FURTHER STUDIES ON THE REDUCTION OF GASTRIC ACIDITY

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The gastric acidity of patients with duodenal ulcers is more effectively reduced by the continuous sucking of alkaline tablets* than it is by the intermittent administration of antacids (Douthwaite and Batty Shaw, 1952). The above trials were made during the course of the digestive period of gruel test meals, and subsequently by drawing samples from the stomachs of fasting patients. Criticism that results based on a relatively inert gruel meal were of little value must be in part accepted. However, this type of meal has been extensively used in studies of gastric acidity over the past thirty years, and it was therefore chosen as a basis for comparison.

In the above paper were reported experiments made on the gastric pH of fasting patients exhibiting the characteristically low pH of duodenal ulceration. It is probable that this high acidity of the inter-prandial periods is responsible for maintaining duodenal ulceration. The alkaline tablets were shown to raise the pH from figures of 1.5 to 8 during the period of sucking. When food was brought into the ward a fall of pH was often noted, presumably as a result of psychic stimulation. It was therefore decided to carry out a similar series of investigations on patients with peptic ulcer taking ordinary meals, except that solid food was minced. Patients 1 and 12, however, were eating ordinary food, unminced.

Choice of Patients.—Twelve patients were chosen who were suffering from chronic ulceration—one in the stomach, eleven in the duodenum. They gave a typical history and showed the clinical and radiological signs of the disease. Those in the wards were ambulant and were eating a mixed diet, as stated above.

Method

The patients were deprived of all drugs for 18 hours before the tests. Within an hour of their usual ward or home breakfast, or lunch, they came to the laboratory and 2-ml. samples

were drawn from the gastric contents every 15 minutes. During the first hour no medicaments were given, but in the subsequent two hours the patients sucked either alkaline tablets or dummy tablets without alkali. The tests were made on two successive days; in some instances the dummy tablets were given on the first day and in some on the second. A comparison of the gastric acidity during the first-hour periods shows the degree to which the measurements are reproducible on successive days. Where the acidity on the test day is reasonably similar to that on the control day it seems legitimate to attribute differences between the two following periods to the difference in composition of the tablets. Immediately after each experiment was completed the pH of each sample was measured electrometrically.

The composition of the alkaline tablets is:

Solids from whole-milk, combined with		
dextrins and maltose		40 gr. (2.6 g.)
Magnesium trisilicate		3½ gr. (0.23 g.)
Magnesium oxide		2 gr. (0.13 g.)
Calcium carbonate		2 gr. (0.13 g.)
Magnesium carbonate		½ gr. (0.03 g.)
Ol. menth. pip.		q.s.

This tablet, if lodged between gum and cheek, was found to take 20 to 30 minutes to dissolve. Its food value was approximately 11 calories.

Results

The results of the tests in the order of their performance are shown in the accompanying graphs. It may be seen that in every case the alkaline tablets produced an appreci-

Acidity of gastric contents plotted against time. ← → Shows the period of tablet-sucking and the number of tablets taken. ●—●—● = Alkaline tablets; ○—○—○ = Dummy tablets.

*Subsequently given the trade name of "nulacin."

able lowering of the acidity of the gastric contents as compared with the acidity during the sucking of the dummy tablets.

A study of the acidity of the gastric contents during the first-hour control periods does not reveal any systematic difference between the hour preceding the dummy tablets and the hour preceding the alkaline tablets. In those patients who took more than three alkaline tablets in the two-hour period the acidity of the gastric contents at some time fell as low as 1 clinical unit, or 1 mEq per litre. It is an important point that under the conditions of the experiments the patients decided for themselves how many tablets to suck, subject to a tablet being in the mouth during the whole period; yet at no time was a pH higher than 6 recorded in the recovered gastric contents, most of the pH readings of more than 3 being in the range of 3 to 4. Since the alkaline tablet dissolved in water will give a pH of 10, which is probably higher than optimal, this finding that the gastric contents are not made more alkaline than the plasma is reassuring.

It may be seen from Graphs 2 and 8 that the acidity of the gastric contents did not fall immediately the alkaline tablet was sucked by these two patients. This would be accounted for if the volume of the gastric contents was large at this part of the digestive period, so that some time would be required for enough alkali to be swallowed to neutralize the whole.

At first sight it might appear that the increase of pH occasioned by the alkaline tablets was negligible, but this is not so. A slight change of pH at low pH levels represents a large alteration in the more familiar scale of units of clinical acidity. This has been made clear by charting the latter on the left-hand side and the corresponding pH of pure HCl on the right-hand side of the graphs. Thus pH 1.7 corresponds to 20 clinical units, pH 2 to 10 clinical units. In short, a change of 0.3 pH unit always represents a doubling or halving of the concentration of acid.

Discussion

It is generally accepted that reduction of the acidity of gastric contents is desirable in the treatment of patients with peptic ulcer. The experiments quoted above show that this can be achieved by sucking tablets containing quite small quantities of alkali. The question arises, What is the optimum degree of neutralization? To attain the pH of the plasma—namely 7.4—might not be advantageous, because bacterial growth might thus be encouraged. We suggest arbitrarily that an acidity corresponding to 1 clinical unit represents satisfactory neutralization.

In vitro it is found that one of the alkaline tablets neutralizes about 90 ml. of N/10 HCl, using pH 3, corresponding to 1 clinical unit, as the end-point. *In vivo* the food which the patient takes is also effective in reducing the acidity of the gastric contents, so that it is not surprising that sucking only one tablet an hour was effective in some of our experiments. Since it is quite possible to suck four such tablets an hour for a short period, it is clear that the alkaline tablets offer a potent means of reducing the acidity of the gastric contents. The question arises, Are they too potent to be given to patients without close supervision? We are satisfied that this is not the case. Douthwaite *et al.* (1952) considered the possibility of alkalosis arising from these tablets and on theoretical grounds dismissed it, provided that the daily dose did not exceed 15 tablets. Since that time many thousands of them have been used in hospital and private practice, and no such side-effect has been reported.

That the sucking of alkaline tablets will relieve symptoms of duodenal ulcer is certain. Their regular use in the symptom-free patient already seems to reduce the tendency to relapse. It would be unwise to put the case any more strongly than this for the present. It is hoped that significant results will be available after a five-year follow-up period.

Summary

The antacid effect of alkaline tablets on 12 patients with chronic peptic ulcer has been studied and compared with that of dummy tablets containing no antacid. The patients were ambulant and on full meals.

In every case the degree of neutralization was considerable, in marked contrast to the lack of effect of the control tablets.

The degree of neutralization required for therapeutics is considered and grounds are given to justify the belief that the treatment is safe.

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REFERENCE

Douthwaite, A. H., and Shaw, A. Batty (1952). *British Medical Journal*, 2, 180.

INFLUENCE OF CORTISONE ON INDUCED ASTHMA AND BRONCHIAL HYPOSENSITIZATION

BY

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Cortisone and A.C.T.H. have been found by many authors to be beneficial in bronchial asthma. Signs and symptoms of the disorder are suppressed in the great majority of cases as long as either is administered (McCombs, 1952; Schwartz *et al.*, 1952; Lowell *et al.*, 1953; and others).

It seemed of interest to find out whether cortisone would alter the bronchial reaction to a test dose of the allergen, or, in other words, whether it would influence an induced asthmatic attack. If it did, it might also influence the course of therapeutic hyposensitization, which at present consists of a series of injections or inhalations of the allergen, the dose being cautiously increased each time. This increase aims at the gradual build-up of sufficient circulating antibody, and avoids severe reactions. If the increase is too abrupt, not only do severe allergic attacks develop but they are followed by a period of hypersensitivity (Herxheimer, 1951; Herxheimer and Prior, 1952). The mechanism of the development of hyposensitivity and hypersensitivity is, so far, not understood.

From clinical experience it was expected that cortisone would abolish or modify the violence of the reaction to an overdose of allergen, but it seemed also of great practical and theoretical interest whether it would, in addition, prevent hypersensitization.

Method

The inhalation method was used for inducing asthma and hyposensitization in the same way as described before (Herxheimer, 1951). The subject breathes atmospheric air from a closed-circuit spirometer which records his vital capacity and, in the more recent work, expiratory speed. A pump compresses air taken from the circuit and sends it at a standard pressure through an aerolyser filled with allergen extract. The aerosol thus produced flows back into the circuit and is inhaled by the patient. The degree of exposure to the allergen is measured by its duration in seconds. In order to achieve hyposensitization the duration must be