for some months. This can hardly fail to demonstrate that neither dullness nor the other obligatory signs of consolidation but the appearance of moist râles after cough is usually the first evidence of the invading enemy. If this be true of the advancing process in an old case, it should also be true of the incipient stage.

The great and predominant value, then, of localized râles in the diagnosis of incipient tuberculosis consists first, in their almost constant presence at a time when other local signs are absent or at most indefinite. Second, in their practically unmistakable character, thus differing widely from other signs which represent merely deviations from the normal. Third, in the fact that when occurring at an apex they are almost pathognomonic, other conditions which might produce them being exceedingly rare. While, therefore, other local signs are of great value, especially for the few experts who by long experience have learned their limitations and the frequent difficulty of interpretation, the presence of localized râles must ever remain the essential guide to early diagnosis for the rank and file of the profession.

THE THERAPEUTIC VALUE OF SOME DIGESTIVE PREPARATIONS, AND THE INDICATIONS FOR THE USE OF PEPSIN, IN DISEASES OF THE STOMACH.*

BY RICHARD F. CHASE, M.D., BOSTON, MASS.,
Instructor in Clinical Medicine, and Lecturer on Gastro-intestinal Diseases, Tufts College Medical School; Physician to the Boston Dispensary, etc.

THE employment of digestive preparations in the treatment of stomach and intestinal diseases is undoubtedly very extensive. Clinical experience seems to have taught that these agents relieve certain symptoms, and probably some physicians believe they possess actual curative properties. On the other hand, there are physicians who has very little confidence in the efficacy of these preparations, and in consequence do not use them.

Now it is fair to assume that the virtue of these products lies in their power to digest, the purpose for which they are intended. Since they have to do solely with the chemical process of digestion, we can determine accurately the extent of their participation in this process. We have for this purpose certain tests, the conditions of which may be made to approach so near to those of the chemical process of digestion in the human stomach that one has very little reason to doubt the reliability of their results.

The preparations which we are to consider are: (1) an essence pepsin, (2) an ess. pepsine, (3) a scale pepsin, (4) an elixir and tablets lactopeptine, (5) liquor diastos, (6) tablets pepsin and pancreatin, (7) tablets panzyme, (8) tablets peptenzyme, (9) an elixir digestive ferments, (10) and papain.

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These particular preparations were selected simply because they were the most available. Their various menstrua probably exert no marked influence upon digestion.

From extensive advertising, if not from personal experience with them, probably many of these preparations are familiar to you.

We learn from the manufacturers of the *complex* products that their digestive power depends upon the presence of one or more of the digestive ferments,—pepsin, rennin and pancreatin. Tests show that all of these preparations are *acid* in reaction, due to the presence of lactic or HCl acid. In the case of some of these products, very likely the agents representing them have called your attention to this fact and reminded you that pepsin preparations are active in acid media only.

While most of us know something of the action of the simple ferments,—pepsin, pancreatin, etc., of these complex products in acid solutions, or made into tablets and powders which are acid in reaction, our knowledge is less, and too often we accept the statements of the manufacturers regarding their therapeutic properties. It may sound very plausible indeed, when the proprietor of a product tells us that through its diastatic ferment, his preparation digests starch in the stomach the same as saliva, and that by the presence of the active ferments, pepsin and rennin, proteids are converted into peptone and milk coagulated as by the gastric juice itself; also, that when the chyme is forced along into the duodenum the pancreatin of his preparation passes along with it, and there further digests proteids and starch the same as is done by the natural pancreatic juice.

Thus, if one does not stop to give the matter some consideration, he may easily be led into the belief that these complex solutions, some so beautiful in color, and that these tablets, put up in bottles so convenient to carry in the pocket, are in many ways superior to simple pepsin and pancreatin preparations.

We know that pepsin in a properly acid medium digests proteids, both in the stomach and in test tubes. We are told that all of the complex preparations here mentioned, contain pepsin. We find by tests that the liquids, tablets and powders are acid in reaction. In fact, we are told by the manufacturers that these products are, in themselves, digestants of proteids.

Hence to determine their digestive power one simply adds a piece of coagulated egg albumen or a piece of fibrin to a given quantity of the liquid digestants, or to a water solution or suspension of tablets and powders, contained in test tubes. The tubes are then left in an oven having a constant temperature of about 110° F., for several hours, being occasionally shaken, to imitate the action of gastric peristalsis. If such fluids are digestants, *per se*, the egg or fibrin disappears. It is converted into peptone.

This was the first test to which these products were subjected and in each case the result was *negative*, no digestion whatever occurred.

In fact, no digestion was expected, because it had been previously ascertained that none of the preparations were acid enough to render their pepsin active. However, the tests proved conclusively that none of these products are digestants of proteids, *per se*, and this was the point to be proven.

But some one may very pertinently ask, "May not these agents become active when taken into the stomach?" Let us see.

One of the gastric disorders in which one would be most inclined to use these agents is chronic gastritis. From a patient with such an affection some of the fresh gastric juice was procured. It contained no free HCl. Twelve test tubes, each containing 5 cc. or 1¼ d. of this gastric juice were used. To tube No. 1 a piece of egg, only, was added. To tube No. 2 a piece of egg and HCl was added. To the ten other tubes pieces of egg and certain quantities of the digestants were added. The tubes were then left in an oven, temperature 40° C. for twenty hours, being occasionally shaken. At the end of this period the following results were noted:

Tube No. 1, containing the gastric juice and egg showed no digestion.

Tube No. 2, containing the gastric juice, hydrochloric acid and egg showed complete digestion, while the ten other tubes containing the gastric juice and egg, and the digestives, showed no digestion at all.

From these tests we learn the following facts:

(1) First, that gastric juice, deprived of its free HCl is incapable of digesting proteids, even if its pepsin is present.

(2) That the same juice, when properly acidulated, becomes active and digests proteids, thereby proving the presence of is natural pepsin.

(3) That the addition of any of these digestives to such a secretion aids in no way whatever its digestive power.

In order to prove this last statement in a more practical way, the following test was made:

To a patient with gastritis, an active essence of pepsin, and tablets of lacto-peptine were given on different occasions after eating. At the end of certain periods the stomach contents were removed and the digestive power of the gastric juice determined. It was always found to be absolutely *negative*, the same as when no digestants were administered.

To some these tests may seem simple, even superfluous, in view of our knowledge of the subject, yet they confirm a fact not universally known and duly appreciated, it is that *as yet we have no digestive preparations depending upon the ferment pepsin for their activity which, in themselves, aid the digestive power of any gastric juice when it is deprived of its HCl.*

This statement applies not only to the ten preparations under consideration, but to *all* similar products.

The reason for this is that no pepsin, not even that of the gastric juice, has any power to digest except in the presence of a properly acid medium. Moreover, no pepsin can be prepared and put upon the market in a strongly acid medium and remain active, for as Mr. B. T. Fairchild [1] says, "If we submit pepsin to long continued contact simply in dilute hydrochloric acid (.25%), we find the pepsin to progressively deterioriate in activity. Therefore, acid cannot, with impunity, be added to pepsin in solution in the manufacture of products necessarily to be submitted to conditions of commerce."

Yet not infrequently we see prescriptions calling for pepsin in combination with HCl of such strength as to immediately paralyze the pepsin used!

The comparative peptic values of these ten preparations were not accurately determined, but, by tests made under various conditions it was always found that the essences and scale pepsins were the most active, while panzyme and the elixir and tablets of lactopeptine were the least active.

Pancreatin: It is a well-known fact that pancreatin in substance, solution or simple tablet, is soon rendered inert by the gastric juice when taken into the stomach. And this is the fate of that ferment as combined in some of these preparations. The recognition of this fact has led to the manufacture of pills and tablets of pancreatin coated with keratin, salol, etc. While such coatings do protect the ferment from the action of the gastric juice, it is a question if they are dissolved early enough in the intestine to allow the pancreatin to be of any service in digestion.

As to the combination of pepsin with the pancreatic ferments in solution, Mr. Fairchild says: "That the ferments combined in solution are antagonistic to each other has often been pointed out. Scheffer early called attention to the incompatibility of pepsin and pancreatin, and pepsin and diastase in elixirs. It is impossible to prepare any media suitable for the preparation of the enzymes of the stomach and pancreas in combination in solution, for whether the reaction of the preparation be neutral, alkaline, or acid, there will be a gradual, sure, progressive deterioration of the product under the commercial conditions to which the preparation must be submitted. If the liquid preparation of the mixed peptic and pancreatic ferments be neutral or alkaline, the pepsin becomes destroyed. If acid, all but the pepsin will perish, and the acid compound will, therefore, be found to be devoid of any pancreatic activity."

According to their formulæ, elix. lacto-peptine, elix. peptenzyme, liquor diastos and elixir digestive ferments are examples of such incompatible preparations, and very likely there are many others not known to the writer.

Just a word more to show why some of these preparations are not what they purport to be.

Papain: The advantages claimed for this product are, that it will digest proteids in an acid, neutral, or alkaline medium. The sample

[1] Mr. B. T. Fairchild: The Evolution and Use of the Animal Digestive Ferments in Medicine. Read before the Pharmaceutical Meeting of the Philadelphia College of Pharmacy, Jan. 21, 1902. Published by the American Journal of Pharmacy, vol. lxxiv, Nos. 2 and 3.

tested showed moderate activity in an acid medium, but none whatever in a neutral or alkaline medium.

Of one preparation the manufacturers state: "This product contains the five digestive agents — pepsin, ptyalin, pancreatin, lactic and hydrochloric acid — combined in the same proportion as they exist in the human system."

This statement is too absurd to warrant any consideration whatever, except the meaning which it is intended to convey. In the writer's opinion, its object is to lead the reader into the belief that the preparation is a digestant *per se* of all forms of food. But this delusion is at once removed by the agent representing this product, who, in a personal interview, said: "To test its peptic value, perform the usual test, using an *acid medium* of .5% HCl." An acidity, by the way, twice that of the gastric juice ever found under normal conditions!

Another product is said "to contain all known ferments and digests albumen, fat, starch and cane sugar without the extra addition of acid or alkali." Yet in a personal letter, dated Jan. 9, 1904, the manufacturers say, "The peptic power of this product must be tested in the usual way, using *acidulated* water, .2% to .25% HCl." In other words, *add* acid.

Such disclosures as these suggest one of two things, either gross ignorance, or brazen attempts on the part of the manufacturers to deceive those who employ these preparations.

Now the very important question presents itself: In what diseases of the stomach is pepsin indicated?

In all gastric affections regardless of their cause, in which free HCl is present, pepsin is not indicated, because the native ferment is always found and in sufficient quantity. In the vast majority of all gastric conditions, characterized by the absence of free HCl, whether due to functional or organic causes, pepsin is not indicated, because after proper acidulation of the gastric juice, it becomes active, showing that pepsin is still present. These two classes of gastric disorders comprise over 90% of all stomach affections, and in their treatment pepsin is never indicated. In all cases of atrophic gastritis, and achylia gastrica and in some cases of cancer of the stomach, both HCl and pepsin are lacking. As a result, here we meet a true indigestion of certain foods in the stomach.

It is upon our knowledge of the existence of such conditions that large doses of HCl and pepsin have been based, and extensively employed. It is perfectly evident that pepsin alone, in these conditions, is of no service, because we know that even the native pepsin, when present, is not active except in the presence of a certain amount of HCl, consequently both HCl and the ferment are used.

By chemical examination of the gastric juice we can determine accurately any deficit of HCl which may exist. Hence, it would seem an easy matter to supply such a deficiency by administering the acid by mouth. This is the object *attempted* by those who use large doses of HCl together with pepsin. But in practice it is found that the large doses necessary for this purpose are impracticable of administration. Such being the case, it is a useless proceeding to use pepsin and then attempt to render it active by giving large quantities of HCl.

While a diversity of opinion yet prevails, regarding this subject, the following quotations will give one an idea on which side of the question the preponderance of evidence rests:

Einhorn:[2] "Pepsin used to be, and is yet, frequently given in combination with HCl. Most writers, however, concur in the absolute inefficacy of this drug, and for two reasons: (1) In most instances, even of diminished secretion, there is yet an abundant quantity of pepsin present. (2) Most pepsins in the market do not, by any means, show as strong digestive properties as the true pepsin of the stomach. Of late years I have entirely abandoned the use of pepsin."

Ewald:[3] "Pepsin was for a long time regularly prescribed with HCl with the pernicious idea that if it did not help, it certainly did no harm. Its use should be restricted to those cases in which an absence can be proven."

Reigel:[4] "In general the administration of pepsin is rarely indicated. The digestion of albumen is rarely improved by the administration of hydrochloric acid even if large doses are given together with pepsin. This is due to the fact that the quantity of HCl that we can administer is very much smaller than the quantity needed to make up the deficit of HCl in the gastric juice."

The theory was that HCl and pepsin given by mouth would take the place of these agents when lacking in the gastric juice, but in practice, it is found they do not. However, stimulation of the functions of the stomach, by means of our various methods of treatment, is probably far better therapy than a useless or even a successful attempt at their substitution.

The facts stated in this article are well known to all physiologists, and may be verified by reference to any textbook that considers the subject. If these facts are brought home for the first time to some of the readers of this article, its object will be attained.

INFECTIONS OF THE RESPIRATORY TRACT WITH INFLUENZA BACILLI AND OTHER ORGANISMS, THEIR CLINICAL AND PATHOLOGICAL SIMILARITY, AND CONFUSION WITH TUBERCULOSIS.

BY FREDERICK T. LORD, M.D., BOSTON,
Physician to Out-Patients, Massachusetts General Hospital; Assistant in Clinical Medicine, Harvard Medical School.

(Concluded from No. 19, p. 540.)

V. PATHOLOGICAL SIMILARITY OF INFECTION WITH INFLUENZA BACILLI AND WITH OTHER ORGANISMS.

THE study of sections from cases of acute bronchopneumonia, associated with influenza bacilli, shows, as Pfeiffer first described,[5] an

[2] Diseases of the Stomach, 1898.
[3] Diseases of the Stomach, American edition, 1900.
[4] Diseases of the Stomach, American edition, 1903.
[5] Pfeiffer: *Loc. cit.*