

# STUDIES ON ANACIDITY: THE HYDROGEN-ION CONCENTRATION OF THE GASTRIC SECRETION, THE GASTROSCOPIC APPEARANCE OF THE GASTRIC MUCOSA, AND THE PRESENCE OF A GASTRIC SECRETORY DEPRESSANT IN PATIENTS WITH ANACIDITY

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Clinicians have customarily used the indicator, dimethyl-amino-azobenzol (Toepfer's solution) to indicate the presence or absence of free hydrochloric acid in the gastric juice. Bloomfield and Polland (1) have pointed out that in many such instances of apparent anacidity with this indicator, the stomach is still capable of secreting hydrochloric acid, and that by determining the hydrogen-ion concentration, the pH may be found definitely on the acid side of neutrality. Furthermore, in these cases there is no regular response to histamine and such secretions as one obtains do not conform to the normal curves but seem to represent a "minimal continuous secretion largely or completely independent of the stimuli which normally cause a flow of juice." In this regard, Martin (2) found a wide variation in the chloride content of the gastric secretion from patients with so-called "benign achlorhydria." The concentration of ammonia and non-protein nitrogen was considerably greater than that found in the acid-secreting patients. This increase was still more pronounced in pernicious anemia and gastric carcinoma with achlorhydria. After histamine stimulation there was usually some change in the acid-base pattern but not to any significant degree.

Many people, without apparent disease, may have a permanent anacidity. Vanzant *et al* (3) noted an incidence of 14.5 per cent after the use of a modified fractional meal. Polland (4) reported an incidence of 10.8 per cent true anacidity in 900 cases (excluding pernicious anemia and carcinoma of the stomach). Furthermore, anacidity increases in frequency with advancing age (3). The relation of gastric anacidity to disease has been considered in detail in the excellent monograph of Bloomfield and Polland (1). Anacidity is an invariable accompaniment of pernicious anemia and occurs frequently in carcinoma of the stomach. Schindler *et al* (5), in describing the anatomic foundations of anacidity, include 6

cases of hypertrophic gastritis, 12 of superficial gastritis and 37 of atrophic gastritis in a series of 120 cases. Brunschwig *et al* (6) have recently reported that, when the gastric secretions from 16 of 18 patients with pernicious anemia (89 per cent) were injected intravenously in dogs with stimulated gastric pouches, they produced a marked inhibition of pouch secretion and achlorhydria. Only 18 per cent of a control group produced similar effects.

The following investigation was undertaken to determine whether significant differences in the anacidity associated with these various conditions would be revealed by a study of the hydrogen-ion concentration of the gastric secretion, and whether or not this could be correlated with the gastroscopic appearance of the gastric mucosa or the presence in the gastric juice of a secretory depressant. For this purpose the pH of individual samples of the gastric secretion obtained after histamine stimulation was determined electrometrically with a Beckman pH meter. The standard histamine test was employed. In every instance the position of the tip of the Rehfuß tube was checked fluoroscopically. The patients were cautioned to avoid swallowing saliva. After the fasting contents were withdrawn, histamine ("imido" Roche) was injected hypodermically in doses of 0.01 mgm. per kilogram of body weight. The stomach contents were then aspirated at 10-minute intervals for one hour. The data comprise pH determinations in 854 specimens of gastric secretion obtained in a series of 72 patients (44 men and 28 women). In 45 patients the absence of free hydrochloric acid (as denoted by the presence of a yellow color with Toepfer's solution) was confirmed by more than one histamine test. The presence or absence of a secretory depressant was determined by Dr. Brunschwig in 19 patients.

*Pernicious anemia*

The 17 patients with pernicious anemia include 8 men and 9 women. The ages ranged from 29 to 69. All except 2 cases (J. C. and F. L.) had received liver therapy. The fasting pH varied from 6.70 to 8.50. After histamine stimulation there was no significant lowering of the pH, the figures ranging from 6.40 to 8.81 (Figure 1). In all but 4 cases the fasting pH was consistently lower than the pH after stimulation. The average values were: 7.43, 7.81, 7.87, 7.95, 8.04, 8.01, and 7.99. In one of the 8 patients gastroscoped (F.M.) a normal stomach was observed. The changes in the other cases varied from a patchy atrophic gastritis to extensive atrophy. There was no direct relationship between the severity of the gastroscopic picture, the presence or absence of anemia, and the hydrogen-ion concentration. Helmer, Fouts, and Zervas (7) found that the pH in 47 patients with pernicious anemia varied from

6.9 to 8.6. In 14, a measurable drop in pH occurred after histamine stimulation. Streicher *et al* (8) observed a pH range of 6.5 to 7.2 in 4 cases of pernicious anemia. Six patients of the present series were found to possess a gastric secretory depressant, but there was no correlation between these findings and the hydrogen-ion concentration of the respective gastric secretions.

*Atrophic gastritis*

In this group are included 19 patients (10 men and 9 women); the ages ranged from 28 to 68. The blood counts in all cases were within normal limits. The fasting pH varied from 6.51 to 8.60. After histamine stimulation, a definite drop in pH occurred in 8 cases. The figures ranged from 4.52 to 8.59 (Figure 2). The average values were: 7.47, 7.74, 7.60, 7.00, 6.97, 7.09, and 6.90. Although the pH curve resembles that of pernicious anemia, the range is distinctly greater. It is

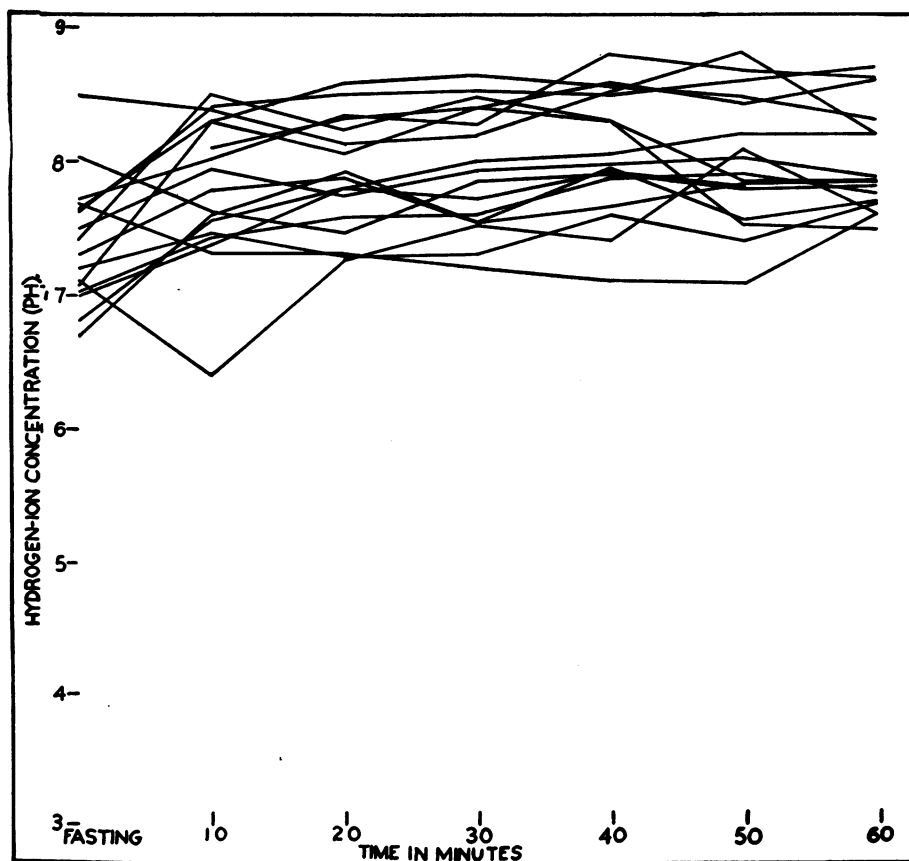


FIG. 1. INDIVIDUAL pH VALUES IN PERNICIOUS ANEMIA (HISTAMINE STIMULATION)

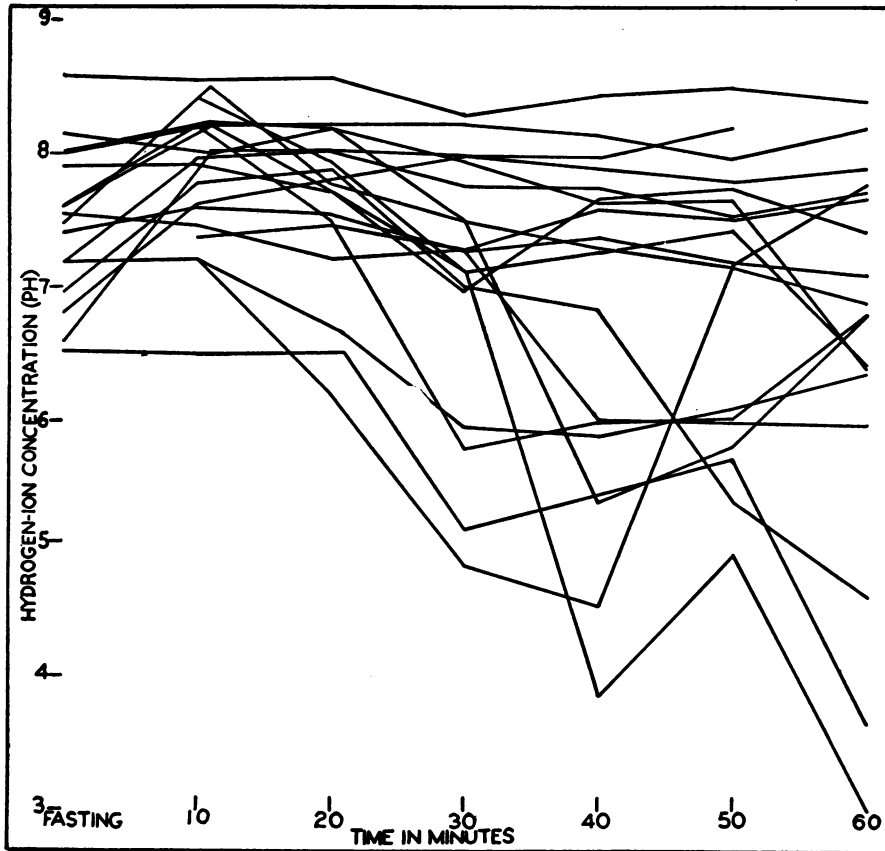


FIG. 2. INDIVIDUAL pH VALUES IN ATROPHIC GASTRITIS WITH ANACIDITY (HISTAMINE STIMULATION)

interesting to note in this connection that Schindler and Serby (9) were unable to differentiate gastroscopically between the atrophic gastritis seen in pernicious anemia and that seen in other types of anemia or in cases without anemia. The extent and severity of the atrophic gastritis in this group could not be correlated with the hydrogen-ion concentration of the gastric secretions. Five patients were tested for the secretory depressant of Brunshwig; positive results were obtained in 3 and negative results in 2. These observations were related neither to the pH nor to the degree of inflammation. Some patients had been treated with liver extract and ventriculin without significant change in the pH values after such therapy. The case of J.M. is interesting in that it represents an instance of subacute combined cord degeneration without anemia and with anacidity. Palmer and Porter (10) have described this patient in detail previously. Oliver and Wilkinson

(11) have observed an incidence of 100 per cent achylia gastrica in 39 such patients.

#### *Carcinoma of stomach*

The 8 cases included in this group were all males with ages ranging between 50 and 70. Secondary anemia was present in 4 patients. The fasting pH varied from 6.68 to 8.50. After histamine stimulation, a definite drop in pH occurred in 4 cases, the pH ranging from 4.81 to 8.54 (Figure 3). The average pH values were: 7.46, 7.36, 6.99, 6.51, 6.45, 6.98, and 7.37. In all patients the carcinoma was extensive. Five patients were gastroscoped; in 2 there was an associated extensive atrophic gastritis, in 2 a patchy atrophic gastritis, while in the fifth case there was no evidence of atrophy. Brunshwig *et al* (12), continuing their important studies, found that the gastric secretions from 21 of 27 patients with carcinoma of the stomach (78 per cent) contained

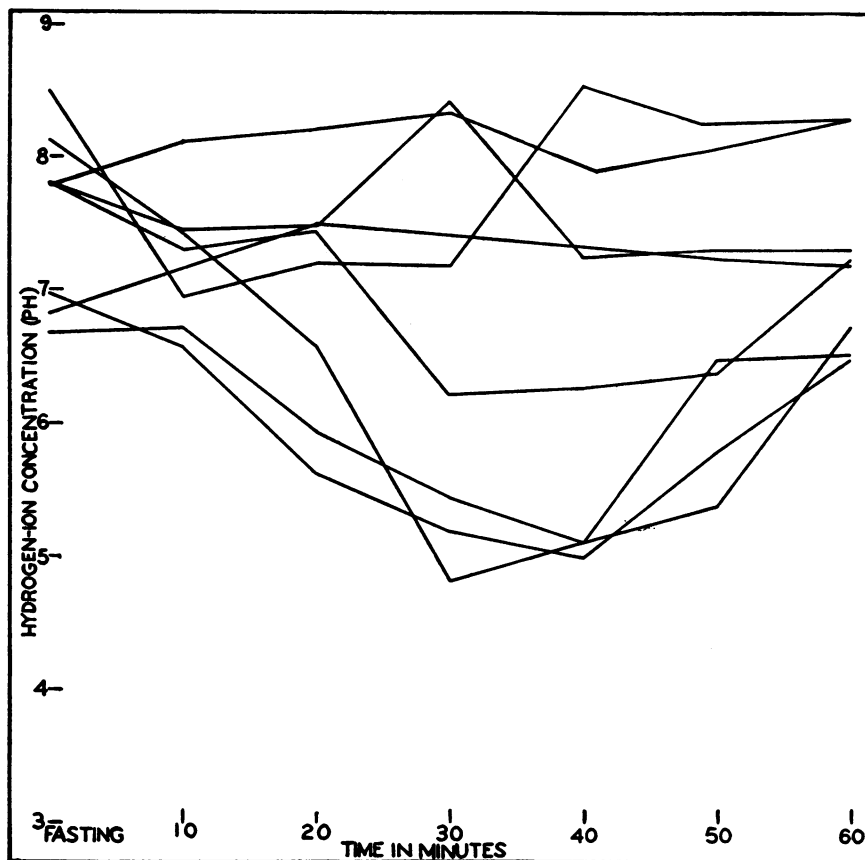


FIG. 3. INDIVIDUAL pH VALUES IN GASTRIC CARCINOMA WITH ANACIDITY (HISTAMINE STIMULATION)

a secretory depressant. Of 3 patients in this group similarly studied, 2 yielded positive and one negative results. The pH could not be correlated with any of these observations.

Polland and Bloomfield (13) determined the hydrogen-ion concentration (colorimetrically) of the gastric juice in some cases of carcinoma of the stomach. When a complete absence of acid existed, the pH reading was usually 6 to 8. In several of the cases, even though no test for free acid was obtained with di-methyl, the pH fell in successive specimens after stimulation to a pH of 3 to 5, indicating that traces of acid were being secreted. These observations are in substantial agreement with the present data.

#### *Anacidity after radiation therapy*

Palmer and Templeton (14) recently have described the effects of radiation therapy on gastric secretion. The purpose of such treatment was

the production of anacidity artificially by x-ray therapy in ulcer patients, thus removing one of the causes essential to the formation of chronic gastroduodenal ulcer. Ten such cases with anacidity to Toepfer's solution are included in this study. All were men with ages ranging from 20 to 52. The amount of radiation therapy varied from 1055 R to 2930 R. The red blood counts and hemoglobin were uniformly normal. The fasting pH varied from 5.65 to 8.19. After histamine stimulation, there was a significant drop in the pH in 8 cases, the figures ranging from 4.13 to 8.00 (Figure 4). The average values were: 7.17, 7.31, 6.89, 6.02, 5.79, 6.20, and 6.31. In 2 patients a superficial gastritis was seen, while in the third case a mild hypertrophic gastritis was observed. Negative results were obtained in 3 patients studied for the presence of a secretory depressant. The variations in pH after histamine stimulation were most pronounced in this group.

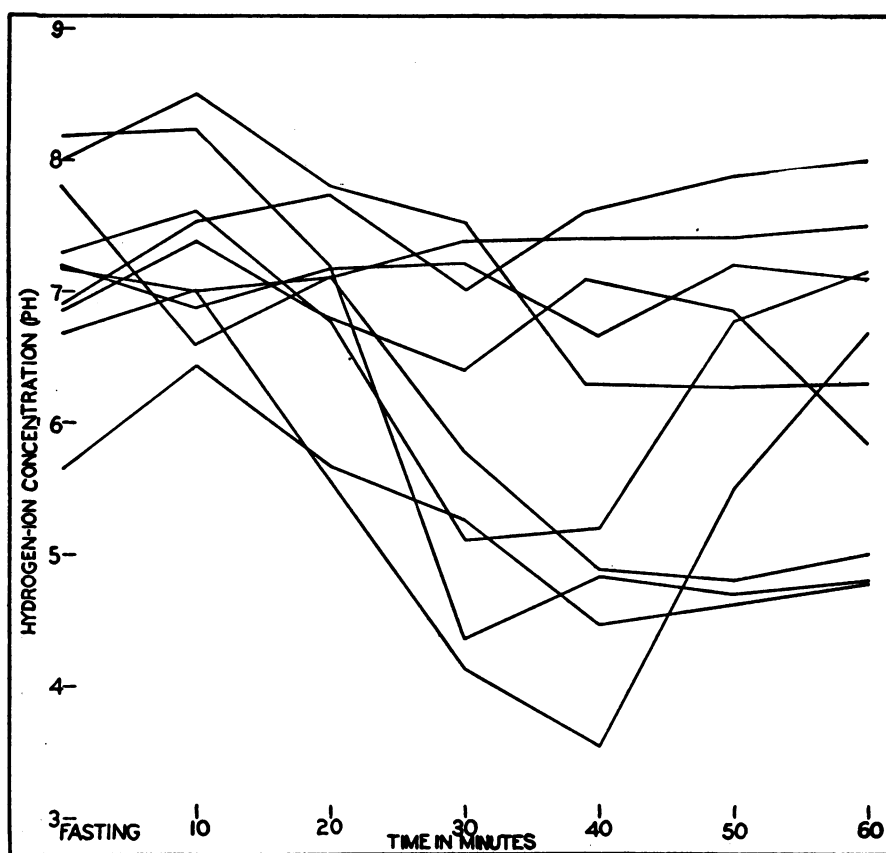


FIG. 4. INDIVIDUAL pH VALUES IN POST-RADIATION ANACIDITY (HISTAMINE STIMULATION)

#### *Miscellaneous conditions*

Eighteen patients with various miscellaneous conditions were studied. In 3 cases, all males, an extensive superficial gastritis was present. The secretion of one of these (J. E.) was found to contain the secretory depressant of Brunshwig. Cholelithiasis was found in 3 cases. Eight patients (3 men, 5 women) were diagnosed as functional bowel distress after complete roentgen studies of the gastro-intestinal tract were interpreted as normal. In 2 of these, a definite lowering of the pH occurred after histamine stimulation. The pH of the gastric secretions in some instances was similar to the values obtained in pernicious anemia or atrophic gastritis. Since none of these patients (excluding those diagnosed as superficial gastritis) were gastroscoped, the possible presence of an atrophic gastritis is not excluded.

#### DISCUSSION

The data presented in this study indicate that anacidity is most complete and constant in pernicious anemia. The pH varied between 7.0 and 8.0 with only slight variations after histamine stimulation. The pH in atrophic gastritis resembled that of pernicious anemia but was more variable. It is interesting to note that not only are the pH curves similar but also that the two conditions cannot be distinguished gastroscopically. In addition, although the series is small, a majority of the patients tested from these two groups were found to possess a secretory depressant in the gastric secretions. The pH values in carcinoma of the stomach and radiation therapy were distinctly lower than in the two preceding groups. These differences are well shown in the individual graphs and the average curves (Figure 5).

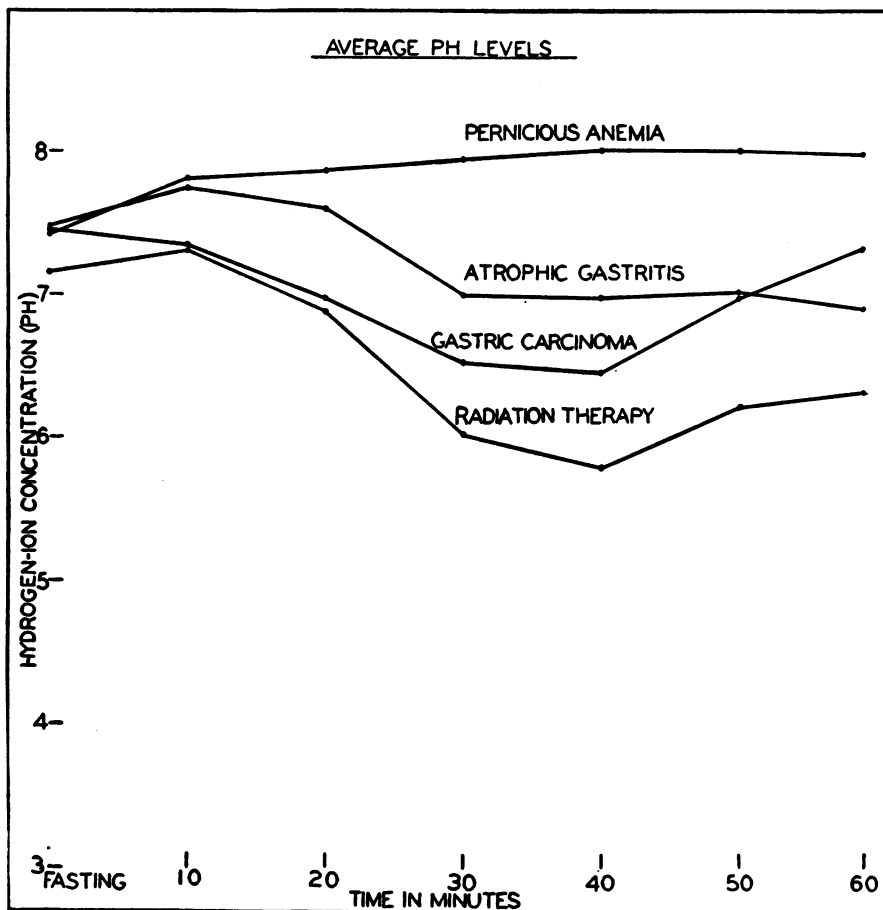


FIG. 5. THE pH OF THE GASTRIC SECRETION IN ANACIDITY. AVERAGE CURVES IN PERNICIOUS ANEMIA, ATROPHIC GASTRITIS, GASTRIC CARCINOMA AND POST-RADIATION ANACIDITY (HISTAMINE STIMULATION)

The pH curves in the anacidity associated with superficial gastritis, cholelithiasis or functional bowel distress may resemble those obtained for pernicious anemia, atrophic gastritis or carcinoma of the stomach, indicating no specific values for any particular type. The artificial anacidity which follows radiation therapy obviously is not as complete as in the other groups. Palmer and Templeton have shown, furthermore, that such an anacidity is not permanent.

No conclusions can be drawn from this study as to the mechanisms involved in the pathogenesis of spontaneous histamine-proved anacidity. The pH levels cannot be correlated with the gastroscopic picture, the presence or absence of a secretory depressant in the gastric secretions, or the presence or absence of anemia. Pollard (15)

likewise attaches no significance to anemia as a cause of anacidity.

#### SUMMARY AND CONCLUSIONS

The hydrogen-ion concentration of the gastric secretion obtained after histamine stimulation and showing a yellow color ("anacidity") to Toepfer's reagent was determined in 72 patients (44 males, 28 females). The series comprised 17 patients with pernicious anemia, 19 patients with atrophic gastritis, 8 patients with carcinoma of the stomach, 10 patients with anacidity after radiation therapy, and 18 patients with miscellaneous conditions.

The pH of the gastric secretion in pernicious anemia falls within a range of pH 7.0 to 8.0 and shows no appreciable drop after histamine stimu-

lation. The pH of the gastric secretion in atrophic gastritis resembles that of pernicious anemia but varies more than pernicious anemia after histamine stimulation.

The pH of the gastric secretion after histamine stimulation in carcinoma of the stomach with anacidity and in the anacidity which sometimes follows radiation therapy is lower and more variable than that found in pernicious anemia.

The individual pH curves in these groups may resemble one another, thus suggesting that there is no specific pH curve for the anacidity associated with a particular disease process.

There is no correlation between the hydrogen-ion concentration of the gastric secretion, the gastroscopic appearance of the stomach mucosa, the presence or absence of a secretory depressant factor in the gastric secretion and the presence or absence of anemia.

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