reff upon the basis that the small intestine could not tolerate and would not accept an acid stronger than from 0.1 to 0.15% HCl. While, undoubtedly, regurgitation of duodenal contents plays probably the most important role in the neutralization mechanism, one cannot escape proper evaluation of the work of Shay, Katz and Schloss (10) who have shown that regurgitation from the duodenum is even greater when alkalis (1-1½% $NaHCO_3$) are introduced into the stomach than when either weak or strong acids are used. We have frequently noticed that the greatest amount of regurgitation occurs in patients with achylia gastrica during a plain water meal. Furthermore, we have been unable to change the color of bromsulphthalein with the regurgitated duodenal contents, even in the presence of achylia gastrica, although this dye changes color at a pH of 7.2. Therefore, it is doubtful if the duodenal content is sufficiently alkaline to markedly lower gastric acidity even in the presence of considerable regurgitation. Reference to Figure 2, Graph II, reveals an increased neutralizing power in the presence of marked pyloric obstruction in both cases where duodenal regurgitation is inhibited. McCann (*Am. Jour. Physiol.*, 89:483, 1929) utilizing the Mann-Williamson operation which shunts all duodenal contents into the terminal ileum and short circuits the gastric contents into the upper jejunum, found that the neutralizing power of the stomach remained the same before and after operation. Since Hill and coworkers (*Am. Jour. Physiol.*, 106:381, 1933), using isolated pyloric pouches, have shown that the secreted mucus is neither sufficient in amount or alkalinity to account for the acid reduction, we must give considerable attention to the possibility of resorption or diffusion of hydrogen ions through the stomach itself or that the stomach is actually capable of secreting an alkaline juice as advocated by Author.

That dilution plays some part in the mechanism is indicated by adding a coloring matter (sodium salt of phenolsulphonphthalein) to the acid test meal and determining its concentration in the fractional specimens by means of a colorimeter. The strength of the acid in the meal and fractional samples was determined by chemical analysis and not by titration. It was found that from 55 to 60 per cent of the reduction was due to dilution and 45 to 50 per cent due to neutralization. Both clinical and experimental recent reports tend to show that the emptying time of the stomach plays very little if any role.

The work of Elman and McLeod and of Levy in connection with ulcer and pylorospasm has been confirmed. Since the neutralizing power in the other diseases studied was within normal variations with the exception of liver and gall bladder disease, it would appear that its diagnostic value in ulcer is even greater and more specific than has been previously emphasized.

A modified technique has been introduced which is less difficult of application by the individual clinician who must refer his cases to a laboratory for analysis since by this technique both the secretory and neutralizing curves can be determined at a single sitting. Total volumes of the test solutions have been reduced which has eliminated discomfort and frequent vomiting both of which are aggravating factors to accuracy of the tests.

CONCLUSIONS

1. The clinical value of the neutralizing functional test of the stomach in ulcer and pyloric spasm as established by other investigators has been confirmed. It apparently is of little or no value in other gastrointestinal and several general diseases investigated in this study except the possibility of liver and gall bladder pathology.

2. By modifying the technique of Elman and Levy both the neutralizing and secretory tests can be accurately performed at one appearance of the patient.

3. Evidence is submitted suggesting that the regurgitation of duodenal juices, while undoubtedly the main factor, is not the only one in the mechanism of neutralization.

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The Acidity Reduction Test Versus the Fractional Test Meal*

By

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THERE is now abundant evidence that the rate at which acid in the stomach is diluted and neutralized is a much clearer indication of gastric function in health and in dyspepsia than is the degree of acidity alone. The reasons for this will be discussed later.

In 1914 Boldyreff (8) first showed that when acid is placed in a dog's stomach the acidity is rapidly reduced. (Fig. 1). This fact was not, so far as I am aware, applied to the investigation of the human stomach until 1923, when I showed that there was a

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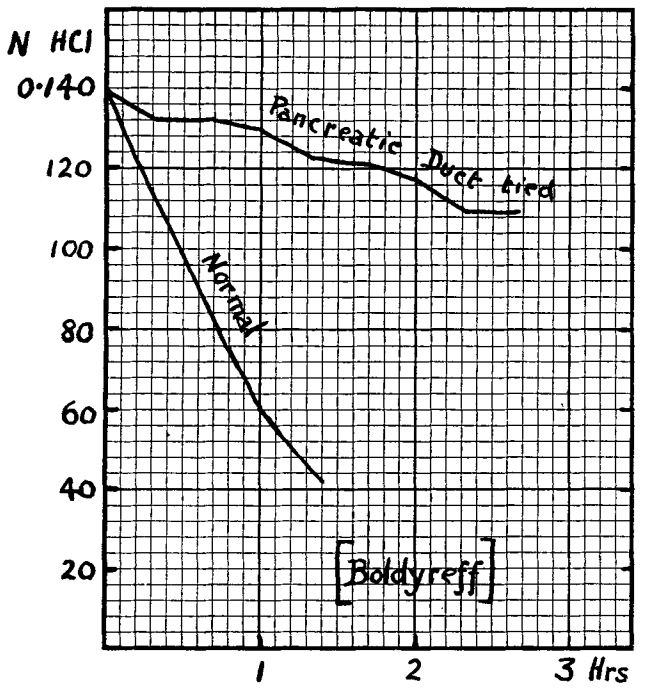

Fig. 1. Showing reduction of acidity when 0.140 N HCl is placed in a dog's stomach (a) under normal conditions, and (b) after ligature of pancreatic duct. (Redrawn from Boldyreff's figures).

delayed reduction of acidity when acid was artifically placed in the stomachs of people who had hyperchlorhydria with the ordinary gruel-meal test (Apperly 1). Fig. 2 shows the gruel-meal acidity curves of a group of eight students, and Fig. 3 shows the results in the same group when 250 c.c. of 0.4% HCl was placed in their stomachs. It will be seen that, in general, those who have high (or low) acidity in the former also have high (or low) acidity in the latter. In other words gastric acidity is a matter of dilution and neutralization rather than of secretion of acid. In the same year Apperly and Cameron (4) showed a similar failure to reduce acid placed in the stomach in cases

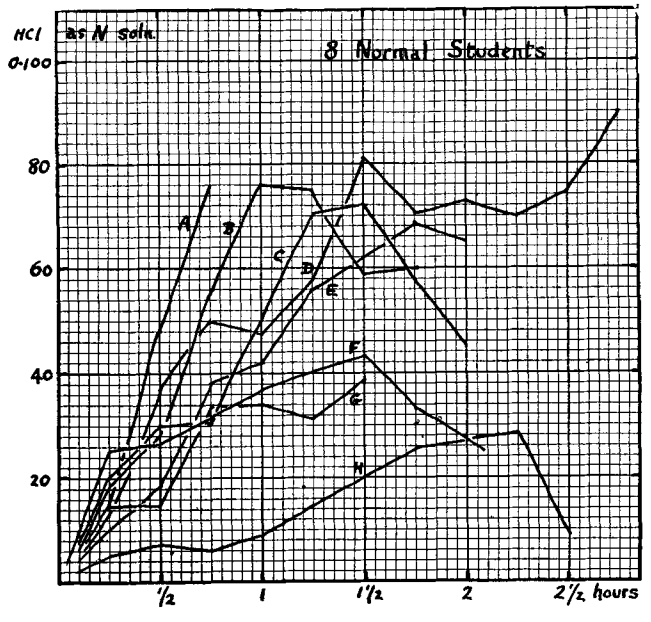

Fig. 2. Fractional test-meal curves (gruel meal) in eight normal students.

of known pancreatic disease (Fig. 4) and first suggested the "acid test" for disease of this organ. Favorable reports concerning this test have since been received. In 1924 I (2) also showed the rapid reduction in the acid test following gastro-enterostomy. (Fig. 5).

Very little further use was made of this test until 1929 when Elman (9) showed that in duodenal ulcer there is some failure to reduce acid in the stomach (Fig. 6—Compare this with Fig. 5). In 1935 he published a further series of cases of duodenal ulcer before and after gastro-enterostomy.

Levy (13) in 1934 showed among other things a diminished acid reduction in cases of chronic appendicitis before operation. (Fig. 7). He believes this failure to reduce acid is due to pyloric spasm. He

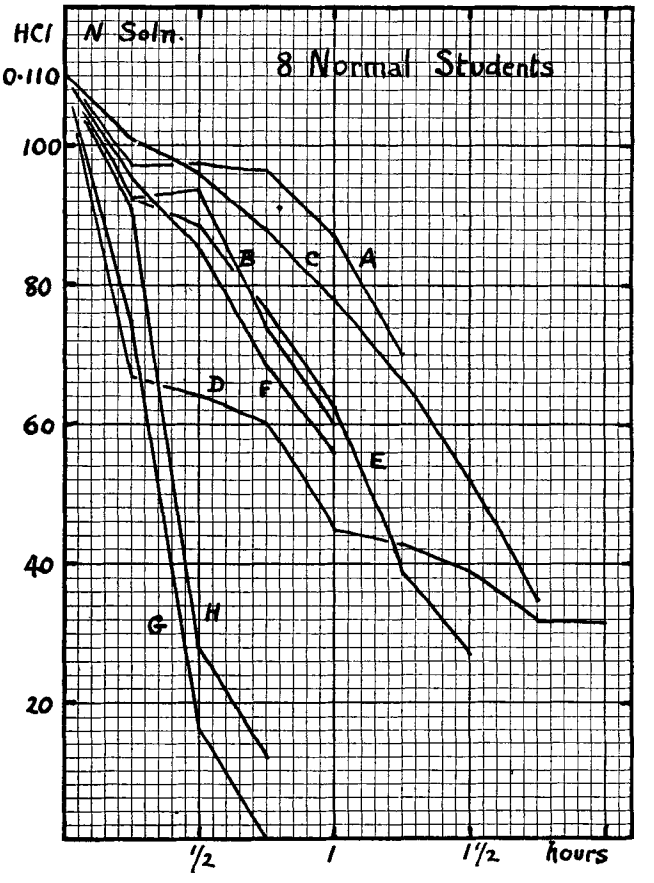

Fig. 3. Showing the fall of acidity in eight normal students (same as those of Fig. 2) when 250 c.c. of 0.110 N HCl is substituted for the gruel meal.

concluded that "as compared with the ..... Ewald test-meal, the neutralization test showed a greater uniformity and in general a closer correlation with the physical and clinical findings and would seem, therefore, to be of greater diagnostic importance."

Various writers have referred to this test as the Neutralization Test. This is a misnomer, since it has been shown by several authors (Apperly (3), MacLean and Griffiths (14) and others) that acid placed in the stomach is reduced almost wholly by dilution, and to only a small extent (and often not at all) by neutralization by duodenal fluids. Hence the term "Acidity Reduction Test" would appear to be better.

One further point should be noted. Most of those

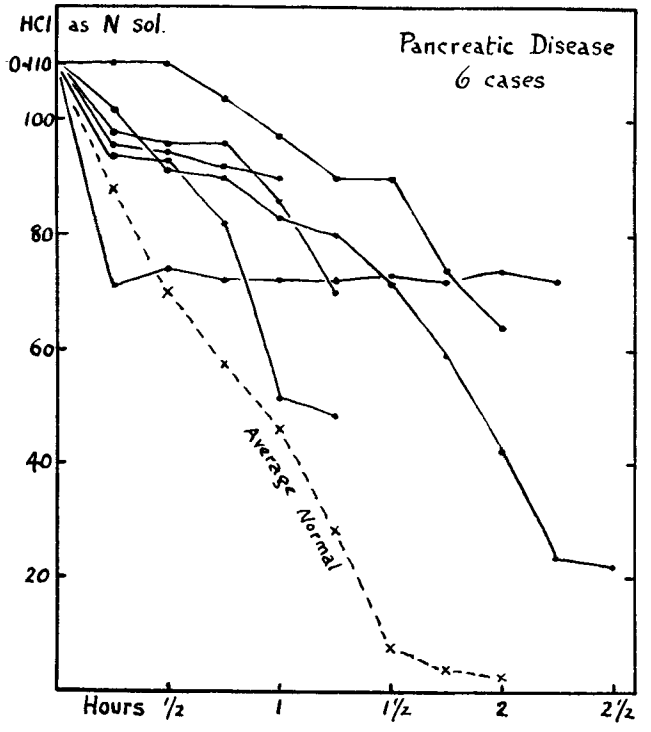

Fig. 4. Acidity Reduction Test in pancreatic disease.

using the test have assumed, following Pavlov (15), Ivy and Whitlow (12), and MacLean and Griffiths (14), that, when acid is artificially placed in the stomach, secretion of hydrochloric acid by the gastric mucosa is suppressed. Generally this appears to be true, but in a certain proportion of cases considerable additional acid may be secreted (Apperly and Norris (7)). In practice, however, this does not seem to vitiate the general results of the test.

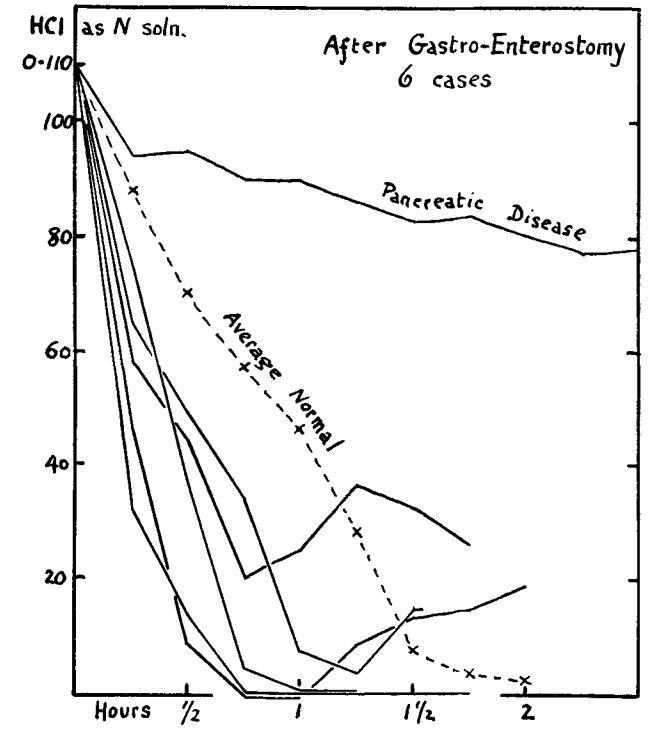

Fig. 5. Acidity Reduction Test After Gastro-enterostomy (one of these cases was found to have pancreatic disease. See Reference 2).

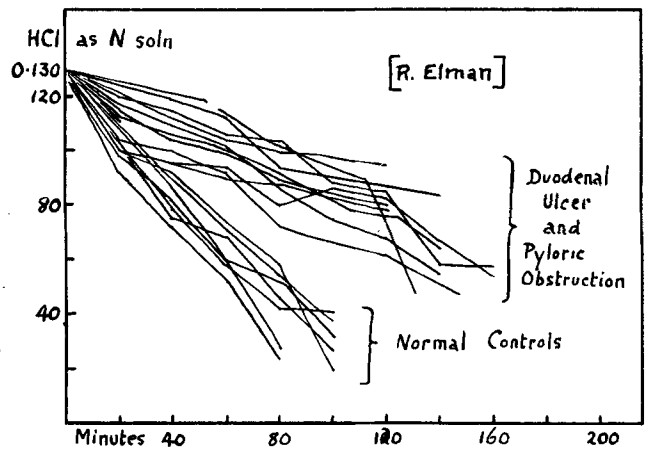

Fig. 6. Acidity Reduction Test in duodenal ulcer and pyloric obstruction. (After Elman (9)).

TECHNIQUE OF TEST

The Rehfuss tube is swallowed by the fasting patient and all fasting contents withdrawn. 250 c.c. of 0.4% (0.110 N) HCl, previously warmed to body temperature, is drawn up into a large (100 c.c.) pipette, which is then attached to the free end of the tube. By holding the pipette above the level of the head, the acid runs into the stomach by gravitation. The test is then conducted as in the usual fractional test-meal, i.e. samples are withdrawn every ¼ hour and titrated for free acid. Insufficient stress however has been laid on one very important point, viz., thoroughly mixing the gastric acid before withdrawing a sample, by moving the piston of the withdrawing syringe back and forth about 6 or 8 times. Experience has shown that this insures a uniform mixture in the stomach.

DISCUSSION

The degree of acidity of the gastric contents does not, of itself, give rise to any sensation. Thus acid, of an acidity far greater than that found in any pathological condition, when placed in the stomach is not in any way appreciated. On the contrary, Hurst (11) has shown that the only adequate stimulus for the production of the sensations of fullness, discomfort and pain in the stomach and intestine is increase of ten-

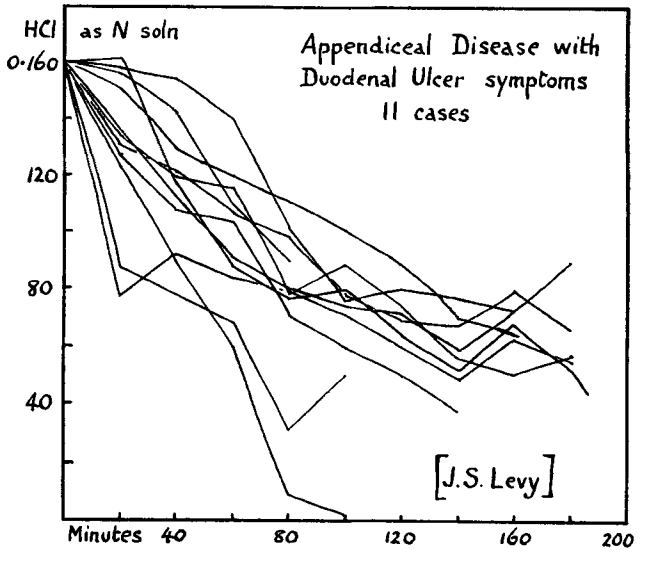

Fig. 7. Acidity Reduction Test in appendiceal disease with ulcer symptoms. (After Levy (13)).

sion or pressure of contents above a certain critical level in that organ. Thermal, chemical, or tactile stimuli, provided they do not cause spasm and rise of tension, are not felt by the patient. This has been shown in operations under local anesthesia.

From the foregoing facts it follows that these symptoms of indigestion can be brought about by such incoordinations of gastro-intestinal muscular activity as give rise to increased intra-gastric or intra-intestinal pressure. Thus a stomach powerfully forcing its contents against a pyloric obstruction gives rise to fullness, discomfort or pain according to the degree of pressure produced.

On the other hand we know from common experience that high or low acidity is often found in certain different forms of indigestion—but not necessarily. In order to clearly understand the relation of acidity to gastro-intestinal muscle function let us consider the series of events following a meal.

When a gruel test-meal is placed in the stomach, hydrochloric acid of concentration 0.174 N (Hollander and Cowgill (10)) is secreted into the fluid food. Usually the acidity rises for one to 1¼ hours and then falls. This fall is brought about chiefly by a regurgitation of duodenal fluids which dilute and to some extent neutralize the gastric acid. The acidity curve can be raised by: (a) increased secretion of acid. (b) increased rate of gastric emptying, which leaves a smaller residue of food to be acidified, thus raising the concentration of the acid, and (c) a diminution or failure of duodenal regurgitation. An opposite set of conditions lowers acidity.

With this double response of the stomach to the introduction of food, viz. 1. acid secretion, and 2. gastro-intestinal movements of flux and reflux, it is obvious that if we could eliminate the former, then any variations in the acidity curve must be brought about wholly by the latter, and so give a much clearer indication of the nature of the faulty gastro-intestinal muscle activity, which is the cause of the symptoms. Hence the origin of the Acidity Reduction Test. In fact, by substituting hydrochloric acid for the Ewald meal, we eliminate both (a) and (b) above.

The figures shown demonstrate these faulty mechanisms. Thus there is a retardation of acid reduction in cases of pyloric obstruction or spasm (Figs. 6 and 7) and in cases of insufficient production of pancreatic alkali, whether brought about experimentally (Fig. 1) or by disease of the pancreas (Fig. 4). Norris and I (7) also showed a retarded rate of reduction in chronic nephritis and in diabetes, two diseases commonly associated with a diminished blood alkali reserve, which in turn brings about a diminished secretion of pancreatic alkali. In all of these cases there is delayed emptying. Even in cases of rapidly emptying hypertonic stomachs, in which flux dominates over reflux, I have found that the acid remains high.

Conversely, when reflux or regurgitation is facilitated, as by gastro-enterostomy (Fig. 5) or where there is an abundant secretion of alkali (Apperly and Crabtree (6)), the stomach empties rapidly with a sharp fall in the acid curve (shown in some cases in Fig. 3).

I have found no definite deviation from the normal in patients with gall bladder disease or with achylia gastrica.

Some other physiological factors governing this test have been discussed elsewhere (Apperly and Cary (5)).

CONCLUSION

From experimental and clinical evidence it is concluded that the Acidity Reduction Test is superior to the gruel or Ewald fractional test-meal.

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