OBSERVATIONS

ON

THE DIGESTIVE FERMENTS, AND THEIR THERAPEUTICAL USES.*

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You all know that before food can be absorbed into the blood and made available for the nutrition of the body it must first be digested. By digestion, the albuminous and collagenous constituents of our food are liquefied and converted into diffusible peptones; the starchy matters are converted into sugar, and the fats are emulsified and partly saponified. Cane-sugar is also changed into glucose. Native glucose, which exists in abundance in all our sweet fruits, is absorbed unchanged, and may be regarded as a ready-made digested food, or rather as a starchy food predigested for us by the agency of plants. The digestive processes are all of a purely chemical and mechanical nature; and they can be imitated successfully in the laboratory, and even in the sick room and nursery.

The agents concerned in these processes are the several digestive juices: saliva, gastric juice, pancreatic juice, bile, and the intestinal secretions. These juices owe their activity to a very remarkable group of bodies, called soluble (or unorganised) ferments; and it is to these ferments—to certain points in their modes of action and mutual relations—that I propose to direct your attention.

In the annexed table I have arranged, in the first column, the digestive juices in their natural order of succession; in the second column are indicated the ferments proper to each of them; in the third column, the nature of the action of each ferment on food-stuffs; and in the fourth column are placed the various medicinal preparations, which are the equivalents or substitutes available for administration to patients in whom this or that digestive juice may be supposed to require artificial assistance.

Table of the Digestive Juices and their Ferments.

Digestive Juices.	Ferments contained in them.	Action on Food-stuffs	Medicinal Substitutes.
Saliva.	Diastase.	<i>Amyolytic</i> , changes starch into sugar.	Various preparations of malt; extracts of malt; malt flour; extract of pancreas.
Gastric juice.	a. Pepsin.	<i>Proteolytic</i> , changes proteids into peptones in an acid medium.	Various preparations of pepsin; pepsin-wine; liquor pepsinæ; lacto-peptin, etc.
	b. Curdling ferment.	Curdles the casein of milk.	Rennet.
Pancreatic juice	a. Trypsin.	<i>Proteolytic</i> , changes proteids into peptones in an alkaline medium.	Pancreatine.
	b. Curdling ferment.	Curdles the casein of milk.	Glycerine extract of pancreas.
	c. Diastase.	<i>Amyolytic</i> , changes starch into sugar.	Liquor pancreaticus.
	d. Emulsifying ferment.	Emulsifies and saponifies fats.	Pancreatic rennet.
Bile and intestinal juice.	?	?	o

An examination of the table shows that a complicated series of ferment-actions is required to complete the digestion of our food; and it is certain that our information is still imperfect on several points, especially in regard to the uses of the bile and the intestinal secretions. It is no part of my purpose to attempt a general account of the digestive processes, but only to pick out certain points in regard to which I may have something to say, which is either novel or has a practical bearing on the treatment of our patients. Of the bile and succus entericus I do not propose to say anything. I shall divide my remarks under the three

headings of saliva, gastric juice, and pancreatic juice; and shall conclude with some observations on the preparation of peptones, and the feeding of patients on peptonised food.

I. SALIVA.—Saliva has but one ferment—namely, diastase, or, as it is sometimes called, ptyalin—and its sole action is to convert starch into sugar. Saliva acts with energy on gelatinised or cooked starch, but with extreme slowness on the native unbroken starch-granules. This is the reason, or necessity, for the practice which has arisen and become universal among mankind, of cooking farinaceous articles of food before they are eaten.

The action of saliva on starch goes on in the mouth and gullet, and for a while after the morsel has reached the stomach; but the action is arrested as soon as the meal is thoroughly permeated by the gastric juice. In the case of a meal of farinaceous food, this arrest occurs long before all the starch is digested; and the work is taken up and finished, after the food has passed the pylorus, by the pancreatic juice.* When the digestion of starchy matters is at fault—or supposed to be at fault, for we really possess little exact knowledge of the indications of such a condition—we resort to one or other of the preparations of malt which contain diastase. At the present moment, the most popular of these preparations are the malt-extracts; and, to judge by the scale on which these extracts are advertised in the medical journals, they are very popular indeed. Several of these preparations are on the table before you; and I think they are likely to prove a valuable addition to our stock of remedies. They resemble a thick brown treacle in appearance, and their taste and smell are not unlike treacle. The statements made in the advertisements as to the nutritive value of malt-extracts are preposterous exaggerations; they are little better, merely as food, than so much syrup. Their real value lies partly in the diastase they contain, and partly in the important pharmaceutical uses to which they may be put as vehicles for other drugs, especially cod-liver oil. If properly prepared, malt-extract is rich in diastase, and has a high power of digesting starchy matters. But you will be surprised to learn, as I was, that a large proportion of the malt-extracts of commerce have no action on starch. This is owing to a too high temperature having been used in their preparation. Any heat above 158° Fahr. is destructive to diastase in solution; so that if the extract be evaporated, as is directed by the German *Pharmacopœia*, at a temperature of 212° Fahr., it is necessarily inert on starch. Out of fourteen trade samples of malt-extract examined by Messrs. Dunstan and Dimmock, only three possessed the power of acting on starch; all the rest were inert.† I myself examined three brands of malt-extract in regard to this point, and found all three very active.‡ But even the most active of the three was feeble when compared with an extract of pancreas which I shall show you presently.

It is important to choose the right time for giving preparations of diastase, otherwise you may obtain little or no help from them in the digestion of the starchy constituents of the meal. The labels on all the malt-extract bottles I have examined direct a dose to be taken after meals. This is evidently a mistake. I told you a while ago that the action of diastase is arrested in the stomach; and I have reason to believe that this arrest is permanent, and that, under the ordinary conditions of digestion, not a particle of active diastase escapes through the pylorus. If, therefore, you wish to get a full amount of work from a dose of malt-extract, you should administer it, like the natural saliva, with the food; or, better still, mix it with the food beforehand. The malt-extracts lend themselves exceedingly well to this latter mode of administration. They have a sweet agreeable flavour, and a teaspoonful or two may be added as a sweetener, and mixed with tea, cocoa, coffee, arrowroot, sago, or any other farinaceous dish. The only precaution to be observed is that the food should be sufficiently cooled down to be endurable in the mouth before the malt-extract is added. I have found on trial that you cannot eat or sip, even in teaspoonfuls, any substance which has a temperature above 150° Fahr., and, at this heat, diastase not only remains uninjured, but is highly active.

2. GASTRIC JUICE.—Gastric digestion has been the subject of numerous and successful studies in times past, and our knowledge thereof to-day is little in advance of what it was when most of us were students. For this reason, it will not detain us long.

* It is generally stated in text-books of physiology that the digestion of starch is only suspended in the stomach, and that the saliva resumes its activity in the duodenum. I greatly doubt this. In observations on artificial digestion, I found that both saliva and malt-diastase became permanently inert after a comparatively brief (thirty minutes) contact with artificial gastric juice—even when greatly diluted, and when the proportion of hydrochloric acid did not exceed 0.05 per cent.

† *Pharmaceutical Journal*, March 8th, 1879.

‡ These three brands were: Corbyn, Stacey, and Co.; Kepler Malt-Extract Company; and the "Maltine" of the Maltine Manufacturing Company. The activity of Trommer's malt-extract is vouched for by Professor Redwood.

* This paper is the substance of an address delivered before a meeting of the Lancashire and Cheshire Branch of the British Medical Association, at Northwich, on April 26th, 1879.

Pepsin.—The special ferment of the gastric juice is pepsin, and its office is to digest the albuminous and the gelatinous constituents of our food. Pepsin is only active in the presence of an acid; and the normal acid of the stomach appears to be hydrochloric acid; other acids, however—lactic, phosphoric, citric, etc.—render pepsin active, but not so energetically as the hydrochloric.

Under the influence of pepsin proteids are changed into peptone, or peptones. The word is often used in the plural number, because the products arising during the digestion of proteids show considerable variation *inter se*; and this has led physiologists to conclude either that there are several varieties of peptone evolved in the process, or that the same body is encountered in different stages of transformation. The change impressed on a native proteid by its conversion into peptone is probably simply a hydration—a change similar in character to the hydration undergone by starch when it is changed into sugar by diastase. That the change does not involve a profound disturbance of the molecular constitution of the proteid, would seem to be indicated by the fact that the first thing that happens to peptone when it has been absorbed into the blood-current is to be immediately depeptonised—that is, to be again restored to the condition of a native proteid (serum-albumen). So quickly does this re-transformation take place, that no peptones can be detected in the lacteals, nor in the blood of the portal vein.

The Curdling Ferment of the Stomach.—Everybody knows that one of the most striking properties of the gastric juice is its power of curdling milk. This property is quite independent of the acid of the gastric juice, and is effective in neutral and even in slightly alkaline milk. Under the name of rennet, which is simply a brine-extract of the calf's stomach, this property has been known from time immemorial, and has been utilised for the making of cheese. Until quite recently, it was not doubted that the curdling power was an essential attribute of pepsin; but, in 1876, Brücke published a process by which he obtained a pepsin which was strongly proteolytic, but which was powerless to curdle milk. Quite recently, Mr. Bengel has made an observation which may be regarded as the complement of that of Brücke. He finds that a concentrated brine-extract of calf's stomach has intense curdling powers, but is almost devoid of proteolytic powers. On the ground of these observations, we are justified in concluding that two distinct ferments have been heretofore included under the old term pepsin—namely, a proteolytic ferment, which peptonises proteids in the presence of an acid, to which the name pepsin should in future be confined—and another ferment, of which the only property now known is that of curdling the casein of milk.

The Medicinal Equivalents of Gastric Juice.—These are so familiarly known as the various and numerous preparations of pepsin, that I need not linger over them. There is no doubt that formerly a number of inert preparations were sold under the name of pepsin, and dispensed to a confiding public; but matters have improved since then; and I have authority for saying that now all the leading brands of pepsin are reliable. Pepsin preparations are especially suitable for administration by the mouth immediately after a meal. Those of you who, from past experience, have lost faith in pepsin, may be encouraged to try again the more active preparations which are now within our reach. A *liquor pepsinæ* prepared by Mr. Bengel, of which a specimen is on the table, is a digestive agent of extraordinary power. A teaspoonful of this preparation in six ounces of acidulated water dissolved an ounce of chopped white of egg completely in three hours.

3. PANCREATIC JUICE.—Formerly, the pancreas was held in little esteem as a digestive agent; it was not thought to have any function except to assist in emulsifying fats. But of late, through the researches chiefly of Corvisart and Bernard in France, and Kühne and Haidenhain in Germany, our estimate of the pancreas has been revolutionised. The pancreas is now known to be rich both in the quantity and variety of its digestive ferments. Extract of pancreas—and we may presume also the natural pancreatic secretion—has at least four distinct kinds of action on food-stuffs, namely: 1. It converts proteids into peptones in alkaline media; 2. It curdles the casein of milk; 3. It transforms starch into sugar; and, 4. It emulsifies fats. I shall have a word to say about each of these modes of activity.

Proteolytic Ferment of Pancreas.—This has been named trypsin by Kühne. It differs from pepsin in requiring an alkaline (instead of an acid) medium for the exercise of its powers. Although the action of pepsin and trypsin on proteids is the same in its ultimate result—i.e., both convert proteids into peptones—certain differences have been noted between them, not only in the reaction of the medium suitable to each, but also in their manner of achieving their work, and in the by-products which attend their action. I am also led to believe that an important practical distinction *between* pepsin and trypsin will prove

to be the difference in the facility of their attack on the different kinds of proteids. Thus, I found it more easy to peptonise milk by trypsin than by pepsin; on the other hand, egg-albumen was attacked more energetically by pepsin than by trypsin.

The mutual reactions of pepsin and trypsin, when present together in solution, are of some practical interest. Kühne has stated that pepsin in an acid medium destroys trypsin, but that trypsin in an alkaline medium has no such effect on pepsin. The latter part of this statement is, I believe, incorrect. My own experiments on this point gave the following results. When pepsin and trypsin were infused together in a large dilution of simple water, at blood-heat, they proved mutually indifferent, and retained their respective activities even after three hours' companionship. But when the mixture was acidified with a few drops of hydrochloric acid, the trypsin was speedily destroyed; and conversely, when the mixture was feebly alkalisied with sodium bicarbonate, the pepsin was quite as speedily destroyed. But I found, further, that pepsin was destroyed apparently as quickly in the simple alkaline solution, without any trypsin; and similarly, that trypsin was speedily destroyed in the simple acid solution when no pepsin was present.

These reactions involve a point of practical interest in regard to the medicinal administration of pancreatic preparations. They lead directly to the inference that acid gastric juice is destructive of the proteolytic activity of pancreatic preparations, and that it is useless to administer such preparations by the mouth, unless means be adopted to safeguard them against the action of the gastric acid. It is also plain that some of the new digestive remedies which are being sent out by eminent firms of druggists, and which are recommended expressly on the ground that they contain the combined energies of the gastric and pancreatic juices (two of these are styled respectively *peptocolos* and *peptodyn*) are compounded on erroneous principles. Pepsin and trypsin cannot possibly be combined in action. If the two ferments be present together in solution, there is no work to be got from either so long as the reaction is neutral; if you acidify, so as to waken the pepsin into activity, the trypsin is thereby rendered permanently inert; and conversely, if you quicken the trypsin into activity by adding an alkali, the pepsin loses its powers.

The Curdling Ferment of the Pancreas.—The property of curdling milk has hitherto been regarded as the special appanage of the gastric ferment; and I was surprised to find a curdling agent also associated with the pancreatic ferments. All extracts of pancreas, however made, were found to have this power. The action seems identical with that of rennet made from calf's stomach, and takes effect both in neutral and in alkalisied milk.

I found that a piece of perfectly fresh pancreas infused in warm milk had only the feeblest possible curdling power. The extract of fresh pancreas, likewise, when newly prepared was inert, but after the lapse of a few weeks it became active. In this respect, the curdling ferment shows parallel behaviour with trypsin, and the explanation is probably the same in both cases, namely, that the pancreatic cells do not contain either ferment in a perfect state, but rather in the condition of zymogen or mother-of-ferment. It may be assumed that, in the living animal, the zymogens are converted into active ferments during the process of secretion. In the artificially made extracts, the change takes place more gradually, and is probably of the nature of a slow oxidation.

Pancreatic Diastase.—The pancreas is exceedingly rich in diastase. An aqueous extract of the gland (of which seven ounces represented one ounce of gland-tissue) was found to have about tenfold the starch-converting power of the best malt-extracts. We therefore possess, in pancreatic extracts, an efficient medicinal substitute for saliva in the digestion of starch.

The emulsifying properties of pancreatic juice have long been known; and Bernard demonstrated that this power depended not simply on the free alkali of the secretion, but on the presence of a special ferment.

Medicinal Equivalents of Pancreatic Juice.—There are two pancreatic preparations which have long been before the profession, namely, pancreatic emulsion and pancreatine, both sent out by Savory and Moore. I found that pancreatic emulsion contained no active ferments; they had probably been destroyed by the heat used in the manufacture; but it was the most perfect possible emulsion, and when mixed with water, the milk-like fluid showed no tendency to separate after several days.*

The single specimen of pancreatine which I was able to examine was found to have an energetic proteolytic activity, and it also curdled milk; but it had no action on starch, a fact which supplied an unex-

* This excellent preparation would be much improved if the strong ethereal and spicy flavour of it could be removed.

pected confirmation of the opinion that the four pancreatic ferments are perfectly distinct bodies.

The most complete, active, and convenient medicinal equivalents of pancreatic juice are, however, the liquid extracts of the gland. These may be prepared from the pancreas of the pig, with glycerine, with water, or with brine. The glycerine extract leaves nothing to desire on the score of activity, and it keeps perfectly; but the taste of glycerine is to some persons objectionable, and it seems sometimes to provoke nausea, and even vomiting.

The aqueous extract, as prepared for me by Mr. Benger, will, I think, prove a valuable preparation. It is simply an extract of the gland in water, with just enough spirit added to keep it from decomposition. I propose to call it liquor pancreaticus. A sample of it is on the table before you. It is a limpid, straw-coloured fluid, with very little taste or smell of its own, and of nearly neutral reaction. But though so pale and bland, it is an elixir of really remarkable powers; it curdles milk like rennet; it changes starch into sugar with unrivalled energy; with the aid of a little alkali, it transforms albuminous substances into peptones; finally, it emulsifies fats more perfectly than any other known agent. Extracts of pancreas are destined, if I am not mistaken, to play a considerable part in the dietetic therapeutics of the future. Whether the full powers of these preparations can be made available when administered by the mouth, must be regarded as uncertain. As an aid to the digestion of starch, the propriety of giving them by the mouth cannot of course be doubted; but the propriety of giving them by the mouth as proteolytic agents is a less simple question, seeing that it requires the addition of an alkali to bring the trypsin into activity; and the addition of an alkali is an interference with gastric digestion which may, or may not, be advantageous in a particular case. I commenced to employ pancreatic extract by the mouth about two years ago, and have now had considerable experience of its use. Guided by theoretical considerations, I have usually directed the dose (a teaspoonful) to be given, with twelve or fifteen grains of bicarbonate of soda, one and a half or two hours after a meal, when gastric digestion might be supposed to be approaching its termination, and the later portions of the meal to be passing into the duodenum. There is at this late period of digestion a tendency to excess of acid in the stomach, and the alkali alone is undoubtedly of service; but I have had, in several instances, striking results from the combination of the extract with the alkali, which I had previously failed to obtain from the alkali alone. I am, therefore, pretty strongly convinced that, by administering a pancreatic preparation towards the tail of gastric digestion, you can, under the guardianship of a dose of alkali, convey it into the duodenum, where it arrives opportunely to aid in the important work of intestinal digestion. But, however useful pancreatic extracts may prove to be for administration by the mouth, I anticipate far more important results from their employment in the preparation of peptones and peptonised aliments; and to this subject I now beg to call your attention.

[To be continued.]

PORTSMOUTH.—The two most interesting features in Mr. George Turner's last report are the account of an epidemic of typhoid fever due to milk, and a critical study of infantile diarrhoea. Into the latter question we need not now go, as Mr. Turner's opinions have been already sufficiently explained in the JOURNAL (vol. i, 1879, page 821); but we may, in passing, pay a tribute of admiration to Mr. Turner for the earnest and laborious investigation which he is making into this very difficult question. The history of the milk epidemic is not very exactly told; but it may be broadly stated that, of 153 cases of typhoid fever, during the third quarter of 1878, in a town which stands worst as regards the disease of the twenty large towns, 64 per cent. obtained their milk directly or indirectly, from a particular farm. At this farm, there had been a case of typhoid fever, and the well of the house was within a few feet of the cesspit of the common privy. There seems, therefore, little reason to doubt that the milk supplied by this dairy contained the contagium of enteric fever, which was thus distributed to the consumers. During the year, the general death-rate was 19.02 per 1,000, which, though higher than that for 1877, is slightly below the average for the last six years. The increased mortality has been due rather to a general rise in the death-rate from all causes than from the presence of any large amount of zymotic disease. The greatest blot on the character of the borough is the high death-rate from typhoid fever. The reasons why Portsmouth seems to be so much subject to this disease are the flatness of the sewers, the insufficient ventilation of sewers and house-drains, and the defective construction of houses. The typhoid fever-rate in 1878 was 0.71 per 1,000, and the disease is always most prevalent at the end of the third and the beginning of the fourth quarter of the year. The figures for the other zymotic diseases call for no remark.

CLINICAL LECTURE

ON

AMPUTATION AT THE HIP-JOINT:

WITH CASES ILLUSTRATING THE USE OF THE LEVER
FOR CONTROLLING HÆMORRHAGE.

By RICHARD DAVY, M.B., F.R.C.S.,

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GENTLEMEN,—Some few years ago, I drew the attention of surgeons to the *per rectum* compression of the aorta and iliac arteries for the temporary arrest of hæmorrhage during the performance of operations, and practically demonstrated the efficacy of the method in cases of amputation at the hip-joint. I shall endeavour to interest you to-day, first, by practical observations on amputation at the hip-joint; and, second, by recording the ascertained experience of operating surgeons in the use of the lever for controlling bleeding during amputation at the hip-joint.

Firstly, in considering how surgeons may best restrain bleeding in amputation at the hip-joint, just look at a side view of the pelvis, with the arteries injected (Royal College of Surgeons' Museum, 939, Q. f. Homo); you will notice how that the anterior flap is principally fed by the external, the posterior by the internal iliac artery; therefore, the common iliac artery must be compressed to secure both. And Nature has so focussed her blood-courses at the common iliac artery for the nourishment of the lower limb, that it really seems strange that compression of this vessel should not have been earlier practised.

I would insist strongly on the absolute necessity for restraining loss of blood from the posterior flap; much as I respect the femoral artery in the anterior flap, yet more do I beg you not to underrate the large and numerous muscular branches of the gluteal and sciatic trunks in the posterior. In an interesting discussion at the Clinical Society of London, following a paper read by my colleague, Mr. A. Pearce Gould (*vide* BRITISH MEDICAL JOURNAL, May 10th, 1879), the use of the rectal lever was received with favour, and a comparison was drawn between it and digital compression. I can only state that, after a surgeon has proved practically how very easy it is to prolong indefinitely compression by the lever, he will not care to submit to the fatigue, uncertainty, and anxiety of the digital pressure. Nor can I see why the whole thickness of the abdomen should be squeezed, now that it has been shown that the common iliac artery may be compressed, with only the thin rectal wall intervening.

Mr. Newman of Glasgow has sent me a pamphlet, in which he describes a special knife and India-rubber bands for compressing the flaps during amputation at the hip-joint. It seems to me that, as Pancoast's tourniquet applied over the aorta is too high up, so also Mr. Newman's apparatus on the flaps is applied too low down; and that operating surgeons in future will act on the spirit of the motto,

"In medio tutissimus ibis",

and compress the common iliac artery *per rectum*.

I will just say one word on the perfect safety and absence of inconvenience in using the lever. I have personally compressed the common iliac artery in a man suffering from aneurism of the right external iliac artery, aged 60, for twenty minutes, and without chloroform or other anæsthetic. The only pain felt was the presence of a foreign body; showing how tolerant of pressure the upper part of the rectum is. In no case (so far as I am aware) has any blood or stain been seen in the stool, though I have watched carefully for this event.

On anatomical grounds, the situation of the common iliac artery is perfect for the ends of compression; the lever drops between the psoas magnus muscle and the bodies of the lumbar vertebræ, having the spring (sacral margin) of the true pelvic brim as a counter-resistance to the lever, and no large nervous trunks in the way. I tried to pass the lever once on a dead body at the Westminster Hospital, and failed; I dissected this rectum *in situ*, and found syphilitic stricture in it; in short, the gut was tied up like a boy's cracker; this is the only case in which any difficulty has been met with at present.

The lever is turned out of ebony, and varies in length from eighteen

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to twenty-two inches. Its surface is very smooth and polished; and its ends are rounded off much like the finger-tips. The maximum trans-