same oil, one perfectly neutral and the other containing a little free fatty acid, is exceedingly striking. I have here before me two specimens of cod-liver oil—one of them is a fine and pure pale oil, such as is usually dispensed by the better class of chemists; the other is the brown oil sent out under the name of De Jongh. I put a few drops of each of these into these two beakers, and pour on them some of this solution, which contains two per cent. of bicarbonate of soda. The pale oil, you see, is not in the least emulsified; it rises to the top of the water in large clear globules;

* Claude Bernard, *Leçons sur les Phénomènes de la Vie*, tome ii, page 346. Paris: 1879.

* Hoppe-Seyler, *Physiologische Chemie*, p. 257. Berlin: 1878.

the brown oil, on the contrary, yields at once a milky emulsion. The pale oil is a neutral oil, and yields no acid to water when agitated with it—in other words, it is quite free from rancidity; but the brown oil, when treated in the same way, causes the water in which it is shaken to redden litmus paper. I was surprised to find that olive oil (salad oil), which appeared quite sweet and had not the slightest taste or smell of rancidity, gave a milky emulsion with the soda solution. This oil did not yield any acid reaction to water when agitated therewith. Nevertheless, it evidently contained a little free fatty acid (probably oleic acid, which is insoluble in water, and therefore does not acidify water shaken up with it); for, when a portion of this oil was washed with a strong solution of carbonate of soda, and then allowed to separate, the oil thus freed from acid no longer gave an emulsion with the weak soda solution. It would appear that an admixture of only a very small proportion of free fatty acid is sufficient to induce emulsification—a quantity so small as not to cause any appreciable rancidity to the senses of smell or taste. This specimen of almond oil is to all appearance perfectly sweet; but it communicates a rather sharp acid reaction to water shaken up with it, and it gives, as you see, an instantaneous and perfect emulsion with the soda solution.

The bearing of these observations on the digestion of fat is plain. When the contents of the stomach pass the pylorus, they encounter the bile and pancreatic juice, which are alkaline, from the presence in them of carbonate of soda. Thus the fatty ingredients of the chyme, if they only contain a small admixture of free fatty acids, are at once placed in favourable circumstances for the production of an emulsion without the help of any soluble ferment, the mere agitation of the contents of the bowel by the peristaltic action being sufficient to effect the purpose.

This view of the matter renders it necessary that fresh inquiries should be made into the effect of gastric digestion on fats. It has hitherto been supposed that fatty and oily substances undergo no change in the stomach; but it is quite possible that something may have been overlooked. It was noticed by Richet, in the patient with a gastric fistula, that the fatty matters were detained a long time in the stomach, and that they only passed through the pylorus with the last portions of the meal. It is also a familiar experience to most dyspeptics, that rancid eructations are a frequent occurrence in the later stages of gastric digestion. If it should turn out that, among the complex operations taking place in the stomach, there occurred some slight decomposition of the neutral fats, and a liberation of a small quantity of free fatty acid, such a result would supply the necessary condition for the emulsification of the neutral fats in the duodenum. In speculating on this subject, it is difficult to shut one's eye to the possibility of the intervention of formed or organised ferments in the digestive process. It is well known that fatty acids are liberated in the decomposition of neutral fats by bacterioid ferments (zymophytes); and the presence of ferments of this class in the living stomach has been so repeatedly observed that it may well give rise to the suspicion that they are a normal ingredient of the gastric mucus, and have a normal function to perform in the digestion of some portions of our food. It is not, however, desirable to push speculations of this kind in advance of observed facts; and I only mention them as hints for further inquiry in regard to the digestion of fat.

MR. FURNEAUX JORDAN'S LITHOTOMY.

IN reply to Mr. C. Heath's remarks, I would say that in the fullest notes of my clinical lecture, from which the published report was condensed, I refer to his useful suggestion respecting the use of a probe at a certain stage in the operation for lithotomy. Mr. Heath and Mr. Teevan differ so widely touching the incision at the neck of the bladder, that there is plenty of room for an "infinite variety" of opinion. Mr. Heath says any incision at the neck of the bladder is, as a rule, "uncalled for". Mr. Teevan tells us to cut the neck of the bladder even in little boys with a "big knife". He refers with just pride to twenty-two successful cases so cut. Mr. Teevan is quite correct in saying that the lateral method is very safe in boys. I have performed the operation in upwards of forty cases without a death. But I also agree with Mr. Heath, that it is not necessary to carry the knife into the bladder in every case. Twice within the last few months, and frequently before, I have removed small calculi with more limited incisions.

So far, the criticisms on my operation have been based on opinion, not on experience. I do not complain of this. An expert has a right to give opinions on new operations before he tries them; and a wise man will certainly not relinquish an operation which he knows, and likes, and excels in, for an untried operation. I have suggested a method of lithotomy which must stand or fall on its intrinsic merits. In one case, it served me well when no other proceeding was open to me. Whether it be found of general utility, or only of exceptional utility, or of no utility at all, time will show.

FURNEAUX JORDAN.

ABSTRACT REPORT OF LECTURES ON THE COMPARATIVE ANATOMY OF MAN. *Delivered at the Royal College of Surgeons of England.*

By W. H. FLOWER, LL.D., F.R.S.,
Conservator of the Museum, and Hunterian Professor of Comparative Anatomy
in the College.

LECTURE IV.—THE RACES OF AMERICA.—(*Continued.*)

THE physical or anatomical characters of the American native people taken as a whole, leaving out for the present the Eskimo, may be described as follows. In stature, they vary considerably. Among them are the tallest known people on the earth, the Tchuelches or Patagonians, who, though not the fabled giants of the earlier voyagers, appear by all trustworthy accounts to attain an average in the male sex of from 178 to 183 centimètres, which exceeds that of any other race. Some of the North American Indians—for instance, the Iroquois—are also very tall. On the other hand, the Fuegians, and especially the Peruvians, are small. There is, however, no pigmy race on the American Continent like the Bushmen, Negritos, and Lapps of the Old World. The hair, always a characteristic of primary importance in zoological anthropology, is remarkably uniform. Its prevailing, if not universal, colour is black or very dark brown. The pale and auburn colour of the hair of Peruvian mummies is probably due to accidental bleaching, and the fair hair said occasionally to be met with in existing tribes may be the result of European admixture. It is always straight and lank, though sometimes coarse and sometimes silky in texture, depending upon the thickness of the individual hairs. In transverse section it approaches the circular form perhaps more nearly than in any other race, though in this and in other characters it resembles that of the Asiatic Mongolian people. On the scalp, the hair grows abundantly and often to a great length; in many North American Indians it has been known to trail upon the ground when the person is standing upright. Not less characteristic is the rarity or absence of hair on the face and other parts of the body. The skin is smooth and soft, and of various shades of brown, though cinnamon, or as it is usually termed copper colour, is the most characteristic. Some Californian Indians and the now extinct Charruas of Uruguay were said to be nearly black; and some scattered tribes, both in North and South America, are described as being nearly as fair as Southern Europeans. The tint of hair appears to have no relation to the external conditions, such as heat, moisture, etc.; though the features of various tribes and of particular individuals in each tribe show considerable diversity, a characteristic type prevails throughout the great majority of the whole people from north to south. The forehead is usually retreating; the face wide in the molar region, narrowing towards the chin; the brows prominent, overhanging rather small, sleepy, half-closed eyes; the nose long from above downwards and narrow. The nose, as seen in profile, is usually arched, rather sunk at the root, then projecting somewhat horizontally, and making a tolerably sharp bend down to the tip, which is not produced down below the septum. Though this form is very frequently found amongst all tribes, there is some diversity, and the profile is sometimes simply arched and sometimes straight, but a broad flat nose is very rarely met with. The mouth is wide and prominent; the lips rather thin; the chin well formed, narrow, but prominent; the whole face below the eyes long and large, the malar bones projecting laterally, and the lower jaw large.

With regard to the cranial characters of the Americans, the same difference of statement has been made respecting their external appearance. Morton's assertion of the general sameness in the skulls from all parts of the Continent has been contested by others. But the controversies relating to this subject have nearly all turned upon one character alone, that is, the relative breadth of the cranium compared to its length, to the neglect of many others of probably equal importance. The prevalence of artificial cranial deformity, spoken of in a previous lecture, causes much difficulty by limiting the number of crania possessing their natural form at our disposal; but still there is sufficient evidence to show great variation in the cephalic index in American