Effect of Cimetidine and Antacid on Gastric Microbial Flora

RICHARD SNEPAR, GEORGE A. POPORAD, JOSEPH M. ROMANO, WILLIAM D. KOBASA, AND DONALD KAYE*

Department of Medicine, The Medical College of Pennsylvania, Philadelphia, Pennsylvania 19129

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The effect of a standard regimen of cimetidine on the gastric flora of 20 male volunteers was studied in a double-blind manner and compared with the effects of a standard antacid regimen. Postprandial microbial titers in gastric aspirates were significantly higher at 4, 8, and 16 weeks of therapy in subjects taking antacids and at 4 weeks in subjects taking cimetidine when compared with their pretreatment titers. Although not significant, there was a tendency for fasting microbial titers to be higher in subjects receiving cimetidine as compared with pretreatment titers. The higher titers were primarily related to increases in survival of mouth flora (viridans streptococci and Neisseria spp.); Enterobacteriaceae and other nitrate-reducing organisms were unusual isolates. There was no significant difference in the total titers or types of organisms isolated when subjects taking cimetidine were compared with those taking antacid.

In 1939 Garrod demonstrated the bactericidal activity of hydrochloric acid and gastric juice (6). Others have subsequently reported that the type and numbers of microbial flora present in the stomach are affected by gastric pH (3, 8, 9). Drasar et al. (3) and Giannella et al. (7) showed that, unlike normal stomachs, which contain few bacteria, stomachs of patients with hypochlorhydria or achlorhydria maintain high bacterial counts. Bacterial overgrowth in the stomach increases the risk of wound sepsis after gastric surgery (14).

Gastric pH, as well as affecting gastric microbial flora, has been shown to be inversely correlated with the amount of nitrite present in gastric juice (17, 18). Patients with achlorhydria, hypochlorhydria, or gastric carcinoma have significantly higher concentrations of gastric juice nitrite than normal humans or duodenal ulcer patients. Reduction of dietary and salivary nitrites by bacteria has been postulated as the source of these nitrates (17).

Nitrites and secondary amines, which are present in gastric juice in both the normal and achlorhydric states, can combine, catalyzed by the presence of bacteria, to form nitrosamines (10, 11, 17, 18). These compounds are carcinogenic in laboratory animals (13), have been thought to be carcinogenic in humans, and have been postulated to be implicated in the increased incidence of gastric carcinoma seen in achlorhydric patients (17).

Although it is presently possible to reduce gastric acid secretion with the H₂ receptor antagonist cimetidine, its effect on gastric bacterial flora has not been thoroughly studied. There have been only three previously published papers on the effect of cimetidine on gastric flora. One paper (16) on peptic ulcer patients reported an increase in enterococci and nitrate-reducing organisms (among others) in gastric aspirates; however, there was no attempt to standardize specimens as to relation to food intake, a factor known to influence gastric flora (2). The other two reports (14, 15) were both from the same investigators. One (15) found no increase in gastric bacterial titers in six volunteers in either the fasting or postprandial state; the other (14) reported a marked increase in bacterial titers in fasting gastric aspirates from patients receiving cimetidine (the postprandial state was not studied). In all three studies (after excluding lactobacilli), enterococci were the bacteria most commonly isolated.

The purpose of the present study was to determine the effects of cimetidine on the gastric flora in healthy volunteers both in the fasting and postprandial states and to compare these in a double-blind fashion with the effects of antacids which are also commonly used to elevate the pH of gastric secretions. Cimetidine and antacids were both found to increase postprandial bacterial titers, but enterococci were not isolated.

MATERIALS AND METHODS

Patient population. Twenty male volunteers (19 white and 1 black) between the ages of 20 and 35 years were studied. The subjects were free of organic disease and were taking no medication. Eighteen of the 20 subjects were medical students, residents, or male nurses.

Study protocol. Subjects were randomly assigned in a double-blind manner to receive either: (i) cimetidine
and placebo antacid; or (ii) aluminum hydroxide and magnesium hydroxide with simethicone in liquid suspension (Mylanta II) and placebo cimetidine. The regimen for cimetidine (or cimetidine placebo) was 300 mg four times daily with meals and at bedtime for the first 4 weeks of the study and 400 mg at bedtime only for an additional 12 weeks. Thirty milliliters of Mylanta II or placebo Mylanta II was taken 1 and 3 h after each meal and at bedtime for the first 4 weeks of the study and 1 h after each meal and at bedtime for an additional 12 weeks (four times daily). In the event that diarrhea occurred, 30 ml of aluminum hydroxide (Amphogel) or Amphogel placebo was substituted for Mylanta II in that subject. These regimens of cimetidine and antacid are commonly recommended in treatment of peptic ulcer disease.

Baseline gastric aspirates were obtained in all subjects before therapy to serve as pretreatment control values and again after 4, 8, and 16 weeks of therapy. The procedure was as follows: in the morning after a 12-h fast (except for the bedtime cimetidine and antacid), a nasogastric tube (12 French) was passed, and an aspirate was withdrawn. The first 5 ml of all samples was discarded. A standard meal of Knox gelatin (6 g of protein) was administered, and the subjects then took their medication as described below. The aspiration was repeated 2 h after the meal (again the first 5 ml was discarded after clearing the tube with air). The tube was left in place during the 2 h. Aspirates were tested for pH by pH meter, and cultures were obtained. At 4 weeks the morning dose of cimetidine was given with the Knox gelatin, and the antacid was given 1 h after the Knox gelatin. Thereafter, the cimetidine or antacid was given at bedtime the night before the aspirate, and the antacid was given 1 h after the Knox gelatin. One milliliter of gastric aspirate was diluted in 9 ml of brain heart infusion broth (Difco Laboratories) and immediately plated in dilutions from $10^{-4}$ to $10^{-7}$ in an anaerobic chamber, on Schaedler tomato juice and ragosa SL agars. Plates were incubated at 37°C in GasPak jars (BBL Microbiology Systems) and inspected at 48 h and at 7 days. Gastric aspirates were also quantitatively cultured on Schaedler CNA, chocolate, desoxycholate, and Sabaraud agars and incubated aerobically (in a CO$_2$ atmosphere for chocolate agar) for 48 h at 37°C. Sabaraud agar plates were incubated at 20°C for 7 days. The colonies developing were counted, and the original titer was calculated as colony-forming units (CFU) per milliliter. Organisms were identified by standard laboratory procedures (4, 12). The bacteria isolated were assayed for their ability to reduce nitrate to nitrite (4).

Statistical analysis. The unpaired Student $t$ test, Wilcoxon’s rank sum test, and product-moment correlation coefficient tests were used to analyze the data. $P$ values of $\leq 0.05$ were accepted as significant.

RESULTS

All 20 subjects completed the study. Six subjects in the antacid group developed diarrhea and took aluminum hydroxide without magnesium hydroxide as part of their regimen. No subjects taking antacid placebo developed diarrhea. There were no other side effects noted.

Pretreatment gastric pH. The mean pretreatment fasting pH values of gastric juice for the subjects destined to receive antacid or cimetidine were 2.7 for the antacid group and 3.0 for the cimetidine group (Table 1). Two hours postprandially there was a drop in pH in subjects of both groups to 1.8 and 2.0, respectively, but the decrease was not significant ($P > 0.05$ by paired $t$ test and rank sum test). There was no significant difference in pH values between the antacid and cimetidine group in fasting or 2-h postprandial aspirates.

Organisms isolated pretreatment. The titers of organisms isolated during the pretreatment period are listed in Table 2. There was no significant difference in total microbial titers or in type or titers of individual organisms between those destined to be treated with cimetidine or antacid

### TABLE 1. pH of gastric aspirates

<table>
<thead>
<tr>
<th>Sampling time</th>
<th>pH of gastric aspirate [mean ± SD (median)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fasting</td>
</tr>
<tr>
<td>Pretreatment (no antacid or cimetidine)</td>
<td>2.7 ± 1.8 (1.8)</td>
</tr>
<tr>
<td>4 weeks$^a$</td>
<td>2.7 ± 1.4 (2.3)</td>
</tr>
<tr>
<td>8 weeks$^b$</td>
<td>3.0 ± 2.2 (2.0)</td>
</tr>
<tr>
<td>16 weeks$^c$</td>
<td>3.1 ± 2.1 (2.0)</td>
</tr>
</tbody>
</table>

$^a$ $P < 0.05$ by paired $t$ test.
$^b$ $P < 0.01$ by paired $t$ test.
$^c$ $P < 0.05$ by rank sum test.
$^d$ Cimetidine (300 mg) was taken four times a day (with each meal and at bedtime); antacid (30 ml) was taken 1 and 3 h after each meal and at bedtime. On the morning of the study, cimetidine was taken with the test meal, and antacid was taken 1 h after the meal.
$^e$ Cimetidine (400 mg) was taken at bedtime; antacid (30 ml) was taken 1 h after each meal and at bedtime. On the morning of the study, no cimetidine was taken, and antacid was taken 1 h after meal.
either fasting or postprandially. The 10 subjects destined to receive antacid had a significant postprandial fall in titers of total organisms ($P < 0.05$ by paired $t$ test). The 10 subjects destined to receive cimetidine also had a postprandial fall in titers of total organisms, but this did not reach statistical significance.

There was a striking correlation between pH and the total number of organisms isolated from each specimen: the lower the pH, the lower the titer of organisms ($r = 0.740; P < 0.01$). Fungi (Candida spp. and Aspergillus spp.), viridans streptococci, Lactobacillus spp., and Neisseria spp. were the organisms most often isolated.

**pH in treated subjects.** The mean pH values of the group of subjects receiving antacid or cimetidine are listed in Table 1. In the antacid group fasting pH values were not significantly altered throughout therapy as compared with pretreatment values. The 2-h postprandial pH values of the antacid group were significantly higher at 4 weeks ($P < 0.05$) and 16 weeks ($P < 0.05$) of therapy compared with the pretreatment values by the paired $t$ test.

As in the antacid group, fasting pH values in the cimetidine group while on therapy, although higher, did not differ significantly from the pretreatment values. The cimetidine group also had elevations in 2-h postprandial mean pH values when compared with pretreatment values. A significant difference was noticed at 4 weeks and 8 weeks of therapy ($P < 0.01$ and $< 0.05$, respectively, by the paired $t$ test).

Comparing the group receiving antacid and the group receiving cimetidine, no difference was seen in pH values of either fasting or postprandial samples at 4, 8, or 16 weeks of therapy.

**Total organisms in treated subjects.** The mean values for the total organisms in each group at the various times of aspiration are listed in Table 2. In the antacid group, there were no significant differences in titers of total organisms isolated from fasting gastric aspirates at 4, 8, or 16 weeks compared with their pretreatment values. Postprandially (at 2 h), titers of total organisms at 4, 8, and 16 weeks of therapy were significantly higher than pretreatment values ($P < 0.01$, $< 0.01$, and $< 0.05$, respectively). In contrast to pretreatment where organism titers fell postprandially as compared with fasting values, the postprandial titers were higher than the fasting titers at 4, 8, and 16 weeks, but none of these differences were significant.

In the cimetidine group, the titers of total organisms isolated from fasting subjects at 4, 8, or 16 weeks were higher than the pretreatment values, but these differences were not significant. Postprandial organism titers at 4, 8, and 16 weeks of therapy were higher than pretreatment titers, but the difference was significant only at 4 weeks ($P < 0.01$, by the paired $t$ test). At 4 weeks the postprandial titers were higher than the fasting titers, but at 8 and 16 weeks they were lower; none of these differences were significant.

### Table 2. Titers of total organisms

<table>
<thead>
<tr>
<th>Sampling time</th>
<th>Fasting</th>
<th>2 h postprandial</th>
<th>Fasting</th>
<th>2 h postprandial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretreatment (no antacid or cimetidine)</td>
<td>3.3 ± 2.2 (2.0)</td>
<td>2.0 ± 1.2 (1.9)</td>
<td>3.8 ± 2.5 (4.3)</td>
<td>2.6 ± 1.5 (2.8)</td>
</tr>
<tr>
<td>4 weeks*</td>
<td>2.7 ± 1.6 (2.4)</td>
<td>4.0 ± 2.0 (3.8)</td>
<td>4.4 ± 2.1 (4.9)</td>
<td>5.1 ± 2.3 (5.6)</td>
</tr>
<tr>
<td>8 weeks*</td>
<td>3.5 ± 1.9 (3.4)</td>
<td>3.6 ± 1.9 (3.5)</td>
<td>4.9 ± 2.2 (4.8)</td>
<td>3.9 ± 2.0 (4.3)</td>
</tr>
<tr>
<td>16 weeks*</td>
<td>3.7 ± 1.9 (3.8)</td>
<td>4.2 ± 2.1 (4.5)</td>
<td>4.5 ± 2.1 (4.9)</td>
<td>3.7 ± 1.9 (3.2)</td>
</tr>
</tbody>
</table>

*a* $P < 0.05$ by paired $t$ test.

*b* $P < 0.01$ by paired $t$ test.

*c* $P < 0.01$ by rank sum test.

*d* $P < 0.05$ by rank sum test.

*e* Cimetidine (300 mg) was taken four times a day (with each meal and at bedtime); antacid (30 ml) was taken 1 and 3 h after each meal and at bedtime. On the morning of the study, cimetidine was taken with the test meal, and antacid was taken 1 h after the meal.

*f* Cimetidine (400 mg) was taken at bedtime; antacid (30 ml) was taken 1 h after each meal and at bedtime. On the morning of the study no cimetidine was taken, and antacid was taken 1 h after the meal.
There was no significant difference in titers of total organisms isolated from those subjects taking antacid when compared with those taking cimetidine either fasting or postprandially throughout the study.

There was a striking correlation between low pH and low numbers of bacteria \( r = 0.676 \) for the antacid group and \( r = 0.722 \) for the cimetidine group; \( P < 0.01 \) for both groups.

**Individual organisms in treated subjects.** The distribution of individual organisms isolated in the antacid and cimetidine groups at 4, 8, and 16 weeks of therapy was similar in both groups. As in the pretreatment determinations, *Candida* spp., *Aspergillus* spp. viridans streptococci, *Lactobacillus* ssp., and *Neisseria* ssp. were the organisms most often isolated.

Few anaerobes were isolated, and they were generally isolated from the same three patients throughout the study. Few gram-negative bacilli were isolated, and all were in low titers \( (\log_{10} \text{CFU/ml}, 1.7 \text{ to } 3.3) \). No enterococci were found. The mean titers of the major organisms present are listed in Table 3.

In the antacid group, titers of individual organisms did not differ significantly in fasting aspirates at 4, 8, and 16 weeks of therapy as compared with pretreatment titers. Postprandially, however, titers of viridans streptococci were significantly elevated at 4, 8, and 16 weeks of therapy as compared with pretreatment values \( (P < 0.01 \) by paired \( t \) and rank sum tests for each comparison), and titers of *Neisseria* ssp. were significantly elevated at 4, 8, and 16 weeks of therapy \( (P < 0.05, < 0.01, \) and \( < 0.01 \) by paired \( t \) and rank sum tests). There was no significant difference between fasting and postprandial titers of any individual organism at any time.

In the cimetidine group, fasting titers of *Neisseria* ssp. were significantly elevated at 8 and 16 weeks of therapy when compared with pretreatment values \( (P < 0.01 \) and \( < 0.05 \), respectively, by paired \( t \) and rank sum tests). Postprandial titers of *Neisseria* ssp. were significantly elevated at 8 weeks of therapy as compared with pretreatment values \( (P < 0.05 \) by paired \( t \) test), and postprandial titers of viridans streptococci were elevated at 4 weeks of therapy \( (P < 0.01 \) by paired \( t \) and rank sum tests). There was no significant difference between fasting and postprandial titers of any individual organism at any time.

Titters were not significantly different for any organism when the cimetidine group was compared with the antacid group, except on two occasions. At 4 weeks of therapy fasting titers of viridans streptococci were significantly higher in the cimetidine group \( (P < 0.05 \), by the rank sum test). At 8 weeks of therapy fasting titers of

### TABLE 3. Microorganisms isolated from gastric aspirates

<table>
<thead>
<tr>
<th>Sampling time</th>
<th>Organisms</th>
<th>Mean log_{10} CFU/ml ± SD in aspirate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Antacid Fasting</td>
</tr>
<tr>
<td>Pretreatment</td>
<td>Total organisms</td>
<td>3.3 ± 2.2</td>
</tr>
<tr>
<td></td>
<td>Viridans streptococci</td>
<td>1.5 ± 2.4</td>
</tr>
<tr>
<td></td>
<td><em>Neisseria</em> ssp.</td>
<td>0.6 ± 1.8</td>
</tr>
<tr>
<td></td>
<td><em>Candida</em> ssp.</td>
<td>1.5 ± 1.9</td>
</tr>
<tr>
<td></td>
<td><em>Lactobacillus</em> ssp.</td>
<td>3.0 ± 2.4</td>
</tr>
<tr>
<td>4 weeks</td>
<td>Total organisms</td>
<td>2.7 ± 1.6</td>
</tr>
<tr>
<td></td>
<td>Viridans streptococci</td>
<td>1.0 ± 1.7</td>
</tr>
<tr>
<td></td>
<td><em>Neisseria</em> ssp.</td>
<td>0.6 ± 1.7</td>
</tr>
<tr>
<td></td>
<td><em>Candida</em> ssp.</td>
<td>0.9 ± 0.9</td>
</tr>
<tr>
<td></td>
<td><em>Lactobacillus</em> ssp.</td>
<td>1.8 ± 2.0</td>
</tr>
<tr>
<td>8 weeks</td>
<td>Total organisms</td>
<td>3.5 ± 1.9</td>
</tr>
<tr>
<td></td>
<td>Viridans streptococci</td>
<td>2.3 ± 2.3</td>
</tr>
<tr>
<td></td>
<td><em>Neisseria</em> ssp.</td>
<td>1.9 ± 2.4</td>
</tr>
<tr>
<td></td>
<td><em>Candida</em> ssp.</td>
<td>0.5 ± 0.6</td>
</tr>
<tr>
<td></td>
<td><em>Lactobacillus</em> ssp.</td>
<td>2.3 ± 2.0</td>
</tr>
<tr>
<td>16 weeks</td>
<td>Total organisms</td>
<td>3.7 ± 1.9</td>
</tr>
<tr>
<td></td>
<td>Viridans streptococci</td>
<td>2.5 ± 2.5</td>
</tr>
<tr>
<td></td>
<td><em>Neisseria</em> ssp.</td>
<td>2.5 ± 2.3</td>
</tr>
<tr>
<td></td>
<td><em>Candida</em> ssp.</td>
<td>0.5 ± 0.9</td>
</tr>
<tr>
<td></td>
<td><em>Lactobacillus</em> ssp.</td>
<td>2.2 ± 1.6</td>
</tr>
</tbody>
</table>
Neisseria spp. were significantly higher in the cimetidine group \((P < 0.05, \text{ by the rank sum test)}\).

**Nitrate reductase activity.** Nitrate reducing organisms such as staphylococci, Enterobacteriaceae, and Veillonella spp. were unusual isolates in this study. Only occasional isolates of viridans streptococci, Neisseria spp., Lactobacillus spp., and Candida spp. were found to reduce nitrates. There were no differences in isolation of nitrate reducers between the cimetidine and antacid groups.

**DISCUSSION**

The data from this study show that postprandial microbial titers in gastric aspirates were significantly higher in subjects receiving either antacid or cimetidine as compared with postprandial titers before starting antacid or cimetidine regimens. This effect was significant at 4, 8, and 16 weeks with antacid, but only at 4 weeks with cimetidine. The higher titers were primarily related to increases in viridans streptococci and Neisseria spp.

Although not significant, there was a tendency for fasting microbial titers to be higher in subjects receiving cimetidine (but not antacids) as compared with fasting titers before starting antacid or cimetidine regimens. The higher titers were primarily related to increases in Neisseria spp.

These data can best be explained by the fact that antacid taken at night would not be expected to have any buffering effect in a fasting specimen taken the next morning. Whereas the effect of postprandial antacid on the postprandial specimen (antacid taken 1 h after the meal which was 1 h before the aspirate) would be major. With higher pHs, higher bacterial titers would be expected. In contrast, cimetidine taken the night before might have a slight residual effect on raising fasting gastric pH the next morning, approximately 10 h later. The inhibition of secretion of gastric acid by cimetidine loses clinical effectiveness at 5 to 7 h after an oral dose (5), and with lower pHs, lower bacterial titers would be expected. However, cimetidine taken 2 h before the aspirate (as for the 4-week postprandial aspirate) would have a major effect on raising pH.

Therefore, both antacid and cimetidine had significant effects in raising microbial titers. Furthermore, there were no significant differences in total titers or types of organisms present between subjects receiving antacid or cimetidine. However, fasting titers of viridans streptococci were significantly higher in the cimetidine group than in the antacid group at 4 weeks, and fasting titers of Neisseria spp. were higher in the cimetidine group than in the antacid group at 8 weeks.

As in previous studies (3, 7–9, 16), the numbers of organisms present in the gastric secretions correlated directly with the gastric pH. In both the antacid and cimetidine groups, a significant blunting of the normal postprandial fall in pH occurred during therapy and was most marked at 4 weeks. This was associated with higher postprandial titers of organisms isolated in both groups.

There have been three previously reported studies on the effect of cimetidine on bacterial flora (14–16). Ruddell et al. (16) studied patients with peptic ulcers who were given 1 g of cimetidine daily for 1 month, whereas Muscroft et al. (14, 15) studied healthy volunteers and duodenal ulcer patients who received 1 g of cimetidine daily in divided doses or a single 400-mg nighttime dose. The gastric aspirate was obtained 3 to 4 h after a first morning 200-mg cimetidine dose in the study by Ruddell et al. (16), and the relationship of the aspirate to food ingestion was not specified.

After a month of cimetidine the total microbial count in gastric juice rose from a mean of 1.8 to 4.6 \(\log_{10}\) CFU/ml in the study of Ruddell et al. (16). Muscroft et al. found no increase in morning fasting or postprandial bacterial titers in volunteers receiving either 1 g of cimetidine daily or 400 mg nightly (15); however, fasting titers were elevated in duodenal ulcer patients receiving either 1 g of cimetidine daily or 400 mg nightly (14). In the present study, after 4 weeks of cimetidine, fasting titers were not significantly higher than pretreatment titers. However, postprandial titers were higher than pretreatment titers (5.1 as compared with 2.6 \(\log_{10}\) CFU/ml). The studies are not strictly comparable because of differences of timing in relationship to cimetidine dosage, differences in size of cimetidine dosage, differences in relationship of aspirates to eating, and differences in patient population (i.e., peptic ulcer patients versus healthy volunteers).

Giannella et al. (7) reported mean total bacterial titers of 3.4 \(\log_{10}\) CFU/ml in fasting aspirates of normal subjects which is similar to the 3.3 to 3.8 \(\log_{10}\) CFU/ml found in the pretreatment fasting aspirates in the present study. The bacteria isolated were also similar to those in the present study with Enterobacteriaceae as unusual isolates. In contrast, in patients with hypochlorhydria (basal gastric pH > 6.0) or with pernicious anemia, mean titers of total organisms were over 7.0 \(\log_{10}\) CFU/ml with mean titers of Enterobacteriaceae over 4.0 \(\log_{10}\) CFU/ml. Others (3, 7, 9) have also demonstrated that achlorhydric patients have high titers of bacteria including Enterobacteriaceae in gastric aspirates.
rates. It is apparent that patients receiving cimetidine are not comparable to patients with perni-
cious anemia or with hypochlorhydria. Both the
pH and titers of bacteria in gastric juice were
much higher in these patients than in the groups
receiving cimetidine studied by Ruddell et al. (16), Muscroft et al. (14, 15), or in the present
report. In all of these studies, Enterobacteri-
ceae and anaerobes were unusual isolates. How-
ever, the enterococci commonly isolated by
Ruddell et al. and Muscroft et al. were not
isolated in the present study.

The major organisms isolated in the present
study were Candida spp., Aspergillus spp., viri-
dans streptococci, Neisseria spp., and Lactoba-
cillus spp. These organisms were similar to
those isolated in previous studies of gastric flora
in normal individuals (8). The postprandial rise
in total titers of organisms that occurred in both
groups during the study were mainly secondary
to rises in titers of viridans streptococci and
Neisseria spp. This suggests that the rise in
organism titers was related to better survival of
swallowed organisms normally found in the oro-
pharynx.

Ruddell et al. (16), studying gastric aspirates
in peptic ulcer patients, found a significant rise
in numbers of enterococci and unspecified nit-
rate-reducing organisms in gastric aspirates af-
after a month of cimetidine as compared with
before cimetidine. They noted a rise in “fetal
organisms” in patients receiving cimetidine, ap-
parently referring to the enterococci as the fetal
organisms. Similarly, Muscroft et al. (14, 15)
found enterococci to be the most common bacte-
ria isolated (after excluding lactobacilli). The
lack of enterococci in the present study may be
due to differences in populations (e.g., Great
Britain versus the United States).

Nitrate, which are produced by nitrate-re-
ducing bacteria from dietary and salivary nit-
trate, can be further converted to nitrosamines
(10, 11, 17, 18). However, the low titers of
nitrate-reducing organisms isolated in the pre-
sent study suggests little difference in nitrite
concentrations between treatment and pretreat-
ment aspirates and between cimetidine or antac-
id regimens. This study has shown that cimetidine or antac-
ids per se do not result in major changes in the
microbial flora of the stomach in healthy volun-
tees. Furthermore, microbial titers in gastric
juice of those receiving cimetidine did not differ
from those receiving antacids with only two
exceptions: titers of viridans streptococci at 4
weeks and Neisseria spp. at 8 weeks were
significantly higher in fasting volunteers receiv-
ing cimetidine than in fasting volunteers receiv-
ing antacids.

The lack of striking effect of cimetidine is
probably related to two factors. First, the gastric
pH and not the total gastric acid secretion was
measured. Cimetidine reduces both acid produc-
tion and volume of gastric juice (1, 5), but the pH
may not be markedly elevated (i.e., a small
amount of acid in a small volume may result in a
low pH). Bacterial survival is probably related
much more to pH than to the amount of acid
produced. Second, subjects were receiving ci-
metidine 10 h before the fasting aspiration of
gastric contents, and the effect of cimetidine is
mainly lost by this time (5). Although differences
in microbial flora may possibly be more marked
at other time periods after cimetidine (e.g., 3 to 4
h), it is clear that in healthy volunteers there are
no sustained major differences during a 24-h
period.

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