Gastric Acidity in Older Adults

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Context.—Early studies suggested that gastric acidity declines as people age. However, sequelae of achlorhydria are uncommon in older people, making this conventional wisdom unlikely.

Objective.—To ascertain the prevalence of basal gastric acidity and atrophic gastritis (indicated by serum pepsinogen ratio) in older adults.

Design.—Cross-sectional study in a volunteer sample.

Setting.—Retirement communities in suburbs of Kansas City, Mo.

Subjects.—A total of 248 white male and female volunteers aged 65 years or older living independently.

Main Outcome Measures.—Presence of basal unstimulated gastric acid was evaluated noninvasively by having subjects swallow quininium resin. Gastric acid with a pH lower than 3.5 releases quinine, which is then absorbed and excreted into urine. Atrophic gastritis was defined as a ratio of serum pepsinogen I/pepsinogen II of less than 2.9.

Results.—Basal unstimulated gastric content was acidic (pH <3.5) in 208 (84%) of 248 elderly subjects. On retesting 66 subjects (35 normals and 31 hyposecretors), 28 (80%) of 35 had pH less than 3.5 both times, and 22 (71%) of 31 had pH of 3.5 or higher twice; in the remaining 16 subjects, low vs high gastric pH changed between tests. Weighted population prevalence estimates in this sample were 67% for consistent acid secretion, 22% for intermittent secretion, and 11% for consistent gastric pH higher than 3.5. Whereas 14 (67%) of 21 consistent hyposecretors had serum pepsinogen ratios of less than 2.9, indicating atrophic gastritis, only 2 (5%) of 44 consistent or intermittent secretors of acid had ratios in this range (P<.001).

Conclusions.—In contrast to what is commonly stated, nearly 90% of elderly people in this study were able to acidify gastric contents, even in the basal, unstimulated state. Of those who were consistent hyposecretors of acid, most had serum markers of atrophic gastritis.

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GASTRIC ACID is needed to suppress bacterial growth and for absorption of some drugs and nutrients.1-4 While numerous studies, mainly in people with gastrointestinal symptoms, have demonstrated impaired acid secretion in the elderly,5 age-related achlorhydria has not been found in small cohorts of disease-free subjects.6-10 Colonization by enteric pathogens or malabsorption of drugs and nutrients, sequelae of hypacidity readily shown in other populations with achlorhydria, have not been reported in the aged. This led us to suspect that achlorhydria may not be as common as believed. We chose to ascertain the prevalence of basal gastric hypacidity in a group of older adults with typical health problems and assessed acidity before breakfast, when many would ordinarily take their medications.

For editorial comment see p 681.

METHODS

Participants

Unpaid volunteers were recruited by means of notices and group presentations from the independently living populations of 2 retirement communities in suburban Kansas City, Mo, from May 1991 through September 1993. Of 258 volunteers who chose to participate and were aged 65 years or older, 10 were excluded for the following reasons: prior gastric surgery or omeprazole ingestion (n=3); inability to postpone morning medications (n=1); renal insufficiency or urinary incontinence (n=2); drug allergy (n=2); and ingestion of quinine or quinidine, which would have interfered with the study (n=2). We studied 73 men (mean ±SD age, 78.8 [5.4] years; range, 65-91 years) and 175 women (mean ±SD age, 79.5 [6.34] years; range, 66-96 years); all but 1 were white. Men and women had mean (±SD) weights of 76.4 (11.8) kg and 61.8 (10.5) kg, respectively. Mean (±SD) blood hemoglobin (140.0±10.1 g/L), serum creatinine (100.8±19.5 μmol/L [1.14±0.22 mg/dL]), and albumin (40.2±2.4 g/L [4.2±0.24 g/dL]) levels were normal. A total of 219 (88%) of 248 volunteers reported at least 1 illness, and 225 (91%) of 248 were taking medication (Table 1). The study protocol and consent forms, signed by all volunteers, had been approved by the institutions' human subjects committees.
Gastric Acid

Tubeless gastric analysis with quinininium or azure-A resin had been validated and extensively used in the 1950s.11 We prepared quinininium resin by mixing 100 g of IRP-64 carboxyl cation-exchange resin (Rohm and Haas, Philadelphia, Pa) with a solution containing 2 g of quinine sulfate. After repeated water washes the resin was dried and stored in 2-g aliquots. Titration of 2 g of this resin with hydrochloric acid resulted in maximum release of 48 mg of quinine at pH 2.0. Since 0.3% to 1.5% of released quinine is normally excreted in urine in 2 hours,8 and renal excretion of quinine is reduced by 30% in the elderly overall,12 the lower limit for urine quinine within 2 hours of swallowing 2 g of the resin was calculated to be 90 μg.

After fasting overnight and withholding all morning medications, subjects swallowed a slurry of 2 g of quinininium resin in 120 mL of water. At gastric pH lower than 3.5—the negative logarithm of the acid ionization constant (pKₐ) of the resin—acid displaces the quinine, which is then absorbed systemically and excreted in urine. Without acid, the marker remains bound to resin and little is absorbed, and the total urine quinine in 2 hours remains less than 90 μg. With preresin urine as blank, quinine was determined fluorometrically in a photomultiplier fluoromicrophotometer (American Instrument Co, Silver Spring, Md).13

To validate the use of quinininium resin in this population, a pH radiotelemetry capsule (7 mm in diameter by 20 mm in length) (Heidelberg Inc, Norcross, Ga) was used for direct measurement of gastric acidity.8,14,15 Subjects lying in a semirecumbent position swallowed untethered capsules with the resin slurry. Signals reflecting gastric pH were transmitted, detected by a belt antenna over the abdomen, and recorded on a strip chart. The lowest consistent pH in the next 2 hours indicated maximal basal acidity (Figure 1).

Atrophic Gastritis

Pepsinogen I (PGI) and pepsinogen II (PGII) in serum was measured by radioimmunoassay.16 A serum PGI/PGII ratio less than 2.9 indicated atrophic gastritis; PGII less than 20 μg/mL indicated severe atrophy.17

Bacterial Overgrowth

Breath hydrogen after glucose ingestion served as a marker for intestinal bacterial overgrowth.18,19 After an overnight fast, nondiabetic volunteers removed dentures, rinsed their mouths with chlorhexidine, and ingested glucose, 80 g in 300 mL of water. Serial breath samples were assayed for hydrogen in a gas chromatograph (QuinTron Instrument Co, Model 121 microlyzer, Milwaukee, Wis). Two consecutive values exceeding 20 ppm of hydrogen were considered positive.

Statistical Analysis

A necessary sample size of 246 was calculated to obtain an estimate of population prevalence within ±0.05 of the true value, with α=.05 and an estimated population prevalence of 0.20.20 Data for continuous variables are presented as mean±SD. Categorical variables are presented as percentages. Groups were compared by t test or analysis of variance and the Newman-Keul procedure for continuous variables, and results were confirmed using the Scheffe test. For categorical variables, groups were compared by the χ² test. P values (2-tailed) less than .05 were considered statistically significant.

RESULTS

Of 248 subjects, 208 (84%) excreted more than 90 μg of quinine in urine, consistent with gastric secretion to pH lower than 3.5. Hyposecretors (n=40) did not differ from normal secretors in numbers or categories of diagnoses or medications. Of 40 subjects with hyposecretion on initial study, 31 (78%) agreed to repeat the study; 35 normal acid secretors also agreed to a second study. Restudied subjects differed from the total population only in having more men. Though the second resin study most often corroborated prior results, 7 (20%) of 35 who initially secreted acid were hyposecretors on a repeat study; 9 (29%) of 31 hyposecretors in the first study secreted acid on a repeat study. Extrapolating these findings to the entire study population, 67% would secrete acid in 2 studies, 22% would be intermittent hyposecretors (hyposecretion in 1 of 2 studies), and only 11% would have 2 tests consistent with basal gastric hyposecretion. With the second resin

Figure 1.—Effect of gastric pH on excretion of quinine from resin. Urine was collected for 2 hours after the patient swallowed a suspension of 2 g of quinininium resin in water together with a radiotelemetry capsule to measure gastric pH. Relationship of gastric pH to atrophic gastritis (low serum pepsinogen ratios) is shown for each subject. The lower left box represents false-positive hyposecretors; the upper right box represents false-negative hyposecretors.

Figure 2.—Distribution of gastric hypoacidity and abnormal serum pepsinogen ratios. Acidity (pH ≤3.5) was indicated by excretion of more than 90 μg of quinine into urine within 2 hours after the patient swallowed 2 g of quinininium resin. A low ratio of serum pepsinogens (pepsinogen I/pepsinogen II ≤2.9) indicated atrophic gastritis.
study, 58 (88%) of the 66 subjects swallowed radiotelemetry capsules for direct measurement of gastric pH. Only 1 (5%) of 21 subjects with gastric pH of 3.5 or higher eliminated more than 90 µg of quinine (sensitivity of 95%), while 30 (81%) of 37 with pH lower than 3.5 excreted this amount of quinine (specificity of 81%) (Figure 1).

Serum pepsinogen levels were measured in 243 of the subjects. Prevalence of hypochlorhydria was not different between the 243 and the entire sample of 248 (Table 2). Of 204 with normal gastric acid by resin test, only 5 (2%) had a PGI/PGII ratio of less than 2.9, indicating atrophic gastritis; evidence of atrophic gastritis was found in 17 (44%) of 39 hyposecretors ($P<.001$). Among subjects who were studied twice, 95% of those secreting acid in at least 1 resin study had normal serum PG levels; ratios of PGII/PGII were abnormally low in two thirds of those who did not secrete acid either time ($P<.001$). Only 1 (3%) of 37 proven acid secretors (gastric pH lower than 3.5 by radiotelemetry) had a PGI/PGII ratio of less than 2.9 (Figure 1); 14 (67%) of 21 subjects with measured pH higher than 3.5 had PGI/PGII ratios of less than 2.9 ($P<.001$ compared with normal secretors). In 11 (5%) of 243, PGI was less than 20 µg/L, indicating severe atrophic gastritis. The mean PGI/PGII ratio in these 11 was 0.94, much less than 2.9.

There was no age-related increase in achlorhydria (by quininum resin test) or in atrophic gastritis (by ratio of PGI/PGII) in subjects older than 65 years (Figure 2).

Abnormal breath study findings suggesting bacterial overgrowth (more than 20 ppm of hydrogen after glucose ingestion) were detected in only 4 (2.9%) of 138 subjects studied. (None of the 4 was taking H₂ blockers or antacids.) Neither quininium resin test nor serum PG indicated achlorhydria or atrophic gastritis in any of these 4 subjects. Since the prevalence of abnormal breath hydrogen was so low, and no correlation could be shown between gastric acid and breath hydrogen in this subgroup, breath hydrogen was not measured in the remaining subjects.

In these analyses we did not exclude subjects taking histamine H₂-receptor antagonists. Of 17 subjects taking these agents, 13 had low pH after remaining drug-free overnight. If the other 4 were actually acid secretors with persistent pharmacological suppression, the corrected prevalence of hypochlorhydria would be 36 (15%) of 245. In subjects not taking H₂ antagonists the prevalence of hypochlorhydria was 36 (16%) of 231, the same as in our entire population.

**COMMENT**

In their 1993 monograph, *Chronic Gastritis and Hypochlorhydria in the Elderly*, Holt and Russell state that "gastric hypo- and achlorhydria occurred commonly in elderly."21 In the past 7 decades numerous studies have reinforced this belief that "changes in the function of the gastrointestinal tract in old age include a reduction in gastric parietal cell function, leading to impaired acid secretion and an elevation in gastric pH."22 In contrast to other studies of gastric acid that selected subjects with gastrointestinal symptoms or specifically excluded subjects with concomitant illnesses,23,24 we enrolled elderly men and women with the spectrum of disease found in this population.

All resin tests were performed in the morning in fasting subjects in the basal unstimulated state, when gastric secretion is lowest.25-27 Despite these conservative conditions, under which some normal younger people secrete no acid,25-27 we found only 16% of our older population to be hyposecretors of acid. This is similar to the prevalence of basal acid secretion in 91 healthy young men and women (mean age, 30 years), which is slightly more than 14%.28 Fasting pH has been shown to be "a sensitive method for diagnosing bona fide hypochlorhydria," with upper 95% confidence limits more than 5.09 for men and 6.81 for women.28 The resin test, which identifies gastric pH higher than 3.5, would thus detect true hypochlorhydria. Basal gastric acid may be secreted intermittently in repeated studies of normal persons,29 and resting acid secretion in the same person may vary from day to day by more than 100%.14 On repeat study nearly one third (9 of 31) of our elderly subjects who had been initial hyposecretors were secreting acid, suggesting intermittent basal, unstimulated achlorhydria. Since such intermittent hyposecretors are capable of secreting acid, they do not have true achlorhydria. Extrapolating from subjects who underwent repeated studies, the prevalence of achlorhydria in our population does not exceed 11%. This does not differ from younger people15 and does not increase with subjects older than 65 years (Figure 2).

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**Table 1.** Self-reported Diseases and Medications of Study Population (N=248)*

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Cardiovascular</td>
<td>99 (40)</td>
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<tr>
<td>Hypertension</td>
<td>50 (20)</td>
</tr>
<tr>
<td>Arteriosclerosis</td>
<td>24 (10)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>14 (6)</td>
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<tr>
<td>Musculoskeletal</td>
<td>83 (33)</td>
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<tr>
<td>Arthritis</td>
<td>65 (26)</td>
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<tr>
<td>Endocrine/metabolic</td>
<td>41 (17)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>19 (8)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>71 (29)</td>
</tr>
<tr>
<td>Hialt hernia</td>
<td>14 (6)</td>
</tr>
<tr>
<td>Ulcers</td>
<td>13 (5)</td>
</tr>
<tr>
<td>Diverticula</td>
<td>12 (5)</td>
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</table>

<table>
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<tr>
<th>Medication</th>
<th>No. (%)</th>
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<tr>
<td>Aspirin</td>
<td>72 (29)</td>
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<tr>
<td>Diuretic</td>
<td>42 (17)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>40 (16)</td>
</tr>
<tr>
<td>Antacid</td>
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</tr>
<tr>
<td>Thyroxine</td>
<td>34 (14)</td>
</tr>
<tr>
<td>NSAID</td>
<td>31 (12)</td>
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<tr>
<td>β-Blocker</td>
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<td>Estrogen</td>
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<tr>
<td>ACE inhibitor</td>
<td>25 (10)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>19 (8)</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>18 (7)</td>
</tr>
<tr>
<td>H₂-receptor antagonist</td>
<td>17 (7)</td>
</tr>
</tbody>
</table>

*NSAID indicates nonsteroidal anti-inflammatory drug; and ACE, angiotensin-converting enzyme.

**Table 2.** Gastric pH* and Relation to Gastritis†

<table>
<thead>
<tr>
<th>Study Characteristics</th>
<th>No. (%)</th>
<th>Atrophic Gastritis, No. (%)†</th>
<th>Pepsinogen II Ratio‡</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Total sample</td>
<td>243 (100)</td>
<td>221 (91)</td>
<td>22 (9)</td>
</tr>
<tr>
<td>Normal acid secretion</td>
<td>204 (84)</td>
<td>199 (98)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Low acid secretion</td>
<td>39 (16)</td>
<td>22 (56)</td>
<td>17 (44)§</td>
</tr>
</tbody>
</table>

*Defined by urine quinine 2 hours after resin; normal >90 µg.
†Gastritis determined by ratio of pepsinogen II; low ratio (≤2.9) denotes atrophic gastritis.
‡Continuous data are expressed as mean (SD).
§$P<.001$ compared with normal acid secretors.

Ellipses indicate not applicable. Percentages for the 2-resin study are extrapolated to entire population sample (243). Of the 204 acid secretors in the first resin study, 35 were studied a second time. Twenty-eight of these 35 had gastric acid in both resin studies. Therefore, the prevalence of normal (2-time) acid secretions is 204(243)×(28/35)×67%. Thirty of the 39 with one resin test showed high gastric pH were similarly restudied. Twenty-one of these had low acidity in both studies. Therefore, the prevalence of consistent (2-time) hyposecretion is 39(243)×(21/30)×11%. Intermittent secretors of acid (pH=3.5 in 1 of 2 studies) account for 22% of the total population sample.

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Some earlier gastric studies were done in regions with higher prevalence of gastritis, such as Scandinavia, where fully half of asymptomatic people aged 20 to 65 years had endoscopically proven chronic atrophic gastritis. 30 In Australian men older than 64 years, atrophic gastritis was so common as to be considered part of normal aging. 31 A reduced ratio of PG I/PGII, indicating atrophic gastritis, 17 22 34 was found in only 9% of our subjects. As expected, we found a higher prevalence (14% [67%] of 21) of atrophic gastritis in consistent hyposecretors of acid. Consistent and intermittent secretors of acid had identical normal levels of PG. As with achlorhydria, prevalence of atrophic gastritis in our population was less than that in a prior US study. 35

We found no evidence for overgrowth by gram-negative or anaerobic bacteria. Though sensitive for detecting such organisms, 18 19 breath hydrogen tests are inadequate for gram-positive organisms 36 37 found in achlorhydria. 20 We were unable to corroborate the claim that with dietary carbohydrate, "elderly subjects show an increased excretion of breath hydrogen due to greater bacterial exposure in the intestinal lumen." 41 Only 22 (9%) of 240 of our subjects had PG levels consistent with atrophic gastritis, a condition associated with Helicobacter pylori. Though we did not test for H pylori, 80% of people in the United States have been found to be seropositive by the age of 75 years. 18 19

We cannot explain the discrepancy between our findings and those of others regarding prevalence of gastric hypoacidity and atrophic gastritis in the aged. No reason was ascertained to account for self-selection of acid secretors into our samples, though there are several possibilities: perhaps our independently living subjects were healthier; existing regional differences might explain it; or maybe the prevalence of atrophic gastritis and achlorhydria has indeed fallen, as has prevalence of gastric cancer, 40 with which they are associated. Our findings demonstrate that gastric hypoacidity is not directly or predictably associated with aging. Sequelae of achlorhydria, including bacterial overgrowth or malabsorption of drugs, should not be expected in elderly white persons.

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References