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PART I.

ORIGINAL COMMUNICATIONS.

ART. X.—*On the Therapeutic Uses of the Digestive Ferments.*
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IF we may judge from the number of advertisements with which the journals are filled, and by the number of testimonials from chemists and practitioners which accompany these advertisements, there are few kinds of medicine more widely used at the present time than are the digestive ferments.

If we neglect the somewhat doubtful lactic acid ferment of the stomach, we know five digestive ferments:—1. A diastatic ferment found in the saliva and also in the pancreatic fluid; 2. A milk-curdling ferment found in the stomach and also in the pancreas; 3. A ferment which decomposes neutral fats, and which is found in the pancreas, and possibly in small quantity in the stomach; 4. A ferment which splits cane sugar into glucose and levulose, and which changes maltose into glucose—found only in the small intestine; and 5. A ferment, or, more properly, ferments, which convert proteid substances into peptone and other products. These ferments, which differ very much in their action, and in the conditions under which they act, are found in the stomach as pepsin, and in the pancreas as trypsin.

Now, as therapeutic agents there are some of these which we may eliminate, since their action is apparently unimportant for the process of digestion. We do not know why milk is curdled in the

* Read in the Medical Section of the Academy of Medicine in Ireland, Friday, January 29, 1886. [For the discussion on this paper, see page 274.]

stomach, and I believe rennet is never given as medicine. The decomposition of neutral fats undoubtedly takes place in the intestine, but we have every reason to believe that this occurs only to a very limited extent, and that the absorption of neutral fats is effected for the most part without their having undergone any chemical change. Moreover, the fat-decomposing ferment of the pancreas is the most delicate of all the ferments, and even if it could be separated and administered it would be immediately destroyed by the acid of the stomach, as it cannot resist the action of an acid medium.

Thirdly, the inversive ferment of the small intestine is not much used in medicine, and we do not know to what extent in normal digestion splitting of the sugars of the saccharose group takes place. We have thus remaining only two ferments—the diastatic and the proteolytic.

The diastatic ferment is given either as preparations of malt or as pancreatic extracts, and there is no doubt that many of these substances do contain a ferment which changes starch to dextrin and sugar. But what is the value of this? In the body the transformation of starch takes place in the mouth and for a short time in the stomach. Then the action is stopped by the increasing acidity of the gastric juice and the salivary diastase is destroyed, not merely suspended in its action. In the intestine the action is again resumed and completed by the more powerful diastatic ferment of the pancreas, and usually there is very little unchanged starch to be found in the fæces. Now when diastatic ferment is given by the mouth it can only supplement the action of the saliva, for, before it can reach the intestine, it is destroyed by the acid of the stomach. The action of the saliva on starch is far less important than that of the pancreas, and, while after a starchy meal much unchanged starch is always found in the stomach, scarcely any is to be found in the intestine. In many of the lower animals who eat their food raw the saliva has scarcely any digestive action, and the starch is digested altogether by the pancreas. Hence the useful effect of diastase given by the mouth must be insignificant, even supposing that the preparation is good, and that the ferment in question is wanting in the saliva. But is this ever the case? I do not remember ever to have heard of an instance in which the physician found this to be so before he prescribed maltin or pancreas preparations; and I believe that the absence of ptyalin from the secretion of the mouth will be found to be

one of the rarest circumstances. I must therefore conclude that as regards diastatic ferments their administration as such is useless and irrational.

We now come to the proteolytic ferments, which are in many respects the most important of all. First, as regards the pancreas ferment or trypsin—it is generally stated that this ferment is destroyed by acid of the strength of that of the gastric juice, and there can be no doubt that this is true of many pancreas extracts. This being so, it is evident that it is useless to administer trypsin as a drug, for its activity will be destroyed if it be given while the stomach is digesting and contains acid, while if it be given during fasting, when the stomach contents are not acid, it is incredible that it could pass through the stomach and lie in wait in the duodenum until the next meal is taken, and, having undergone stomach digestion, has passed through the pylorus.

I have, however, found the statement that the proteolytic ferment of the pancreas is destroyed by acid to be not invariably true. I have lately worked with an example of the liquor pancreaticus made by Mottershead of Manchester, a very active preparation. This is acid, but what the nature of the acid is I cannot say. The liquor has a vinous smell, and the acid is possibly only that of the wine with which the preparation seems to be made. I have found that when the liquor was mixed with about five times its bulk of 0.2 per cent. hydrochloric acid and kept for twenty-four hours at 100° F. in the water bath, then neutralised and added to 1 per cent. solution of carbonate of sodium, it dissolved fibrin readily, although not so rapidly as before acidification. This solution was not due to putrefaction, as it took place when thymol was added to the digestive mixture, and when this lay for many days in the water bath it developed no putrefactive smell. Another statement which has been made by Kühne I have been also unable to confirm. He says that in a mixture of pepsin and trypsin the latter is destroyed, while the former is uninjured, and he suggests that in the body the bile plays an important part in precipitating and killing the pepsin before it can reach the pancreatic fluid. In order to test this I mixed equal volumes of Mottershead's liquor pancreaticus and liquor pepticus together, carefully neutralised the mixture with sodium carbonate, and left it for twenty-four hours in the water bath at 100°–104° F. I then divided the mixture into two equal parts: to one I added 0.2 per cent. HCl, to the other 1 per cent. Na_2CO_3 , and placed fibrin in each. The alkaline fluid digested the fibrin readily; the acid even

after several days showed no signs of digestion. Here it would appear that the pepsin was destroyed, not the trypsin. Although I have repeated these experiments with constant result, I cannot affirm more than that what I have described took place with the particular material with which I worked, and I do not wish to throw any doubt on the contrary results got by other observers. To what the discrepancy is due, must be a matter for further investigation.

Still, even admitting that trypsin is not absolutely destroyed in the stomach, I think there is but little encouragement for its administration as a drug. Mixed up with the acid chyme such part of it as escaped absorption in the stomach would be precipitated by the bile along with the pepsin when the contents of the stomach passed into the duodenum, and even if it were again dissolved it would be so enfeebled in its action as to be of little use in digestion. But beyond this, is there any evidence that this ferment is wanting in the pancreatic fluid? Has any attempt ever been made to show this, or is there any known way by which it may be determined? It is more than probable that so long as pancreatic fluid continues to flow into the intestine it contains trypsin in far better condition than this ferment would be after having undergone stomach digestion. I would therefore condemn the administration of trypsin as I have done that of diastase.

We finally come to pepsin, and here, if anywhere, we have the ferment whose administration rests on a scientific basis. This ferment is easily prepared and kept, as it keeps well in an acid solution which is not prone to decompose. It can be introduced into the stomach without having undergone injury by the action of any other gland, and we can time its administration so as to introduce it when it is required. Is its administration, then, founded on sound principles? I believe not. In the first place, pepsin is very rarely absent from the gastric secretion.* I have repeatedly examined matters ejected from the stomach. They were sometimes alkaline, or fœtid—on one occasion smelling strongly of ammonia, but always when they were filtered and acidified they digested fibrin or albumen readily. It is, therefore, not to the want of pepsin that the failure of stomach digestion is usually due, but to some failure in the conditions under which only the pepsin will act. I do not deny, however, that there are cases in which pepsin is absent, and

* This is in accordance with the large experience of Dr. C. A. Ewald. *Berliner klinische Wochenschrift*, 1886. P. 51.

that it may be possible to effect an artificial digestion in the stomach, but is that an experiment which any chemist would like to undertake?

If the condition of the stomach is so seriously affected as to cause a cessation in the secretion of the pepsin, it is most likely that the viscus is not a very favourable receptacle in which to carry on an artificial digestion. The matters introduced are withdrawn from observation and removed from control; we have no power of keeping them from hurtful mixture or of regulating the conditions so that they may be favourable to the process. In short, it seems to me that the stomach is about the worst place possible in which to perform a prolonged and delicate chemical experiment. Since, then, pepsin is very rarely absent from the stomach, and since, even in those cases where it is wanting, the conditions for its action are not favourable, I think that pepsin, like the other ferments, should be banished from the list of drugs employed for administration as internal medicine.

In what I have said I have supposed that the ferments in question are genuine, and capable, under favourable circumstances, of producing their digestive actions on the different alimentary substances. The pepsin preparations are usually good. As I have said, it is easy to make a good stomach extract. Many of the diastatic and pancreatic preparations are utterly worthless, while others are very good.

I suppose, too, that the different ferments are given with some regard to common sense, and not all mixed together regardless of whether they are mutually antagonistic, or whether they act in acid or alkaline solution. But even so, and considered as a question of physiological chemistry, I hold that these substances are not suitable for internal administration.

Of course it will be urged that everyone has seen cases in which the use of these ferments has been attended with marked success. To this I answer—firstly, that the treatment is never confined to the administration of the ferments, but that dietary and other precautions are adopted, to which more than to the medicine the improvement of the patient is due. Secondly, the fact that a patient takes a drug and gets better is no proof that the drug is the direct cause of the improvement. How many patients are cured yearly by homœopathic globules in the thirtieth dilution? how many patients are relieved of the most severe symptoms by having bits of metal fastened on their limbs, by breathing through a solenoid, or

by being put to bed with a horseshoe magnet? and yet does anyone really believe that these cures are produced by the treatment directly, and not through the mental effect the impressiveness of the treatment produces. When a patient gets a bottle of one of the digestive ferments he finds around it a sheaf of testimonials from the most eminent practitioners, and on the label of the bottle is a farrago of nonsense, which passes with him for science. He is told how these ferments (which, as every physiologist knows, have never been isolated or weighed) are here combined in the exact proportions in which they are found in the stomach; that he has here the means of digesting everything that can be swallowed; that he has in his hands a "medical certainty" which will cure all the disease the human frame is liable to. Is it any wonder that he feels comforted both in mind and body? Besides, these drugs have a great advantage over many others—they can do no harm. As placebos, then, I do not object to them, but do not let the medical man suppose that he is walking in the paths of physiological science when he prescribes them.

Are the ferments, then, of no use to the physician? On the contrary I believe them to be of great utility. The attempt to perform an artificial digestion in the living stomach I have deprecated; but the artificial digestion of food in clean vessels outside the body and the administration of the digested material is a mode of treatment scientific in itself, and one which is attended with the very best results. Here we have no interference of one ferment with another; no uncertainty of whether the ferment will find in the body the suitable conditions for its action. The whole process is carried on under our eyes and in circumstances which are under our control. This use of the ferments inaugurated by Liebig, and so much extended in late years, chiefly through the labours of Sir William Roberts, is I believe the true one, and destined to replace altogether their internal administration as drugs.