

On pepsine / by M. Boudault ; translated by W. Stevens Squire.

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(1)

ON PEPSINE.

BY

M. BOUDAULT.

TRANSLATED BY

W. STEVENS SQUIRE, Ph.D., F.C.S.

THIRD EDITION,

WITH REMARKS BY ENGLISH PHYSICIANS.

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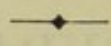
1863.

Price Sixpence.



ON PEPSINE

INTRODUCTION.

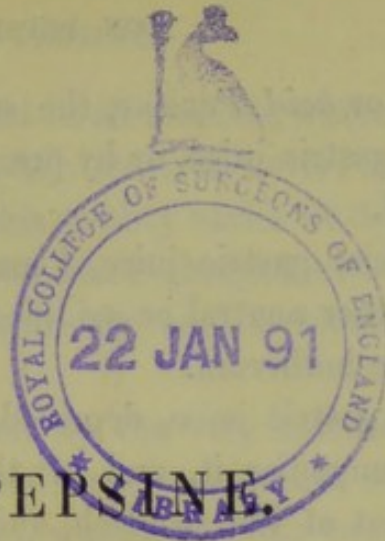


THE translation of M. Boudault's pamphlet "ON PEPSINE" being out of print, it has become necessary to issue a second edition. Since the publication, however, of the first edition, Pepsine has been so extensively used by English Physicians, that an immense amount of valuable information, and experience in the use of this agent, has been accumulated by them.

I have, therefore, for the use principally of medical men, but also to a great extent for the benefit of the general public, appended to this edition of M. Boudault's memoir extracts from the writings of, as well as special and original communications from, some of the eminent Physicians who have employed M. Boudault's preparation.

W. S. S.

LONDON:
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ON PEPSINE.

A PROCESS for preparing Pepsine from the rennet of the sheep was described by me a year ago in a paper read before the Academy of Medicine, and I endeavoured, at the same time, to explain some of the very interesting properties of that secretion of the stomach.

Being now able to obtain considerable quantities of it, whether in solution or powder, I have endeavoured to complete the chemical investigation of this substance, and to indicate the most convenient means of employing it in medicine.

Some of the facts that I am about to detail are already well known to scientific men, but I have thought it necessary, with a view to proving the affinity, that chemically prepared Pepsine has to natural Pepsine, to bring forward all the reactions of each.

The objects that I have in view in this memoir are—to compare the physical, chemical, and physiological properties of artificial Pepsine with those of natural Pepsine, and, to ascertain the best mode of exhibiting Pepsine as a medicine.

I have employed in my experiments the method proposed by Dr. Blondlot for procuring the natural gastric juice; and by means of fistulæ inserted into the stomachs of a large number of dogs, I have succeeded in procuring a certain quantity of *natural gastric juice*.

I wish it to be understood that by the term *natural gastric juice*, I mean the liquid product secreted by the stomach, and

by *neutral* or *acid Pepsine*, the substance obtained by evaporating the gastric juice, or by precipitating it with neutral acetate of lead.

By artificial gastric juice, I mean the solution, in water, of Pepsine, either neutral or acidified, but obtained from the stomach of the herbivora.

Properties
of Pepsine.

Natural gastric juice, deprived, by filtration, of the mucus which accompanies it, and of the alimentary matters which line the coat of the stomach, and which contaminate it when it is collected, is a limpid liquid of a light amber colour, astringent and rather saline taste, and a density slightly greater than that of water. Its odour is characteristic, more especially when it is heated; it then resembles that of broth. When exposed for six hours to the temperature of 50° Centigrade (122° Fahrenheit), it becomes slightly turbid, and loses its power of digestion. When the gastric juice is pure, it can be kept out of contact of air for many years without alteration, and without losing its chemical and physiological properties. Alcohol precipitates Pepsine from its solution, and separates it from its acid. Absolute alcohol dehydrates Pepsine, and deprives it, if not quite, at least in part, of its property of digesting *fibrine*.

Tannin produces a precipitate in gastric juice; but the precipitate possesses none of the physiological properties of Pepsine. Metallic salts also produce a precipitate in the gastric juice; and this precipitate, when decomposed, reproduces the Pepsine, with its physiological properties.

The quantity of water which the gastric juice contains is considerable; amounting to 97 per cent. of the liquid secretion in its greatest state of purity: about 1.25 per cent. is Pepsine. There remains, consequently, 1.75 per cent. for salts, which are always much about the same, but in differing proportions—viz. carbonate and phosphate of lime, chloride of sodium, minute traces of sulphates, and often a trace of ammoniacal salts. Lastly, the gastric juice contains a free acid.

The gastric juice must always be acid to be endowed with digestive properties. It is, in fact, demonstrated, that the

gastric juice is constantly acid in all animals, whatever be their age, species, or even food. We shall, however, have to draw attention to the fact, that this acidity varies in degree. It is greater when the food has been much charged with amylaceous principles, which indicates what the acid is which forms part of the gastric juice.

I shall not attempt to open up the very extensive question of the presence of other acids, such as acetic acid, butyric, hydrochloric, phosphoric, etc., whether in the free state, or in the form of acid salts. I have undoubtedly verified the presence of a certain number of these acids and these salts in the gastric juice, but in very minute proportions, compared with the quantity of lactic acid. It may even be presumed that the acids were set at liberty by the action of the lactic acid upon their salts; for it was more especially after the concentration of the gastric fluid that I succeeded in establishing their presence.

Acid of the
gastric
juice.

The acid in it gives to the gastric juice the reactions of a dilute acid; it attacks iron filings, and decomposes the alkaline carbonates.

Many physiologists assert that the gastric juice is neutral when it is secreted; others, on the contrary, contend that it is secreted in an acid state.

This point I have endeavoured to determine by approaching it with the combined resources of chemistry and physiology.

I killed some animals at the time when digestion was most active, and separated from the rennet-bag the mucus with the greatest care; I next removed, with distilled water, all the soluble matters, until litmus paper was no longer reddened; the bag was then scraped, and the cells bruised, and, on treating it again with distilled water, I obtained a perfectly neutral liquid. When this liquid was exposed for some hours in contact with fibrine, to a temperature of 40° Centigrade (104° Fahrenheit), *no* digestion took place. But another portion of this fluid under the same conditions, to which a small proportion of lactic acid was added, yielded, at the end of two hours, complete digestion.

From this experiment, repeated a great number of times

upon the carnivora and herbivora, it is fair to conclude that Pepsine is secreted in a neutral state.

As it is admitted that lactic acid is always found in the gastric juice, and is one of the principal agents, let us inquire how the lactic acid is formed. Is it formed from the amylaceous substances by the action of the alimentary matters, or by the action of Pepsine?

Action of
Pepsine.

In point of fact, Pepsine has always been considered as a true ferment; but it certainly does not act as common ferments, yeast, for example. It acts upon the alimentary matters by dissociating them, and causing them to undergo an isomeric transformation, so to speak, but not a decomposition.

It is, indeed, already admitted that acid Pepsine—that is to say, gastric juice itself—is able to transform glucose into lactic acid. I have, however, found, by numerous experiments, that neutral Pepsine acts as a true ferment in the presence of glucose, and transforms it into lactic acid, and so reconstitutes the gastric juice.

If I take a certain quantity of Pepsine in solution and perfectly neutral, and add to it some glucose, and submit the whole to a temperature of 40° C. (104° Fahrenheit), for twelve hours, I find at the end of this time that lactic acid has been formed; and if I add to this mixture some fibrine, I find that after some hours I have complete digestion. It is therefore perfectly proved that, by means of neutral Pepsine, we cannot obtain digestion, and that with Pepsine and glucose no immediate digestion takes place; it does not act, in short, until the glucose is converted into lactic acid.

This experiment enables us to explain the presence of the large quantity of lactic acid present in the gastric juice. The amylaceous matters are transformed by the salivary diastase into glucose, which is thus found in the stomach in considerable quantity, and the Pepsine determines its conversion into lactic acid.

The other acids can certainly play the same part as lactic acid in the stomach, when this acid is deficient; but we have never obtained such complete artificial digestions with Pepsine

acidified by hydrochloric and acetic acids, as we have with Pepsine acidified with lactic acid.*

Having described the properties of natural Pepsine, we shall now examine those of artificial Pepsine, and follow them in all their reactions.

In the first place I endeavoured to ascertain whether the natural Pepsine obtained from the gastric juice of carnivora, and that obtained from the stomachs of herbivora, have the same chemical composition in 100 parts; but I tried in vain to obtain Pepsine chemically pure, by employing either the gastric juice from the stomachs of dogs or the rennet-bags of sheep. It was difficult to obtain twice running a product which had the same percentage composition. I obtained products, physiologically speaking, perfectly similar, and the chemical reactions of which were precisely the same; but, when I submitted them to ultimate analysis, I found discrepancies so great, either in the nitrogen, the carbon, or the water, that I was unable to arrive at any exact percentage formula. Whenever I arrived at great purity of product—that is to say, had isolated it completely from the salts and acids—it lost its physiological properties.

Identity of Pepsine in carnivora and herbivora.

In order to prove the perfect similarity of the two Pepsines, I was obliged to have recourse to its physical and chemical, and especially its physiological properties.

I have taken as a standard of comparison, or rather as a normal type, the gastric juice of the dog, obtained under the following conditions, and in all cases from healthy animals. The food which these animals received was always equal in weight, and always contained the same amount of nitrogenous matter. This food was administered every day at twelve o'clock; and on the day on which I wished to collect the gastric juice, in place of giving them their usual food, I caused them to eat tendons of beef, which had been boiled for a very long time in water, and were subsequently well washed, so

* This is an oversight, for hydrochloric acid succeeds quite as well as, if not better than, lactic acid.—Ed.

that no matter remained which could rapidly dissolve in the stomach of the animal.

I dried them in a stove, cut them into small pieces, and then administered them to my animals.

Then I attached to a tube, communicating with the stomach, an India-rubber bag, and I collected, under these conditions, a gastric juice nearly always identical, that is to say, possessing the properties I have indicated above; and especially that of digesting a definite quantity of fibrine by a definite weight of juice; that is to say, 100 grammes of the gastric juice of the dog ought always to digest 40 grammes of desiccated fibrine, when submitted for four hours to a temperature of 40° Centigrade.

I thus found it easy to make all my comparative experiments.

Having a certain quantity of artificial Pepsine dissolved in water, I could reduce it to the normal type—that is to say, proportion its digestive power by adding water if it was too concentrated, or evaporating it at a gentle temperature if it did not digest the same quantity of fibrine as the juice of the dog.

In this way, by making numerous artificial digestions (of course always under the same conditions), and comparative digestions with the gastric juice of the dog, I eventually succeeded in obtaining a Pepsine similar to the normal type.

In the preparation of Pepsine by chemical processes, the greater part of the lactic acid is eliminated. This acid must be restored, and the gastric juice of the dog will again serve as a standard of comparison. By means of a standard solution of litmus, I succeeded in determining the quantity of acid which should be added to artificial Pepsine to give it all the properties of the gastric juice of the dog.

The amber colour and density were found to be the same, and the odour might be confounded with that of the gastric juice of the dog. But one of the most important chemical and physiological characters which the natural and artificial gastric juices have in common, is, that when maintained for six hours at a temperature of 50° Cent. (122° Fahr.), chemical Pepsine

decomposes in the same manner as the natural. It becomes slightly turbid, and loses its digestive properties. It may be kept for an indefinite time if air be excluded; and when the bottle is opened, it resists putrefaction as long as the gastric juice of the dog, if the proportion of lactic acid is not augmented.

Alcohol precipitates it from its solution; tannin does the same; the salts of lead and mercury produce abundant precipitates, which can, by their decomposition, again reproduce the Pepsine.

Thus far I have succeeded in proving an entire similarity between the properties of the two Pepsines. We will now compare the products of digestion, in order to leave no doubt upon this subject; but first let me describe how I performed the artificial digestions, and consequently, under what conditions I tested comparatively the two fluid Pepsines.

Products of
digestion
compared.

I brought into contact definite quantities of fibrine and of each kind of gastric juice in small flasks, the necks of which were furnished with a bent tube dipping into lime-water. These flasks were submitted to a temperature of 40° C. (104° Fahr.) for four hours, in a water-bath. The flasks were agitated as often as possible; at the end of this time the fibrine was entirely digested, and the resemblance of the two products was apparent at first sight.

In order to imitate as much as possible the natural conditions, I employed bags of India-rubber as thin as possible, having the form of pears, and very long. These bags were introduced into the stomachs of the dogs through the fistulous openings. In these bags I placed the substances to digest, some containing the natural, others the artificial Pepsine, and in the same proportion as in the first experiment with the flasks. The digestions took place in precisely the same way, only quicker, in consequence of the peristaltic movement.

Not satisfied even with these almost natural means of obtaining the products of digestion, I have had recourse to the natural functions themselves. I deprived a dog of nitrogenized food for some days, and satisfied myself that the

stomach was perfectly free from alimentary matters, and that the gastric juice which passed through the fistula in the stomach was perfectly normal. I then administered to the animal a tolerably large quantity of fibrine; digestion took place rapidly, and I succeeded in collecting a viscous fluid, which I could compare with those previously obtained. It remains now to examine these different products of digestion.

When a digestion is complete, it should not precipitate by boiling. The assimilable product is then soluble in water; this is one of the most certain tests for distinguishing a product of digestion from a simple solution of fibrine in diluted acids.

All the various products of digestion obtained under the different conditions described above, possessed this property; when boiled they did not precipitate: they perfectly agreed therefore in this respect. When submitted to the action of chemical reagents the results were precisely similar. Precipitates were produced by salts of lead and mercury, by tannin, by alcohol, and the solution was coloured by nitric acid; in short, the Pepsine of the juice of the dog, and the Pepsine obtained by chemical processes, afforded perfectly similar products of digestion.

If, on the contrary, we compare the solution of fibrine in acids with the digestions thus produced, we no longer obtain the same reactions.

To obtain digestion, we must have the combined action of acid and Pepsine. The acid acts first; it disintegrates, it diminishes the aggregation of the fibrine; then comes the Pepsine, and finishes the digestion. I have employed the process of M. Longet for comparing the products of digestion. This most ingenious process consists in adding a mixture of glucose and bitartrate of copper and potash (the solution of M. Barreswil) to a nitrogenized product of digestion. If the digestion is complete, there is no reduction of the salt of copper by the glucose; in short, the nitrogenized nutriment masks the glucose.

In fact, when a definite quantity of M. Barreswil's solution

and a definite quantity of glucose are brought into contact with a solution of the product of digestion, the liquid becomes violet, and does not change by ebullition. If the quantity of glucose is much increased, a reduction then takes place, but still no precipitation, such as we obtain from a mere mixture of glucose and bitartrate of copper and potash.

This experiment was repeated with the products of digestion obtained both by the artificial Pepsine, and by that obtained from the dog, the results being perfectly similar, even to the violet colour. In this case, as in the others, we may come to the conclusion that the products are identical. I think that I have now shown the perfect similarity not only in the chemical and physical properties of the two Pepsines, but even in their physiological properties. We shall therefore be justified in substituting one for the other.

M. le Dr. Corvisart, in his paper upon nutriments and aliments, first proposed to employ Pepsine in cases of dyspepsia; for this purpose a large quantity of Pepsine is necessary, and it is most important that it should be uniform. As we are able to replace the Pepsine of the carnivora by the Pepsine of the herbivora, the question is solved.

It remains only to determine the best form of administration for this new medicine.

I have stated above that acidified Pepsine is soluble in all proportions in water, but these solutions change very easily, if they are exposed to the air. It would therefore be difficult to keep them in this state. Again, the taste is not very agreeable, and there would be a great repugnance on the part of invalids to take the liquid Pepsine, even if it were associated with sugar, or with substances capable of masking the taste.

Objections
to Pepsine
in a fluid
form.

I have therefore endeavoured to remedy these inconveniences. After many researches I concentrated the Pepsine to a syrupy consistence; but in this state it attracts moisture, and does not keep much better than when more diluted with water. I have therefore sought for a body that I could so incorporate with it as to enable me to reduce it to powder.

It is especially necessary that this body should be tolerably inert; it should not alter the Pepsine, and at the same time the Pepsine should not transform it into nutriment, or rather it should not act upon it as a true ferment. This body should likewise be able to absorb the humidity of the Pepsine, without, however, being so hygrometric as to attract moisture from the air.

Best form
for admi-
nistration.

I have had recourse, after a number of trials, to starch, powdered and dried at 100° C. (212° Fahr.)

Starch does not undergo any change in contact with Pepsine; it fulfils all the conditions that we wish for, and, more than this, it does not interfere in any manner with the digestion.

Mixed with starch thus dried, the Pepsine can be reduced to powder and preserved in well-closed bottles; it undergoes no alteration, and may be kept indefinitely without losing its physiological properties.

Its disagreeable taste is singularly modified; the odour only remains, and that is diminished in consequence of the dryness of the product.

The amount of starch to be added should always be specially determined, otherwise we should not obtain a product possessing constantly the same digestive power. Now it is of the utmost importance that a medicine should always have the same properties. I have once more availed myself of artificial digestions to determine the digestive power. I add, in fact, starch gradually in such quantities to the Pepsine that a gramme (fifteen grains) of the mixture is in a position to digest four grammes of dry fibrine, or that it will in the stomach cause the meat of a mutton chop to be digested.

Cases where
Pepsine is
suitable.

It is in cases of want of appetite, of sluggish and painful digestion, of diarrhœa, and of vomiting, in the weakness of stomach which still remains at the commencement of the convalescence of severe fever, and in the course of most chronic diseases, and lastly, in consumption arising from want of nourishment, that Pepsine is indicated as a powerful digestive agent.

It may be administered either in the acid or neutral form.

When acid, it possesses all the properties of gastric juice, and may be exhibited in all those cases where there is not too much acid already in the stomach. On the contrary, when diseases of the stomach give rise to an excess of acid, it should be administered in the neutral form: I will not say chemically neutral, but neutral at least if compared to the former.

Pepsine
No. 1, or
acid.

Pepsine
No. 4, or
neutral.

Pepsine can easily be taken before meals enveloped in a small piece of unfermented bread;* if it is taken in the first spoonful of soup, care should be taken that the temperature does not exceed 45° C. (113° Fahr.), otherwise its digestive properties will be inevitably lost. After meals it may be taken in syrup of cherries,† which entirely masks the taste.

I have endeavoured to give Pepsine in the form of a syrup, as it is as easy to obtain a definite solution in syrup as it is to mix it with starch; but I found that after a short time a very decided action took place of the Pepsine upon the cane-sugar.

Pepsine mixed with cane-sugar, and allowed to remain for several days, ten or twelve for instance, transforms it into glucose, and finally into lactic acid; it acts as a ferment. This would not be due to any salivary diastase present in the Pepsine which we prepared, as it was obtained not from the compound fluid found in the stomach, but from the mucous membrane previously well washed. It was therefore impossible to prepare this mixture of Pepsine and syrup of cherries in advance.

Pepsine can be mixed with certain medicines which do not modify its digestive properties in the least.

Hydrochlorate of morphia, in the proportion of 1 centigramme ($\frac{1}{7}$ grain), at a meal, may be added to Pepsine in cases of severe pain in the stomach.

Pepsine
No. 2.

Strychnine, in the proportion of 3 milligrammes ($\frac{1}{20}$ grain) *per diem*, is given in cases of want of peristaltic movement.

Pepsine
No. 3.

Other medicines, such as subnitrate of bismuth, lactate of iron, carbonate of iron, iodide of iron, and reduced iron, may

* Or between two thin slices of common bread.—ED.

† As syrup of cherries is not generally kept in this country, the syrup of orange, lemon, or mulberries may be substituted.—ED.

be mixed with Pepsine, and do not in any way alter its properties.

I have endeavoured to show that chemical Pepsine, or "*poudre nutritive*," can in every way replace the Pepsine of the gastric juice of animals, and that it can be employed as a medicine.

Clinical experience has fully confirmed this idea, and artificial Pepsine may now be employed in those cases where there is a deficiency of gastric juice, for the animal economy derives the same advantage as if the stomach had secreted a natural juice.

277, OXFORD STREET, LONDON,
28th January, 1857.

Extracted from the LANCET.

PRACTICAL LECTURES
ON THE
MANAGEMENT OF THE DIGESTION IN DISEASE.

Delivered at St. Mary's Hospital,

BY T. K. CHAMBERS, M.D., M.R.C.P.,

Lecturer on the Practice of Medicine at St. Mary's Medical School, and Physician
to the Hospital.

LECTURE VIII.—ON PEPSINE.

THE attempt to turn the peculiar powers of gastric juice to advantage in medicine, dates from remote antiquity. Pliny mentions the fluids of the stomach of sucking animals as a remedy in common use for a variety of purposes, such as curing disorders of the intestines, allaying the inflammation from spiders' bites, stopping bleeding from the nose, preventing snakes attacking you, and, in fine, against poisons in general.* Galen, arguing probably on physiological grounds, attributes a "digestive" and "drying" power to it. He mentions having experienced in his own person the relief afforded by it to the weight at the epigastrium after drinking too much milk, and advises a trial of it in abdominal disorders. He remarks that the stomach of one animal differs from another only in degree of power. He gives a warning also that the boiling temperature destroys its virtues, as we now well know; for he found that hens' and cormorants' stomachs, when cooked, were perfectly inert.†

History of
Pepsine

On the strength of his rational advice, the coagulated milk and fluids taken from the paunches of several young animals was a remedy sufficiently often used to retain a place in Euro-

* See the places referred to in any good index to Pliny's Nat. Hist., article "Coagulum."

† Galeni de Simpl. Med. x. 11; xi. 13.

pean Pharmacopœias up to the first quarter of the last century. This is the explanation given by Dr. Schroder, a Dutch pharmacologist, who wrote in 1672,* of the method of preparing, and the reason for using, "*Coagulum leporis† hædi, agni, equi,*" etc.

The disagreeable nature of the remedy in this form probably drove it out of use, for the last London Pharmacopœia in which it appears is that of 1677. In the edition of 1721, the only representative of gastric juice is the mucous membrane of the hen's stomach—"*Pelliculæ stomachi gallinæ interiores.*"‡ In 1746 this also had vanished, along with "*stercus bovinum humanum, pavonis,*" and various similar remedies which patients had got too civilized to submit to, without at least knowing the reason why. Thirty years later, the immortal experiments of the Abbé Spallanzani threw a bright new light into the subject of digestion, and taught the true nature of the gastric juice. With much juster views than of old, its use in medicine was again recommended. Dr. Mongiardini, at Pavia, a pupil of Spallanzani's, at his master's instance, treated indigestion successfully with the gastric juice of crows. Another pupil employed it as a lithontriptic, to break down calculi by destroying the animal matter which holds them together. M. Senebier, a clerical pupil, suggested that its antiseptic power might make it useful in surgery, and advised a trial of sheep's paunch as an application to ill-conditioned wounds.§ M. Boyer, of Strasburg, found that it destroyed the poison of the viper, and thought it might be an antidote to snake-bites.||

* 'Pharmacopœia Medico-Chimica.' Amstelodami, 1672.

† The rennet of the leveret is now usually wasted, but the Roman dairymaids preferred it to that of any other animal for making cheese. Varro ranks it as the best, then that of the kid, then of the lamb. (Varro de Re Rusticâ, lib. ii., xi. 4.) The Roman physicians also had the same preference. Quintus Sammonicus, in a prescription for "colus" (colic), says, "Aut pavidi leporis madefacta coagula pota." (Sammonici de Medicinâ Præcepta, "De colo compescendo.") This accounts for its being named in Pharmacopœias which omit other rennets, as, for instance, in the Vienna priced drug list of 1613 and 1646, in which its price varies from six to sixteen kreutzers the half-ounce.

‡ This is another Italian expedient for coagulating milk rarely used now. Palladius recommends it for making summer cheeses, when you cannot get leverets.—Palladius de Re Rusticâ, Mensis Maius, ix.

§ 'Expériences sur la Digestion de l'Homme, par l'Abbé Spallanzani, avec des Considérations,' etc., par Jean Senebier. Genève, 1783.

|| Falek, 'Handbuch der Arzneimittellehre,' vol. i. p. 275.

But with all the obvious advantages with which the remedy recommended itself to the physician, there was the insurmountable difficulty of obtaining it in a form fit for general use internally. It was of course necessary to administer it at the same time with the food, and any nauseating substance then given does more harm than good, by taking away the already squeamish appetite. Dr. Latham, who practised in Paris some years ago, informed me that Laennec had a preparation of concentrated gastric mucus, which he recommended with great enthusiasm.

But the matter showed itself in quite a new light when an ingenious French pharmacien, M. Boudault, made the very elegant and agreeable preparation now so well known to the profession as "*poudre nutritive*." It is simply Pepsine from the sheep's stomach dried on starch, with lactic acid added or not, according to circumstances. When, one day in the autumn of last year, Dr. Waller Lewis showed me some of this powder he had brought from Paris, I saw in a moment that it was what we had been so long wanting, and instantly ordered a kilogramme over for experiment. You have since that time seen me prescribe it to numerous patients in the wards, and I have also employed it frequently in private practice, so that I think we are in a position now to form an idea of its value to the practical physician.

The cases in which I have administered it with advantage are—six of phthisis pulmonalis, one of cancer near the pylorus, two of gastric ulcer, one of hysterical vomiting, two of nausea, one of hysterical pain after eating, two of atonic pain after eating, one of atonic gout, one of dilated stomach, one of gastric flatulence, three of low fever, and two of pneumonia. In these, all the benefit which physiological reasoning would lead us to expect from the remedy has followed.

I have also injected it *per anum*, mixed with food, in a case of ulcerated œsophagus, and in a case of manio-hysterical vomiting and dysphagia. But in neither did it appear to delay death. Probably the ilia are the only part of the alimentary canal capable of absorbing chyme.

Boudault's
Pepsine.

Successful
cases.

Injection
per anum
useless.

Several other cases of atonic pain after eating, in which I have given Pepsine, I have not since heard of, but probably should have done so had any harm happened.

In one case of chronic dysentery it caused nausea and obliteration of appetite. In one case of consumption, and in one of pendulous tumour of the abdomen (attached probably to the pylorus), it purged the patient. These are the only instances of inconvenience that I have been able to assign to the remedy.

The phthisical cases have been those where a progressive anæmia was accompanied by an inability to digest meat or other albuminous food. This inability is exhibited in three ways: first, by the eating of such diet, even in very small quantities, being followed by a sense of great weight and oppression at the epigastrium, and sometimes by actual vomiting; secondly, by the passage of loose fetid stools, containing much unaltered muscular fibre, lumps of fat, and such-like remnants of a former meal; thirdly, by entire loss of appetite, and an instinctive nausea excited by the bare idea of flesh food. Often all three phenomena exist together; but each one may be found separately, and is of itself a sufficient indication of the patient's state.

Pathological explanation.

The pathological explanation of these symptoms is an excessive secretion, in the upper part of the alimentary canal, of alkaline mucus, which envelopes the food, and prevents the action of the gastric juice upon it. The consequence is, either its rapid ejection unaltered, or its decomposition, and the evolution of fetid gas. If vegetable food is mixed with the meat, it ferments into lactic and acetic acids; and thus you may have acid eructations from the stomach, and acid diarrhœa arising out of the want of acid gastric juice. If this excessive secretion of mucus is recent and moderate, the appetite may remain uninjured, nay, may sometimes be morbidly increased; but a long continuance, joined to progressive pulmonary disease, is sure to induce an anæmic condition of the alimentary canal, which results in a disgust for food.

Now this state of things it is very important to check. If it goes on, the patient cannot take in sufficient quantities the

meat which should refresh his degenerating muscles and pale blood ; he cannot take the cod-liver oil which is to replace his emaciating tissues ; he cannot, from weakness, take the exercise which might renew his whole diseased system. And I do not know any remedy which more readily, obviously, and directly does what it can towards checking it than Pepsine. It does immediately and surely what it can ; but then that is not very much. Do not raise your expectations of its powers too high, or you will be disappointed. Understand clearly what position this agent holds in the rational *Materia Medica*, and then you will know what good results you may demand with reasonable hopes of obtaining them. It is an *artificial*, and therefore a *partial*, substitute for a *natural* process. Gastric juice prepared by a healthy animal is mixed with the food, instead of that which the patient's stomach ought to prepare. And it acts in the body just as it would out of the body under the same circumstances of heat and motion. The chewed meat is dissolved by it, just as you see the white of egg suspended in this beaker dissolved by it ; and the putrefactive process is arrested by it in the intestinal canal, just as you perceive the putrefactive process is arrested by it in the experiment under our eye. For you may observe that this albumen suspended in Pepsine is quite sweet, whereas that soaked for the same time in saliva is most fetid. It is, therefore, a substitute for the natural secretion, and to a certain extent supplies its place. But, like all imitations of nature, it is coarse and imperfect. The solvent, instead of being gradually and continuously poured on to the outside of the mass of food, is mixed up in the middle of part of it, and acts merely chemically, without any of the mechanical and physiological helps belonging to natural digestion, and consequently soon exhausts its energies. The chyme, or albumen prepared for absorption, instead of being wiped off, and swept away by the stomach, remains for some time mixed up with the Pepsine, so that the latter is not freed for the solution of a small portion. By this imperfect process only a very small quantity of meat can be dissolved at once.

Practical
remarks.

Hence, if you hope that, by administering Pepsine with it, you can get a full and sufficient meal eaten at once by your consumptive patient, you will fail. Give half a mutton-chop with the remedy the first day, and, if that is digested well, try a whole chop the next; but remember, then you have got to the end of your tether, and that the digestion of a larger quantity will not be at all assisted by artificial solvents. Also, after a chop has been digested and absorbed twice, or even once a day, by this means for about a week or ten days, the expedient has probably done all the work that can be asked of it, and the stomach has either recovered sufficient energy to digest alone, or will require different remedies to enable it to do so. Therefore, for the Pepsine to be completely successful in these cases—first, it must be given only to those who cannot digest half a mutton chop without it; secondly, more than a chop must not be given at once; thirdly, it must not be required to go on alone improving the patient's condition for more than a week or ten days.

But for the time named, I do advise its being given alone, and the action not interfered with in general by other drugs. Many will really prevent its chemical effect, and all will confuse your judgment of the advantage gained. In this time you will generally find that the repugnance of the patient to meat has been overcome, and that a small quantity of it at a time can be relished and digested; the morbid fetor of the stools diminishes, and the flatulence and distress arising during their passage through the bowels ceases. A renewed strength and a renewed power of assimilation commence, the sleep becomes more natural, with the diminution of night-sweats and hectic; while, at the same time, the pulmonary symptoms of cough, dyspnoea, etc., relax, and a step at any rate is taken in the right direction towards the cure of the disease. It is remarkable, too, what a slight improvement in the digestive powers will often enable iron and cod-liver oil to be taken. These drugs are, you know, the mainstays in the treatment of tubercular consumption; and any expedient, however temporary, which will pave the way for their administration, is a great boon.

It would not suit the plan of the present lectures to quote ^{Consump-} in detail these consumptive cases. They differ much from one ^{tion.} another in their unessential characters—namely, in the stage of the disease, their ages, sexes, and general phenomena; while they are closely similar in essential points—that is to say, in those which I have described as indicating a mucous condition of stomach, preventing the gastric juice being poured out on the food, and finally leading to anæmia and atrophy of the secreting membrane. They resemble one another also in exhibiting an immediate and uniform amelioration of limited extent. In one man, who had loss of voice apparently from crude tubercle in the lungs, with ulcerated trachea, the amelioration of voice and cough continued so long, that I let him remain three weeks taking Pepsine alone without other drugs; but, then, he also continued to improve more afterwards on cod-liver oil, so that he might just as well have commenced it sooner. In another, who had tubercular ulcers in the bowels, afterwards fatal, there was an idea that the Pepsine caused a relapse of diarrhœa; but I suspect the coincidence was accidental. These are the only instances where it appeared to do more good or less good than I have attributed to it.

The case I alluded to of cancer near the pylorus is a type of ^{Cancer of} a disease necessarily fatal, being still worthy of the careful atten- ^{pylorus.} tion of the medical man. When the patient came under my care, she was unable to keep anything at all on her stomach; every solid, and even an ounce of beef-tea, was vomited unchanged within half an hour of its ingestion. She had been taking prussic acid, soda, creasote, opium, and a variety of remedies without benefit; and, as might be expected, was dying rapidly of starvation. I ordered her immediately half a mutton chop, with fifteen grains of Boudault's "*poudre nutritive*," twice a day, and an ounce of milk and lime-water every two hours. She kept all that down; it passed the pylorus, and nourished her so far that she had a good night's sleep, and the next day was able to take a whole mutton-chop. So she went on for three weeks, gaining flesh, losing her pain, and acquiring a cheerfulness about the future unwarranted by

the gloomy prognosis which truth compelled me to give her. So far all was right: reason had reasoned well. But I feel it a duty to tell you the mistakes I make, as much as the occasions on which I act wisely. And I find recorded in my notebook a warning, which I advise you to profit by, of the importance of "letting well alone." The patient had from the first jaundice, with pale stools and bilious urine; and now, I thought, had sufficiently recovered strength to bear an endeavour to make the liver clear the blood of its bile a little more briskly. I, therefore, gave her some nitro-hydrochloric acid, which is often of great use under similar circumstances. But the result was most unfortunate. The vomiting returned with violence. The drug was discontinued, and it stopped, but not before the ground gained had been lost. Then, again, contrary, I must say, to my wish, it was judged expedient to give the patient mercury, and she rapidly sank. The jaundice was then proved to be dependent on cancer of the gall-bladder. Now, here it is impossible not to allow that life was prolonged by artificial Pepsine, and would have been further prolonged but for the Anglo-Saxon propensity in both physician and patient for continuous improvement.

Hysterical
vomiting
and nausea.

In one case of hysterical vomiting, and two of nausea preventing due quantity of food being taken by hysterical persons, this remedy has appeared to enable the patient to swallow meat. The mere nutriment thus imbibed has improved the appetite for future meals; and the valerian and salt sponge-baths afterwards administered, seemed to have a more rapid effect than without it. The rational explanation of its good influence is, that both in hysteria and anæmia, the secretion of gastric juice is apt to be irregular and deficient, and that the morbid processes here act, as is so often the case, in a circle; the non-secretion of gastric juice still further starving the blood and aggravating the hysteria and anæmia, and that further aggravation again diminishing the secretion. But once breaking the magic chain, and enabling even a single meal to be well digested, begins a march toward health which it is comparatively easy to guide afterwards.

Closely connected with the last-named complaints is, in the female sex, atonic gastralgia. Indeed, I may say it is practically identical. At the same time that the gastric juice is imperfectly secreted, the muscles of the stomach refuse to perform the peristaltic motions with sufficient activity. Hence, not only is the alimentary mass a greater inconvenience than it ought to be, but it actually lies longer than usual in the first portion of the canal, as may be found on percussion of the epigastrium. It is a common consequence, in the educated classes, of excessive mental and sedentary labour. Where this is very great, I have found Pepsine of some use; but in the slighter cases, which more frequently come before us, I have not seen any apparent benefit accrue from it. A change of habits is here the only permanent remedy, and of drugs strychnine is the most efficacious. I see that M. Boudault prepares a powder in which strychnine is combined with Pepsine and lactic acid. I presume it is for this sort of cases that it is intended, but I do not like mixing up prescriptions in that way, and prefer the strychnine alone, as it is the real active ingredient.

In a case of diarrhœa and mucous vomiting, occurring in an old victim of atonic gout, the stools became more natural and less frequent, and strength was regained, on taking Pepsine and mutton-chops instead of opium and acetate of lead.

As cases of acute disease have an innate tendency to get well, they are not of course such good tests of the essential benefit derived from remedies. And it is only by comparison on a large scale that one could speak of fever and pneumonia being benefited by Pepsine. There seemed, however, in those alluded to, an immediate improvement to take place in the appearance of the tongue and of the evacuations; and it is impossible not to think that the amelioration thus evidenced of the alimentary canal would conduce to lessen the mortality of the disease.

On the whole, then, I cannot but conclude that we have in artificial Pepsine a valuable and safe remedy, and an important aid to rational medicine.

Dose.

The way in which I have given it has depended on the diet on which the patient is. If regular meals are eaten, then it is best taken spread as a sandwich between two thin slices of bread at the commencement of the dinner. Fifteen grains of the starchy powder is the usual dose for an adult. If the patient is so ill that the food is obliged to be administered more frequently and in small quantities, so as to keep up a continuous supply, smaller doses of the Pepsine powder may be given in a draught every four or five hours.

From DR. BALLARD.

42, MYDDELTON SQUARE, E.C.

DEAR SIR,—The second edition of my little work on “Artificial Digestion”* was just out of print, when I received your note, in which you invite me to append to your translation of M. Boudault’s pamphlet any observations that I may be disposed to make, respecting the results of my more mature experience of the use of Pepsine in the treatment of disease. My first edition was published just twelve months ago, when Boudault’s preparation was scarcely known here, and it is highly satisfactory to me to find that the medicine which I was then instrumental in introducing to the Profession in this country has so rapidly attained a position amongst our established remedies. Thus my object has been attained, the medicine has been extensively used, and its value tested, and consequently, any further issue of the work appears unnecessary. At the same time it is not to be concealed that, like every other new remedy laying claim to remarkable powers, its reputation

* *Preface to the Second Edition.*—It is gratifying to find that the subject of Artificial Digestion has excited the interest of the Profession. Nothing that I can add will enhance the force of the facts already put forth, nor have I seen any reason as yet to modify the opinions which those facts have led me to form.

I take this opportunity, however, of warning those who propose adopting this method of treatment, of the spurious character of some of the “*Poudre Nutri-mentive*, or Pepsine,” which is sold. To avoid disappointment, it should be tested as to its transforming power before administration.

42, Myddelton Square, Jan., 1857.

has been endangered by the indiscriminate manner in which it has frequently been prescribed. This error has arisen from overlooking the fact that its operation is restricted to the fulfilment of *one* indication, and of one only—the expectation that it will do more than act as a substitute for a deficient gastric secretion, can only lead to disappointment. As therefore I have determined upon withholding any further publication of my own upon the subject, I avail myself gladly of the opportunity you kindly afford me of protesting against this abuse of the remedy, and of pointing out briefly the class of patients for whom I have used it with success, and who may fairly be expected to benefit from its administration.

Passing over the *nature* of the change which the food undergoes in the process of gastric digestion, and assuming that, unless this change be undergone, alimentary matters are incapable of supplying nourishment to the body, I may just say, that in the healthy state the change is effected by admixture in the stomach with “gastric juice,” the more essential constituents of which, in addition to water, are an acid, either lactic or hydrochloric, or both, and an azotized substance of the nature of a ferment, to which the term “Pepsine” has been applied. After the secretion of the gastric fluid, the mucous membrane of the stomach has no more to do with the process; all that is necessary beyond this lies in an appropriate temperature, and just that mechanical agitation which the healthy stomach imparts to its contents. I am now speaking of the protein articles of food, and especially of animal food, of that food which chiefly maintains the fabric of the body, and not of the oleaginous and amylaceous elements which have a different purpose to serve, and which undergo in the alimentary canal a change of a different character.

It is well known to physicians that the changes in the food which I have referred to, are in disease sometimes arrested; they take place imperfectly, or do not take place at all. The pathological designation of the lesser failure is *dyspepsia*, of the greater *apepsia*; the results, local and constitutional, are, to a certain degree, alike, differing however in degree, and

Digestion :
its nature.

Dyspepsia
and aepsia.

the symptoms varying according to the presence or absence of certain recognized local conditions, the temperament of the sufferer, and other circumstances.

The more important causes of this failure are debility, especially of old age, and that which accompanies and succeeds severe diseases, anæmia, and structural changes which involve the secreting tissue of the stomach.

Unhealthy
digestion.

One class of results arising out of imperfect secretion of gastric juice, pertains to the stomach itself. The leading disturbances thus referred to, are anorexia, a sense of discomfort, weight, or absolute pain accompanying the tardy changes in the aliment; chemical alteration of the nature of decomposition in the aliment, with the production of abundance of gas and acid matters; and, lastly, vomiting, the food sooner or later being thrown off from the stomach in an undigested or almost undigested condition. Where from any cause the stomach is abnormally sensitive, the pain may be almost intolerable. Other sympathetic disturbances may be conjoined, such as overpowering lassitude, headache, tendency to sleep after meals, feverishness, etc.

But the evils consequent upon apepsia may not only be gastric, but intestinal also; the latter may even be the more prominent of the disturbances. It is in young infants and in early childhood that we principally meet with this result. The undigested food, passing along the intestinal canal, acts there as an irritant poison, producing, beside vomiting, diarrhœa and colic. In these circumstances, the undigested food is commonly recognizable in the evacuations. Sympathetic disturbances are often also observed in the form of pyrexia and various nervous systems. Sometimes the diarrhœa is not an immediate result of the apepsia; but a chronic state of ill health arises, in which, as it is well described by Barthez, "the child grows pallid and emaciates, gets flabby and etiolated, loses its strength, cheerfulness, and appetite, and then, after some time, diarrhœa supervenes." Such children at times eat largely, but, notwithstanding, do not thrive. These forms of diarrhœa are well known to medical men, as occasioning a large proportion of

our infantile mortality. The intestinal disturbance of apepsia is, however, not confined to childhood. In grown-up persons, as a direct result of it, we meet with flatulency of the intestines and diarrhœa; while, as an indirect result, an habitual costiveness is very commonly to be observed.

A further and more distant, but equally formidable result of this deficiency is inanition, more or less complete. Inanition. The weakness of the digestive powers may be exhibited chiefly in this way; the food, taken without appetite, soon disgusts, and the meal is left scarcely tasted, or what is eaten produces no influence in renovating the strength, or supplying the waste of the body. This is a condition which is recognized as of common occurrence in the advanced or convalescent stages of severe diseases. We would gladly furnish nutriment to our patient; but he either loathes the food which we present to him, or it fails to restore his powers. It cannot be doubted that this failure of gastric secretion is at the bottom of many instances of progressive chlorosis and prolonged debility, against which we oppose our customary remedies for a long time in vain.

It is to these various effects of apepsia, as resulting from deficient secretion or an imperfect quality of the gastric juice, that the method of treatment by artificial digestion is peculiarly applicable. There are cases also of acute disease which daily claim the most anxious attention of the practitioner, in which the great object at which he aims is to preserve his patient's life till nature has had time to effect her own work of reparation; where experience has satisfied him that, if life can be prolonged only for a limited period, recovery may be fairly anticipated; where, in fact, to gain time is to save life. There are cases also of disease in the digestive canal, where it may be of the first moment to afford nourishment to the patient, and at the same time so completely to utilize the aliment as to leave the smallest possible fœcal residue. In both these classes of cases, the use of this method of treatment is clearly indicated; and in both, the best results may fairly be looked for from its adoption.

Suitable cases for the administration of Pepsine.

An immediate effect of the administration of a dose of Pepsine in appropriate cases of dyspepsia, is sometimes, but not invariably, noticed in the production of *appetite* which had previously been absent. A few doses, in most cases, are followed by an appetite for subsequent meals; and where but little food could be taken without disgust at the commencement of the treatment, it often happens that full meals are shortly taken with pleasure. In those instances where voracious appetite accompanies prolonged diarrhœa, from the aepsia of infancy, the appetite becomes reduced, as soon as the effect of the general improved nutrition becomes marked.

Pain after meals.

The relief and rapid disappearance of painful sensations after meals, is a more marked effect of the use of Pepsine in cases of *dyspepsia*, arising out of defective or imperfect secretion of the gastric juice; and the same thing may be said of the arrest of the vomitings, which are due to the same cause, and also of the flatulent distensions that arise from the chemical decomposition of the aliment.

It is especially in cases where these disturbances succeed the use of animal food, that the employment of Pepsine is chiefly indicated. It often enables a patient, who has not dared to attempt it, and could not do so without suffering, at once to eat it with impunity. Nor is this operation tardy. The first dose usually in such instances produces an effect, and after two or three more no further discomfort is perceived. Even the severest cases of gastralgia after food, are almost as by a miracle relieved by its assistance. Where it fails to give relief to painful digestion, after three doses have been used, and still more so when future doses equally fail to assist the digestion, it is probable either that the dyspepsia does not arise from a defect of the gastric secretion, or that some other condition predominates as its cause, such as hyperæsthesia of the stomach, or atony of its muscular parietes.

Hyperæsthesia.

Where *hyperæsthesia* is conjoined to any great extent, and where, although the painful digestion is relieved by the Pepsine, it does not completely disappear, a small proportion of hydrochlorate of morphia may be prescribed with each dose.

This allays the sensitiveness of the stomach, and does not interfere with the operation of the Pepsine. Where *atony* prevails, the conjoint use of strychnia may be ordered.

It sometimes happens in dyspeptic cases, although acid is freely formed or secreted in the stomach, yet, that the Pepsine of the secretion is so deficient, that digestion is rendered imperfect. High acidity, in fact, of the contents of the stomach, shortly after a meal, is no proof that gastric juice is secreted of a quality adapted to transform the aliment. In these cases, if Pepsine be used, the neutral Pepsine is to be preferred.

But Pepsine does something more than act as a substitute for the natural secretion; its use is shortly succeeded by a restoration of the function of the gastric glands. It is not a merely palliative remedy then, in dyspepsia, as some have feared it might prove, and have consequently declined in my experience to avail themselves of its operation, but it is really curative.

Hence, after a few doses of the medicine, in the majority of cases, the quantity of the dose may be lessened without diminution of its effects, or its use may be limited to dinner or the principal meal of the day. In the less severe cases of dyspepsia, this is the only occasion in which it need be employed from the first—the digestive powers being restored so quickly, as to enable the patient to take meals of secondary importance without distress. The test of this restorative effect having been produced, is a temporary suspension of the medicine. After about six doses, it is not rarely found that digestion is in future perfectly accomplished, and the recurrence to the Pepsine is unnecessary. Should this happy result not follow, it is easy to resume its use. In some chronic and severe cases, advantage is decidedly gained by its employment daily for weeks or months. The presence of ulcer or hypermia of the stomach is no bar to the employment of Pepsine, but in either instance the ordinary treatment should be pursued until the more urgent symptoms are relieved, the proper time for using the Pepsine being that at which an improved diet is permissible. In the cases which have come under my care the amendment of the patients at this stage has been much more rapid, the strength

Atony.

Acidity.

Neutral
Pepsine
indicated.Not pallia-
tive, but
curative.Practical
remarks.

regained more rapidly, and the relapses have been less troublesome than prior to the period when I began to use the Pepsine. I have also seen much benefit accrue from its employment even in cancer of the stomach, where the vomited matter plainly demonstrated that the healthy changes in the aliment did not take place, and when the stomach was manifestly dilated.

In some cases in which I have prescribed it, I have found that the bowels, which were constipated previously, became more regular, and the stools softer under its use. In some, this has gone on to absolute relaxation of the bowels, with griping and borborygmi; but in no case has the debility of the patient been increased by this occurrence, and in all it ceased on the suspension of the medicine. In two instances, my patients have subsequently, on the recurrence of constipation, spontaneously resumed the use of small doses of Pepsine for its relief.

Diarrhœa.

Its operation, in those cases of *diarrhœa* and lientery in which these arise from a defective secretion of gastric juice, or such an atony as permits the food to pass out of the stomach before sufficient gastric juice has been poured out for its digestion, is one of the most remarkable of its effects. It is well known how feeble have been the powers of medical art for the cure of these cases. In Pepsine we have a remedy whose efficacy in such cases is unequalled. Never has the truth of the maxim, "sublatâ causâ tollitur effectus," been more happily exemplified than in the narrative of some cases of this kind, treated with Pepsine. I would refer especially to the cases by Barthez, abstracts of which are given in my work. The improvement is at once seen in the reduction in number of the evacuations, the disappearance from them of undigested portions of food, and the general improvement of the *embonpoint* and vital powers of the patient. A few doses, as in cases of gastric disturbance, suffice to produce an amendment, and the medicine may soon be discontinued. In some instances, the state of diarrhœa is superseded by one of constipation. There is one great advantage also in this remedy in the treatment of infantile diarrhœa, and it is that the restrictions upon the diet

of the young patient, either in respect of its quality or its quantity, are less needed. In the ordinary mode of treating such cases, these restraints are the most essential items of the cure, and are felt to be most irksome both to the parents and the children.

The assistance derived from artificial digestion by Pepsine, is also a valuable addition to our catalogue of remedies for anæmia. Several cases that I have narrated in my work illustrate this, and show that the favourable action of the preparations of iron was not obtained until the digestive powers of the stomach were assisted and restored by this medicine.

The condition of debility, which, whatever may be the local Anæmia. effects of indigestion, sooner or later succeeds to it, rapidly disappears as the work of the stomach is transacted for it, or as its power to perform its own functions is restored. But there are cases in which, although no local symptoms of indigestion may be manifested, we cannot doubt that the stomach is not in a state to undertake the duty of forming the nutriment which we know the wants of the system demand. In the advanced stages of acute and severe diseases, we all know that the life of the patient is often dependent upon the amount of nutriment we can throw into the blood; and we are equally satisfied that the stomach partakes of the general condition of the debility and anæmia, of which we have the clearest evidence in the prostration and pallidity of the invalid; artificial digestion by Pepsine has, in these circumstances, undoubtedly been the means of preserving life. In addition to the cases which I have described in my work on "Artificial Digestion," I may mention a very interesting narrative of a case by Dr. Ross, of Inverness, in the October number of 'The Edinburgh Medical and Surgical Journal.'

Believe me to remain, dear Sir, yours truly,

EDWARD BALLARD, M.D.

To MR. SQUIRE, 277, Oxford Street.

Dr. TODD has authorized me to state, that he has used Boudault's Pepsine with great benefit in many cases of dyspepsia, and also in cases of diabetes.

Dr. PROTHEROE SMITH has employed Boudault's Pepsine very largely. When first brought to his notice by Mr. Squire, he subjected it to the following tests:—Having selected forty-eight cases suffering from dyspepsia, he classified them under the following heads, viz.:—1. Gastrodynia and gastralgia. 2. Sickness, nausea and pyrosis. 3. Flatulence, gastric and enteric.

Under one of these three divisions, as the case might be, he entered the name of each patient, and without restricting the diet, prescribed fifteen grains of Boudault's Pepsine, or "*poudre nutritive*," thrice daily before meals. At the end of a week he found the majority of these cases benefited. In several instances, marked and steady relief was effected, followed after some time by increased bulk, and an improved state of the health generally. In some cases of distressing sickness, during the period of uterogestation, he has noticed a marked benefit from the exhibition of this remedy; and in one case the relief was complete. In two cases, nausea and temporary loss of appetite followed the administration of fifteen grains of the Pepsine. Both these patients were hysterical females, of the ages of twenty-three and twenty-seven. In one of them the remedy was afterwards employed advantageously in smaller (five grains) doses. In one case purging followed the use of this medicine, which was therefore suspended for a time, and afterwards resumed, with a similar result.

From his observation of the effects of this remedy, Dr. Protheroe Smith deduces, amongst others, the following practical conclusions:—

That Pepsine often relieves and sometimes cures hysterical vomiting, nausea, pyrosis, the sickness of pregnancy, gastric and enteric flatulency, gastrodynia, and gastralgia.

That by increasing and perfecting the powers of digestion and assimilation, it is valuable indirectly as a tonic, especially

in subjects of delicate organism, and at the periods of infancy and old age.

That, as seen in two cases of phthisis and uterine cancer, it may be found for a time so to sustain the vital powers, as in some measure to postpone the fatal issue of malignant disease.

That, as a rule, it is best to commence in adults with five grains of the artificial Pepsine, than with a larger dose; but that it may be advantageously increased gradually to fifteen grains or more.

That it is better to administer it at intervals during a meal than to give it at once at the commencement. Thus, he has often prescribed, with apparent advantage, five grains before, five grains in the middle, and five grains after dinner; so that the artificial Pepsine becomes gradually mixed with the food, simulating more the continuous secretion of gastric juice during the process of digestion.

That he has found it beneficial to mix the "*poudre nutritive*" with glycerine, flavoured with orange-peel or raspberry syrup; having observed in some cases, that thus flavoured and combined with glycerine, it was not only more agreeable to the taste, and preserved from decomposition, but that its digestive and nutritive powers were sensibly augmented.

To MR. SQUIRE, 277, Oxford Street.

ON THE INTRODUCTION
OF
PEPSINE INTO THERAPEUTICS.

BY M. LUCIEN CORVISART,

Physician in Ordinary to the Emperor Napoleon III.

THE first experiments of the author having been made publicly in the Hôpital Beaujon, in 1851, and his first communications having been made to the Academy of Sciences in the course of the year 1852,* M. Corvisart summed up the results thus:—
“Whether it is possible to nourish the sick, whose stomachs through weakness or impotence cannot digest, by dispensing, so to speak, with the stomach; performing its functions without it, and as well as it would have done it itself, and with as much benefit to the nourishment and support of life.”

The following paper on this subject was published in the *Bulletin de Thérapeutique*, t. xlvii. p. 320. 1854.

On the Use of “Poudre Nutrimentive” (Acidified Pepsine), and the resources which it affords in the practice of medicine.

The aim of this paper is not to treat of the defective secretion of the stomach, but to show that, by means purely physiological, a remedy is provided for the evils which result from bad digestion, arising from deficiency of the digestive principle; that the patients whose too feeble stomachs reject all kinds of food may recover their own strength and that of their stomach, until it is once more able to resume the exercise of its life-sustaining functions.

* *Comptes-rendus de l'Acad. des Sciences*, t. xxxv. 6 Sept. et 16 Août, 1852.

Gastric juice when employed in these diseases, however efficacious, is nauseous, and therefore not available in practice. Moreover, it has been shown that this liquid is a mixture of detritus eliminated by gastric excretion, and of the useful product of secretion (Pepsine), indispensable for digestion, and well known since the time of Schwann and Wasmann.

This last product, the agent of the vital chemistry at work in the stomach, is obtained in the pulverulent state, by various chemical processes, from the mucous membrane of the fourth stomach (rennet) of calves and sheep. M. Boudault's paper indicates the processes by which all pharmacists may obtain this medicine in its full strength.

But before entering upon the clinical facts connected with its use, and in order to understand thoroughly *à priori* the new remedial agent which I propose, the details which I have furnished in my paper on aliments and nutriments* form a necessary introduction.

It is there shown in effect:—

(a.) 1st. That food is only raw material, without nutritive virtue of itself, and which leaves those who cannot digest it to perish of inanition; that digestion gives it all at once a peculiar vital property, in virtue of which it henceforth contributes to the support of life.

Thenceforward, I expressly designate as *nutriment* all food which has acquired the peculiar vital property, through which it, by itself, without any new preparation, is able, as soon as it is absorbed into a body endowed with assimilative power, to serve for the support of life, either by contributing to the component parts of the body or by sustaining the play of the organs,—that is to say, which is suited to nourish even that which does not perform the digestive functions.

2nd. That there are really several kinds of nutriment, quite distinct in their physical, chemical, and organoleptic characters.

3rd. But that one thing is necessary to produce this transformation from aliment to nutriment,—that is, acidified Pepsine,

* Mémoire sur les Aliments et les Nutriments, par le Docteur Lucien Corvisart. Broch. in-8°; chez Labé, libraire. Paris, 1854.

the powder which, on account of its special action, I call *poudre nutritive*.

4th. That under the influences of this physiological remedy, azotized food undergoes the same physical, chemical, and organoleptic changes, that it would have undergone under the influence of the gastric juice, and in the stomach itself.

5th. That this powder, notwithstanding a variable degree of force, has the same action in transforming aliments into nutriments, whether the pepsine be derived from the mucous membrane of a carnivorous or of a herbivorous animal, that is to say, that its fermentive virtue is always similar,—a matter of the first interest, and on which there cannot remain a doubt after an examination of my physiological experiments and their therapeutic results.

(b.) That having secured the presence of the gastric juice, or of this powder, with the azotized food, and a temperature $+40^{\circ}\text{C}$., the place where the operation is carried on is quite indifferent.

This fermentation, that is to say, this digestion, whether it take place in the living stomach itself, or in an inert vessel, or, to take a middle term, in an Indiarubber bag containing the digestive ferment and the food, but itself introduced into a living stomach, which imparts thus its own action and heat, but not its gastric juice, in every case alike transforms its aliments into nutriments endowed with the same physical, chemical, and organoleptic characters.

If these physiological experiments, infinitely varied, demonstrate that there is an agent absolutely necessary to carry on digestion, that under its influence food becomes always assimilable, and that by the aid of the *vital* force which this *poudre nutritive* contains, we can constantly transform food into nourishment, it follows that we ought by its use so to help those to digest and to be nourished, whose stomach, from defective secretion, is deprived of this agent, of this living force,—agent and force indispensable to nourishment and to life.

The success of my method becomes, then, the most beau-

tiful proof of the truth and solidity of these physiological demonstrations.

The end is sufficiently exalted for me to have attracted much envy; so, in order that I may not be accused either of partiality or of blindness, the facts which I here in the beginning take for examples are not from my own practice, but have been collected and detailed by enlightened colleagues.

We must however first consider the circumstances which in the normal state are adapted to put in action the process of nutrition in all its energy; we shall thus understand better the pathological conditions under which the nutritive doses may succeed, and the explanation of the cause of failure in those cases where the employment of this remedy has been unwisely directed.

The maintenance of life in health, as in disease, requires—

1. That we take food.
2. That the stomach should retain it.
3. That the stomach should secrete the digestive ferment fitted to convert it into nutriment.
4. That the stomach should mix the food with the ferment, in order to unite them intimately, and should warm them.
5. That the system should absorb the product of the action of the ferment on the food,—that is, the nutriment.
6. And that the system should assimilate this.

For in the first and the last case, too long delay might render every ulterior resource useless; thus, in like manner as the too prolonged want of food causes the stomach to lose its digestive power, so that, although we supply the organ with food, it does not digest it; similarly, the too prolonged absence of digestive action causes the system to lose its assimilative faculty; so that even when we have duly converted food into nutriment, either by its own digestive principle or by the *poudre nutritive*, the system cannot take it up.

Thus the prolonged hesitation of the medical man to employ Pepsine may render the method which I recommend ineffectual.

It remains to examine the want of secretion, the deficiency of

trituration, and the deficiency of retention; that is to say, the deficiency of three conditions essential to the digestive faculty, and to counteract this with an appropriate treatment.

(a) *Want of secretion*.—I need not here insist upon the fact that digestion is impossible if the active principle of digestion is not secreted in the stomach; nor point out in detail the mode of supplying this deficiency, and of remedying it, since that is the subject of this whole paper.

(b) *Defective trituration*.—Every one will easily understand the importance of the action of the stomach of patients during digestion, if he recalls the following experiment:—

On dividing the pneumo-gastric nerves of an animal, the stomach, although still secreting the digestive principle, loses its peristaltic and anti-peristaltic action. Thenceforward the digestive principle no longer unites intimately with the food, it receives it only superficially; almost all the mass remains undigested; the surface alone being converted into nutriment.

That which is produced by physiological experiment, as we have just seen, may result from disease only, without vivisection, and the defect of digestion extends only to the immobility of the walls of the stomach. Against this unfortunate immobility we may guard by exciting, by the administration of *nux vomica*, or of its alkaloid *strychnia*, the muscular contraction, which has been diminished or abolished pathologically. But if we fail in this attempt, we must suppose that at the same time that the muscles are weakened, the digestive principle is secreted in less abundance than is necessary to digestion. In this case I prescribe *poudre nutritive* No. 3, thus:—

Pepsine No. 1, one or two grammes; strychnine, three milligrammes; mix, and take at meals.

(c) *Deficiency of retentive power*.—It is superfluous to say that the food which does not remain long enough in the stomach cannot be digested; every one knows that the muscular or mucous membrane of the stomach may become pathologically so irritable, that the least contact of food ill-digested or undigested with that organ excites pain and vomiting. I then advise Pepsine No. 2, thus:—

Pepsine No. 1, one or two grammes; hydrochlorate of morphia, or codeine, one centigramme; mix.

I strongly insist on this mixture, for this reason:—

If narcotics alone are given, as is often done, and if there is really with this irritability defective secretion, the narcotics only prevent the stomach from revealing by pain or vomiting the undigested state of the food. In these cases narcotic treatment alone is homicide, for it prevents us from observing the absence of the most essential act of digestion, the formation of nutriment. An indolent inanition results in the loss of assimilative power, against which medicine is completely unarmed, while the union of Pepsine with narcotics has not this danger.

It remains for the sagacity of physicians to vary these experiments; for, unfortunately, to this day there is no certain differential sign of a want of secretion, of a want of trituration, or of hyperæsthesia, so far at least as a predominant phenomenon characteristic of each; it is, however, these defects, together or separately, that we have to cure. It is true that we have in these remedies excellent means of diagnosis, since they show, by what succeeds, what is wanting.

Poudre nutritive, No. 1, contains the digestive principle entire, endowed with digestive power by itself (acidified Pepsine), which we must first employ.

Poudre nutritive, No. 4, containing Pepsine alone, which is inert until it combines with acid, is prescribed when there is evidently an over-secretion of acid in the stomach.

It would be highly erroneous to conclude that the degree of bitterness or of acidity of what is thrown off, indicates with patients an abundant or over-abundant secretion of gastric juice. Gastric juice, so acid as to be corrosive, contains very little Pepsine, and is not suited for digestion; the two secretions, acid and ferment, are quite independent.

Thus lactic acid, recommended for dyspepsia by Majendie, and revived by Dr. Handfield Jones, has been long disused. For the same reason the mode of preparation of Liebig's broth (with dilute hydrochloric acid) only renders the liquid heavier,

without giving it a higher power of nourishing. No doubt, in those cases in which the acid of gastric juice is deficient, these substances may be useful; but those cases are very rare.

As to the efficacy of Pepsine, the following facts are convincing each in its degree, and I have selected them to show the therapeutic action of this new remedy according to the case.

OBSERVATION I.

Communicated by Dr. A. Longuet, Member of the Institute.

Severe typhoid fever; to the twenty-fourth day the patient could not take any nourishment, even the lightest. The use of Pepsine rendered digestion easy. Relapse; pains in the stomach, diarrhœa, which was suspended by the counteracting influence of the medicine. After ten days of this treatment the patient could digest perfectly without any foreign aid.—Miss —, aged 15, a pupil in the Maison Impériale d'Écouen, reached the twenty-fourth day of a severe typhoidal attack, convalescent, but in a state of debility most distressing, inasmuch as she could not take even the simplest nourishment. I ordered Pepsine powder. The first half-dose was administered in tapioca soup, and passed so easily, that a second and similar one was given to the patient three hours after the first, and it also was digested without difficulty.

The second day the treatment was repeated in three meals of soup and an egg.

The third day the half-dose of Pepsine was purposely omitted from the first meal of soup in the morning; the result was, violent pains in the stomach and bowels, and then a liquid evacuation.

On the other hand, the two other meals, taken on the same day, and which each contained half a dose of Pepsine, were easily and completely digested.

On the fourth day of the administration of Pepsine the patient ate soup and chicken.

From that time, increasingly substantial nourishment was taken; but each time that the dose was not given in any meal, the digestion of that meal was more or less difficult. This state of things lasted for ten days, after which digestion became normal.

During this time there was a marked tendency to constipation, which, however, yielded to the simplest means.

OBSERVATION II.

Communicated by Dr. Berthôlet, of Paris.

Miss B— had for a year complained of a weight at the stomach, and a difficulty in digestion, especially after food in the eve-

ning; and this continuing, in spite of various remedial treatment, I advised her to take a dose of Pepsine with each evening meal. She now digests much better. But whenever she discontinues the doses—and I have repeatedly caused her to omit them—she digests much less easily, and the epigastric pains immediately reappear. Recourse to the nutrimentive preparation again renders digestion painless and easy.

OBSERVATION III.

Communicated by Dr. Cahaguet, Physician at Napoléon Vendée.

After habitual dyspepsia for seven years, with digestive atony and loss of power, which defied tonics, purgatives, narcotics, vegetable carbon, the waters of Seltzer and Vichy, severe endocarditis ensued. After that was removed, dyspepsia returned with redoubled force; in spite of bitters, Vichy water, etc., all food was intolerable; the patient grew weaker, and rejected even broth and the gravy of meat. Syrup of Pepsine alone was administered during eight days. After the first day the digestion was good, and more substantial food, and in greater abundance, was taken, and the patient became so much stronger as to be able to walk in the garden. Endocarditis returned, terminating in death.—M. Savary, a contractor of Napoléon Vendée, aged 45, of a bilious nervous temperament, had suffered during seven years from derangement of the digestive functions. At intervals more or less remote, he was seized with vomiting, which he considered to arise from indigestion. These attacks left the stomach exhausted for some days, after which the disorder yielded to a moderate diet. Independently of this functional disturbance, the frequency of which gradually increased, the digestive organs were slow and feeble in their action.

On being called for the first time to the care of this patient, in August, 1853, I could not discover, after a minute examination, any organic lesion of the digestive organs, and subsequent observation did not cause me to modify my original diagnosis. The tongue was whitish and moist; there was no thirst; want of appetite and constipation were habitual; the stomach was soft, without sensibility or abdominal tension. The patient's mode of life was regular. M. Savary indulged in no excess; he limited himself to a suitable diet, appearing to prefer acid or highly-seasoned food.

I saw in this case only functional derangement, which I treated with remedies slightly stimulant. Some doses of rhubarb, mixed with magnesia and bark, were ordered; but finding that the stomach could scarcely bear them, the patient at once discontinued their use. The symptoms continued and increased, notwithstanding various means which were successively resorted to,—subnitrate of bismuth, vegetable charcoal, various purgatives, tonics, narcotics,

Seltzer and Vichy water, etc. The only remedy which seemed to produce a salutary effect was an infusion of calumba, sweetened with the syrup of the rind of bitter orange. The strength of the patient diminished perceptibly, until early in April, M. Savary, called by business to visit some works under his direction at a distance of some leagues from the town, returned much fatigued with his journey, and sent for me. I perceived at once marked symptoms of acute endocarditis. Owing to the weakness of the patient, I could employ antiphlogistic treatment only with great caution. I succeeded, nevertheless, by repeated applications of leeches, by highly-nitred drinks, by baths and counter-irritation, in arresting an attack which, supervening under such unfavourable conditions, threatened a speedy and fatal termination.

The disease of the heart seemed subdued, when the disturbance of the digestive organs, doubtless aggravated by the antiphlogistic treatment, and the liquids taken by the stomach, received an undesirable development. The tongue was covered with a thick whitish coating; complete dyspepsia supervened. The patient obstinately refused every kind of food. Purgatives, bitter drinks, broth, beef-tea, were tried in vain; the stomach rejected everything. Seltzer and Vichy waters were not more successful, even ice could scarcely be taken. The patient seemed given over to a speedy death, unless this indisposition of the stomach could be overcome. In conjunction with my colleague, M. Merland, I tried Pepsine. A little veal broth, mixed with half-a-spoonful of Pepsine, was taken, and the experiment, several times repeated, succeeded. By degrees, more substantial food, and in greater abundance, could be borne, by increasing the quantity of the Pepsine, which was taken during eight days, in doses of a spoonful morning and evening. The stomach gradually resumed its functions. We were congratulating ourselves on this satisfactory result, which we could only attribute to the use of the Pepsine, prescribed to the exclusion of all other medicine, when the patient, having on one occasion vomited it, refused to continue it. In spite of this, the improvement lasted during some weeks, and M. Savary recovered sufficient strength to take some turns in the garden. Soon, however, the heart disease, which our efforts had only lulled, reappeared in a severe form, and all treatment being powerless against it, the patient sank towards the end of May. I have no doubt that our treatment of the dyspeptic symptoms would have been successful, had not this unfortunate complication existed.

OBSERVATION IV.

Reported by Dr. Parise, Professor in the Ecole de Médecine at Lille.

This was the case of a young woman of weak and irregular constitution, who had long been treated with various preparations of

iron, when she became pregnant for the first time. I then only suspected that she was pregnant.

She suffered so much pain in the coats of the stomach, that I had recourse to nutritive doses. She took them for twelve or fifteen days. On the first day her digestion became much better, and this improvement continued, until very soon she could digest without this help.

OBSERVATION V.

Communicated by Dr. Huet, Assistant Physician of la Maison Impériale de la Légion d'Honneur.

Gastralgia of many years' standing, resisting antiphlogistics, bitters, iron, antispasmodics. Administration of the nutritive doses. *Digestion immediately good. Voluntary suspension of the doses during four days. Reappearance of all the symptoms.* Return to the nutritive doses for twelve days. *Again, disappearance of the malady. Discontinuance of the medicine for twenty-seven days, without any relapse. The cure is undoubted.*—Madame Masc, aged 50, had for some years suffered from gastralgia, characterized by heaviness, by epigastric flatulence, especially after meals; by pains, sometimes very acute, in this region; by acid and acrid eructations; finally, by obstinate constipation.

This lady had been long treated for gastritis, and had undergone both general bleeding and the application of leeches to the epigastrium. Since Madame Masc has been under my care, I have employed bitters, preparations of iron, antispasmodics, and treatment suited to the nature of the disorder, but without great success.

On the 22nd of August, I ordered two nutritive doses in the day, one dose with each meal. On the 23rd I saw the patient again. She told me that she had suffered less, that digestion was easier, and the weight had been less. I recommended her to go on with the doses for four days more, and then to discontinue them, wishing thereby to assure myself that the improvement already manifest in the patient was due to the nutritive doses.

From the 23rd to the 26th, Madame Masc took two doses daily, and during this time digestion was easy, and the patient experienced neither weight at the epigastrium nor acid eructations. From the 26th of August to the 2nd of September, Madame Masc discontinued the nutritive doses. I saw her again September 2nd. She told me that she was again suffering, that she could not digest, that the epigastric pains had returned. The patient requested that I would prescribe for her the doses which she had previously taken.

On September 6th, Madame Masc resumed the doses, and continued them for six successive days. On the 13th, she had no pain, she digested well, and the former obstinate constipation was entirely conquered. From this time her digestion continued good; she had no return of pain; her health was perfect.

These five examples, each different, carry their own conclusion.

Idiopathic or symptomatic disorders of the stomach, when they consist chiefly in a defective secretion, may be cured by the use of Pepsine powder alone, as we see in Observations II. and V.

In certain cases of long illness, often in convalescence after acute disease, where a prolonged course of diet is necessary, it happens that the simplest experiments in feeding cause dangerous relapses, because the stomach has not recovered its arrested secretion; so that either from these unfortunate experiments, or, on the contrary, from the want of alimentation, recovery is hindered; and patients who would have recovered if they had been supported, die without having had, so to speak, time to recover: it is thus in many cases of convalescence after typhus fever. (See Observation I.) Thus we see what heavy responsibility rests upon the medical man, who, from scepticism or from indifference, hesitates to employ reasonable methods, and allows inanition silently to supervene,—that is to say, death. “Inanition,” says Chossat, “is the cause of death, which marches onward in silence with all disease in which the conditions of alimentation are not normal.”

How many times in all these cases have practitioners, impressed with these truths, endeavoured to nourish invalids by giving them aliments; but the deficiency of the digestive principle leaves them undigested.

Medical men, alarmed by the attacks of indigestion, and the dangers of this new disturbance, pause, and prefer, rather than expose themselves to the risk of mistake, to leave patients to themselves,—that is, to inanition, which leads to death.

But will not physicians save many patients if they can attain their end, nourishing without indigestion, nourishing patients, so to speak, by dispensing with their stomach and their powers, and by carrying on within them, by the aid of Pepsine, an artificial digestion, which shall supply, without danger, the assimilating functions with nutriment endowed with all assimilable properties?

Pepsine powder may be given between slices of bread; the patient takes this powder on sitting down to table, and avoids all other internal medicine for two hours before and two hours after the meal, as some medicines destroy its virtue: a temperature above 40° has the same effect.

However ill a patient may be, one or two grammes of *poudre nutritive* will usually suffice for the digestion of a cutlet or more, and of soup; it is necessary to take the meat, or some animal or azotized food with the medicine, as otherwise this latter will have nothing to act upon.

The digestion of aliments called respiratory, feculents, etc., may be facilitated by these preparations, because the transformation of starch necessary to assimilation can take place only on condition that the starch be laid bare by the solution of the azotized matter by means of the digestive principle of the stomach, because then only the diastasic ferment can attack and transform the aliment (starch) into nutriment.

If, after being taken at four meals, Pepsine powder No. 1 has not rendered digestion good, if neither of the others (2 and 3) taken during the same time has any better effect, if especially without them digestion is no worse than during their use, then discontinue them—they are powerless; for if they are to be efficacious, they will act quickly and clearly.

Nevertheless, their action, though appreciable, is perhaps less marked at the commencement than in the course of treatment, because to their power may be added that of the stomach, restored by nourishment, profitably employed by the assimilating forces.

It will be seen in the cases which I have detailed, and I also urgently counsel this course to practitioners, that the *poudre nutritive* which had rendered digestion good, was occasionally discontinued, and that immediately digestion was again disordered,—an experiment almost harmless to the patient, but which compels his conviction, and that of the physician, and shows clearly the suitability of the medicine.

The preceding Paper was only a sketch; M. Corvisart pub-

lished in the same year another work, which was warmly commended, not only in the interest of Pepsine, for the large number of cures which it detailed, and for the names of eminent practitioners who had successfully tested the new remedy, but on account of the valuable practical suggestions which it contained on the subject of nutrition. The title of this work is 'On Dyspepsia and Consumption.'*

In this work M. Corvisart set forth the various forms of dyspepsia, the symptoms which called for the intervention or otherwise of artificial digestion, accomplished by the agent of which we are here treating; the time of administration; the dose; how it ought to act, whether on the defective secretory, muscular, or sensitive action of the stomach; dyspepsia, gastralgia, chlorotic patients, rheumatic patients, pregnant women, etc. The second chapter treats of consumption of the body through defective alimentation; of the striking resemblance which exists between the symptoms accompanying famine and those which terminate the diseases, be they what they may, in which alimentation, for want of sufficient digestive power, is no longer in a normal state; and the silent but implacable advance of those disorders, the cause of which resides in the lack of nutrimentation,—that is to say, of the transformation of aliment into nutriment. In this chapter rules for guidance are clearly laid down, for in this view Pepsine not only alleviates suffering, it has to do also with the conservation of life.

Thirty-two observations, collected and commented upon, which had been drawn forth through M. Corvisart's inquiries, but which were reported by the most eminent physicians, throw light on this important subject.

Considering consumption as first arising from a want of alimentation, then from a want of nutrimentation through weakness of digestion, M. Corvisart comes to the loss of the assimilative function, under which Pepsine can still cause digestion, so certain is its special action, but having been given too late, this action is useless, the system being no longer capable of assimilating what is digested.

* Chez Labe, lib., Paris, 1854.

All this part,—the most important, in truth, of M. Corvisart's work,—especially struck the critics of the journal 'L'Union Médicale;' the whole excited the attention and the endeavours of medical men; and we greatly regret that the extent of the work will not allow us to translate it.

About the same time the following papers appeared in France:—

Professor Rilliet (of Geneva), 'On Apepsia and Dyspepsia, and their Successful Treatment by Pepsine.'*

The author, after various extremely interesting considerations and observations, concludes thus:—

"4th. The effects produced by the '*poudre nutritive*' of Pepsine are ordinarily much more prompt than those which we obtain from the remedies usually employed in the treatment of dyspepsia.

"Digestion is in general much facilitated in the first three or four days of the treatment, but in very different degrees. In some cases there is a complete change of sensation; the weight, the flatulence, the torture of digestion have entirely disappeared; in others, it is only an alleviation.

"When in very chronic cases of dyspepsia the use of the powder is continued for some length of time, the state of the patient sometimes remains stationary; sometimes indeed, after the first relief, there is a reappearance of the symptoms, while at the same time the return of strength, and diminution of thinness, show that the medicine has taken effect.

"The nutritive method of M. Corvisart has this advantage over other remedies, that it may without inconvenience be continued during a long time, and that it does not leave behind it those morbid remains "which are often the effect of very prolonged use of energetic pharmaceutical remedies."

Dr. Louis Henry, of the Hydropathic Establishment of Bellevue,† 1855, thus expresses himself:—

"I have frequently used M. Corvisart's *poudre nutritive*, and I am happy to be able to declare that the results

* Revue de Thérap. Médic. Chirurg. de Marlin Langer, 1 et 15 Dec. 1854.

† Op., chez Labe, lib., Paris, 1855.

have fully confirmed the exactitude of the ingenious and useful researches instituted by that honourable member of our profession."

Dr. Desmartis, in his 'Memoir on Yellow Fever and Cholera,' Bordeaux, 1855, confirms the assertions of M. Corvisart.

"We may say in passing that Pepsine has come very powerfully to our aid, and has given us unhoped-for results in the choleric affections of children, for whom, as we know, we cannot safely prescribe preparations of opium, nor certain other medicines so useful for adults."

Debout, chief editor of 'Le Bulletin de Thérapeutique,' reports evidence furnished by his own personal observation. He says:—

"M. Corvisart's Memoir is too full and too conclusive for us to have deemed it necessary to mention all the new facts which have been developed since. Among the formulized conclusions of our colleague was one which required to be verified. M. Corvisart had asserted that Pepsine would cure diarrhœa, when it was the result of the stomach having allowed aliment, which it should have digested, to pass into the intestines to irritate them. Our own observations in regard to infants at the breast, and those of M. Barthez in regard to older children, testify that the theories of M. Corvisart were well founded."*

The author of the treatise on diseases of children, Barthez ('On the Good Effects of Pepsine in the Diarrhœa of Children') expressed himself thus, as the result of observations made in his practice: †—

"We often find children of the earliest age, with good appetite, consuming eagerly large quantities of aliment diarrhœa exists; the evacuations appear mixed with undigested alimentary substances.

"The children do not benefit, they become fretful; their stomach is large, sonorous, distended. These children move round in a baneful circle:—alimentation too strong for a gastric juice the digestive power of which is diminished; absence of repara-

* Bulletin Général de Thérapeutique, t. liv. p. 97. 1858.

† Union Médicale, 1856, p. 22.

tion, keeping up the voracious hunger which can never be appeased by the injection of new aliments, which will be no more digested than the first. To break this evil round, we must restore to the digestive secretions their solvent power. This I would attempt to accomplish in two ways.

“One consists in diminishing the quantity of alimentation, and in attempting to adapt its quality to the characteristics of the secretions such as they are. The other method is directly to restore to these juices their digestive faculty.

“The first method is not always easy to follow, because parents have not the courage to maintain for long a strict regimen with a child who is incessantly desiring to eat; while Pepsine, if it has the properties indicated in M. Corvisart’s work, is fitted to fulfil the end of restoring directly to the gastric juice its solvent power.

“I leave the facts which can alone settle this question to speak for themselves.

“These facts struck me forcibly; the success was so speedy, so complete, so exactly following upon the administration of Pepsine, that it would be difficult to doubt that the views of M. Corvisart were justified.”

The observations on the pathologico-physiological properties of Pepsine have been everywhere confirmed. Henceforward the use of this remedy becomes each day more general; the doses, the mode of administration originally pointed out, have been scrupulously followed, and always with the greatest success.

THE END.

The first part of the paper is devoted to a general survey of the subject. It is shown that the theory of the differential calculus is a special case of the more general theory of the calculus of variations. The latter is a branch of mathematics which deals with the problem of finding the maximum or minimum of a functional. This is done by the method of Lagrange multipliers.

The second part of the paper is devoted to the study of the calculus of variations. It is shown that the calculus of variations is a branch of mathematics which deals with the problem of finding the maximum or minimum of a functional. This is done by the method of Lagrange multipliers.

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MONS. BOUDAULT

HAS APPOINTED

MR. SQUIRE (HER MAJESTY'S CHEMIST),

277, OXFORD STREET,

HIS AGENT FOR GREAT BRITAIN.

