Diet and Chronic Atrophic Gastritis: A Case-Control Study [1,2]

Elizabeth Fontham,[3] Diego Zavala,[3] Pelayo Correa,[3] Elsie Rodriguez,[3] Fred Hunter,[4] William Haenszel,[5] *and* Steven R. Tannenbaum[6]

ABSTRACT—A hospital-based case-control study of gastric cancer precursor lesions was conducted in a high-risk black population in southern Louisiana. Ninety-three subjects with biopsy-proved advanced chronic atrophic gastritis were compared to two control series: a gastroscopy clinic series and a general hospital-admission series. Dietary case-control differences indicated a protective effect associated with fruit and vegetable intake and with dietary vitamin C and a risk elevation associated with milk consumption. The protective effect associated with consumption of fruits, vegetables, and vitamin C is consistent with findings for gastric cancer and with the etiologic hypothesis of intragastric nitrosation. A twofold increased risk was associated with cigarette smoking. Gastric juice pH, NO_3^-, and NO_2^- were determined for subjects undergoing gastroscopy, and comparisons were made between this high-risk U.S. group and a Colombian population with a much greater magnitude of risk; the latter had higher NO_3^- and NO_2^- levels. An increase in pH was associated with increasing severity of gastric lesions. Levels of pH and NO_2^- concentration were significantly correlated ($P<.0005$); however, in Louisiana the large difference in NO_2^- concentration associated with pH elevation is not associated with histopathologic severity. Divergent trends with severity of lesions for NO_3^- concentration were seen in the two populations.—JNCI 1986; 76:621-627.

It has been postulated that gastric cancer is the end result of a series of carcinogenic stimuli manifested in clinico-pathologic terms by the CAG complex and that the continual formation of N-nitroso compounds over many years promotes this process (*1*). CAG is characterized histologically by loss of gastric glands and in its advanced stages is very frequently associated with IM. These lesions are very prevalent in populations at high risk of gastric cancer (*2*), and study of these lesions has the advantage of decreasing the interval between disease onset and environmental exposures, with particular reference to diet.

The black population of the metropolitan New Orleans area displays high incidence and mortality rates of cancer of the stomach when compared to their white counterparts. Similar racial differences are observed for the United States in general (*3*). A case-control study of advanced CAG in this population is the subject of this report.

MATERIALS AND METHODS

Persons scheduled for gastroscopy at the Louisiana State University Gastrointestinal Clinic of Charity Hospital of New Orleans were asked to participate in this study that began in June 1980. Over 80% of the persons attending the clinic are black. Because the elevated rates in Louisiana are confined to the black population, the analysis was limited to this subgroup. Three percent of the subjects approached refused to participate, and an additional 7% were unable to participate because of incomplete procedures. A total of 442 persons agreed to participate and were interviewed at the clinic.

Neither the interviewer nor the study subject was aware of the subject's diagnostic status. The interview schedule included questions on residential history, occupation, use of alcohol and tobacco, water supply, and diet. The diet section of the questionnaire was developed in conjunction with a Registered Dietician native to the area and familiar with local dietary practices. Detailed dietary questions dealt with usual monthly frequency of consumption of 59 food items. If the subject's eating habits had changed recently due to illness or symptoms, he or she was asked to report usual consumption prior to this change. Also included were questions regarding use of seasonings and use of certain medications. Indices of vitamin intake were calculated by summing the products of monthly consumption frequency and vitamin content of usual portion size over all food items. Usual portion size was obtained from the HANES I survey as described by Pickle and Hartman (*4*). The indices are based on consumption of dietary items only and do not include supplemental vitamin use. Units of measurement for retinol, carotenoids, and total vitamin A indices were in retinol equivalents and in milligrams for vitamin C.

Prior to gastroscopy, all patients fasted overnight. They were premedicated with diazepam and meperidine hydrochloride. An Olympus gastroscope was used to take 4 biopsy samples under direct vision: 2 from the antrum on the anterior and posterior walls near the incisura angularis and 2 from the corpus (anterior and posterior walls). In addition, any local lesion found was biopsied. The specimens were fixed in 10% buffered Formalin. Slides were made and stained with hematox-

ABBREVIATIONS USED: CI=confidence interval(s); CAG=chronic atrophic gastritis; IM=intestinal metaplasia; OR=odds ratio(s).

[1] Received May 21, 1985; revised October 29, 1985; accepted December 6, 1985.

[2] Supported by Public Health Service grants P01CA-28842 and P01CA-26731 from the Division of Extramural Activities, National Cancer Institute.

[3] Department of Pathology, Louisiana State University Medical Center, 1901 Perdido St., New Orleans, LA 70112.

[4] Department of Medicine, Louisiana State University Medical Center.

[5] Illinois Cancer Council, Chicago, IL 60603.

[6] Massachusetts Institute of Technology, Cambridge, MA 02139.

ylin and eosin, periodic acid-Schiff, and Alcian blue. Histologic diagnosis was made by the pathologist without previous knowledge of gastroscopic or clinical findings. Two pathologists of the Louisiana State University Medical Center read the slides independently, and infrequent discrepancies in histologic findings were resolved by mutual consultation and a third reading. Histologically, the specimens were classified as: normal, superficial gastritis, CAG with or without IM, and dysplasia, according to the categories described previously (*5*). Only patients with adequate histologic representation of antral and corporal tissue were selected as controls for statistical analysis. Gastritis is frequently confined to the antrum only, but the reverse, gastritis confined to the corpus only, has not been observed in our material except in cases of pernicious anemia, which were not part of this study. Persons without adequate biopsy material from the antrum, therefore, could be misclassified as "gastritis free" when in fact they are not. A total of 129 such persons were excluded. For the analysis, subjects with normal mucosa and superficial gastritis, based on antral biopsy, who had no history of ulcer served as controls (control group I). Persons with intestinal metaplasia and dysplasia comprised the case series. Persons with CAG uncomplicated by IM ($n=57$), considered an intermediate stage in the process, were excluded from the analysis in an effort to contrast cases and controls. This exclusion is necessary because the diagnosis of CAG, which ranges in spectrum from mild to severe, is subjective at the lower end of the spectrum based on interpretation of the degree of loss of glands from the mucosa. Inclusion of these subjects could therefore introduce a conservative bias in case-control contrasts. A total of 85 subjects were excluded from the study because their histopathology was either unrelated to study criteria (no CAG) or the lesion was too advanced, i.e., gastric carcinoma.

At the time of gastroscopy, a sample of gastric juice was collected and immediately frozen. The samples were later analyzed at the Massachusetts Institute of Technology, Department of Nutrition and Food Science. The pH was determined, and the nitrate and nitrite concentrations in the sample were measured by a modified Griess method (*6*).

Because of the likelihood of overmatching on diet by the use of a control group selected from persons referred for gastroscopy for potential gastrointestinal disorders, a second black control group was chosen (control group II). These comparison subjects did not undergo gastroscopy. They were interviewed at the same hospital during the same time period with the use of the same dietary questionnaire. They originally were randomly selected as age- (±5 yr), sex-, and race-matched controls from general hospital admissions in a case-control study of cancers of the lung, stomach, and pancreas. Patients whose admission diagnosis was chronic lung disease or smoking-related cancer were excluded as lung cancer controls; patients with ulcers of the stomach or duodenum were excluded as stomach cancer controls; and patients with cirrhosis of the liver were excluded as pancreas cancer controls. The major categories of admission diagnoses of this series included diseases of the circulatory system (37%), diseases of the skin and musculoskeletal systems (13.0%), diseases of the digestive system (11.1%), endocrine disorders (8.3%), and diseases of the respiratory system (7.4%).

Crude OR were computed to estimate relative risks, and chi-square tests of homogeneity were performed. When the data were stratified into multiple categories, the 1-degree-of-freedom chi-square test for linear trend was used (*7*). Logistic multiple regression analysis was performed on the data to adjust for covariates by means of the SAS LOGIST procedure (*8*). Means and standard errors were calculated for the results of the gastric juice pH analysis. Because gastric juice nitrate and nitrite were not normally distributed, transformed mean log estimates were computed. The SAS GLM procedure was used to determine covariance by age and sex and to test for statistical significance of differences in the transformed means by analysis of variance (*9*).

For intercountry comparisons of gastric juice parameters, data from an ongoing study in the southern Andes of Colombia (Nariño) are presented. The Nariño population is composed of poor, rural mestizos who are engaged in subsistence farming. The study is a longitudinal gastroscopic survey of the population.

RESULTS

Table 1 presents the age-sex distribution and mean age of cases and controls. The distribution of cases by sex was equal. Control group I had a lower proportion of males, and control group II a higher proportion of males. Cases were older than the clinic controls (group I) and younger than control group II, which was originally selected as an age-matched control group for cancer patients.

Table 2 presents the findings for food groups as well as specific dietary items for each of the 2 control groups separately. Only those foods that had significantly ($P<.05$) elevated or reduced crude OR for one or both

TABLE 1.—*Comparison of cases and controls by age and sex*

Ages	Cases		Controls			
			Group I		Group II	
	n	(%)	*n*	(%)	*n*	(%)
Males						
<40 yr	5	(10.9)	15	(48.4)	4	(6.5)
40-59 yr	26	(56.5)	8	(25.8)	25	(40.3)
>60 yr	15	(32.6)	8	(25.8)	33	(53.2)
Total	46	(100.0)	31	(100.0)	62	(100.0)
Mean (SE)	53.6	(2.0)	45.0	(3.3)	61.2	(1.6)
Females						
<40 yr	5	(10.6)	12	(25.5)	—	—
40-59 yr	19	(40.4)	25	(53.2)	19	(41.3)
>60 yr	23	(48.9)	10	(21.3)	27	(58.7)
Total	47	(100.0)	47	(100.0)	46	(100.0)
Mean (SE)	57.6	(1.8)	47.1	(2.1)	62.0	(1.5)

TABLE 2.—*Estimated relative risk of gastric cancer precursor lesions associated with above median consumption of food groups and individual food items*

Food	Control group I adjusted OR[a] (95% CI)	Control group II adjusted OR[a] (95% CI)
Groups		
Seafood and meats	2.49 (1.26-4.90)[b]	1.09 (0.68-1.98)
Fruits and vegetables	0.98 (0.51-1.88)	0.54 (0.30-0.99)[c]
Vitamin C index	1.02 (0.54-1.93)	0.40 (0.22-0.74)[b]
Items		
Milk	4.29 (1.36-13.54)[c]	7.66 (2.46-23.86)[d]
Bread	1.66 (0.62-4.43)	5.18 (1.37-19.52)[c]
Pork	1.40 (0.71-2.75)	1.85 (0.98-3.48)
Cold cuts	0.99 (0.52-1.90)	1.49 (0.83-2.67)
Merlitons	0.67 (0.35-1.28)	0.55 (0.31-0.99)[c]
Bananas	0.90 (0.47-1.92)	0.45 (0.25-0.81)[b]
Strawberries	0.57 (0.29-1.08)	0.51 (0.28-0.91)[c]
Lima beans	0.49 (0.25-0.97)[c]	1.00 (0.55-1.81)
Cake	0.63 (0.33-1.21)	0.72 (0.40-1.31)
Candy	0.55 (0.29-1.06)	0.88 (0.50-1.56)
Wild game	2.62 (1.31-5.24)[b]	1.33 (0.76-2.49)

[a] Adjusted for age (continuous) and sex.
[b] $P<.01$.
[c] $P<.05$.
[d] $P<.001$.

control groups are shown. In case-control comparisons with the use of controls from the gastroscopy clinic (control group I), three individual food items were associated with significantly decreased risk: cake, candy, and lima beans. After controlling for age and sex differences, only the OR for lima bean consumption remained significantly reduced. Two items, milk and wild game, were positively associated with risk. After adjustment for age and sex, the OR for above median consumption were 4.29 (1.36-13.54) for milk and 2.62 (1.31-5.24) for wild game. The only food group associated with risk of precursor lesions was the combined seafood and meat group, which significantly increased risk approximately 2.5-fold.

When cases were compared to the general hospital control series, control group II, a larger number of dietary items and food groups showed significant positive or negative associations with risk of precursor lesions. A number of fruits and vegetables were found to decrease risk of intestinal metaplasia and dysplasia. These items include bananas, strawberries, and merlitons, a local vegetable pear. As a group, total fruits and vegetables significantly reduced risk of advanced CAG, OR=0.54 (0.30-0.99). Indices of dietary intake of vitamins A and C, and carotenoids, micronutrients found primarily in fruits and vegetables, as well as retinol, were computed based on the frequency of consumption of food items and the vitamin content of each. Dietary vitamin C consumption significantly reduced risk of gastric cancer precursor lesions, OR=0.40 (0.22-0.74). The indices of dietary vitamin A, retinol, and carotenoids were suggestive of a protective effect, although not statistically significant. Crude estimates of risk indicated elevations for several types of meats; however, the positive associations for cold cuts and pork did not persist after adjustment for age and sex. Consumption of bread was positively associated with intestinal metaplasia and dysplasia.

Milk was the only individual food item found to be positively associated with precursor lesions, regardless of the control group selected. The adjusted relative risk of precursor lesions was estimated to be 7.66 (2.46-23.86) for heavy milk consumption when the hospital controls served as a case comparison.

An additional set of questions on the use of salt was asked of a small sample of the gastroscopy series ($n=87$). There was no difference between cases and controls on routine addition of salt at the table. Subjects were asked to classify total salt intake as light, moderate, or heavy. The relative risk for heavy salt use compared to light and moderate use was 3.13 (0.79-12.44) after adjustment for age and sex.

Table 3 displays the association of alcoholic and nonalcoholic beverage consumption with gastric cancer precursor risk by means of separate control group comparisons. A 2.5-fold increased risk of these lesions was associated with beer consumption and with total alcohol consumption for the clinic controls, group I. No such effect was noted for consumption of wine, or distilled spirits individually, or for traditional nonalcoholic beverages, including coffee, tea, and soft drinks. No significant case-control differences were found when the general hospital control series served as the comparison group.

Approximately 70% of the clinic study subjects were current cigarette smokers compared with approximately 50% of the hospital controls. Regardless of comparison

TABLE 3.—*Estimated relative risk of gastric cancer precursor lesions associated with above median beverage consumption*

Beverage	Control group I adjusted OR[a] (95% CI)	Control group II adjusted OR[a] (95% CI)
Alcohol, total	2.49 (1.22-5.08)[b]	0.99 (0.53-1.83)
Beer	2.55 (1.27-5.10)[c]	0.95 (0.52-1.70)
Wine	1.45 (0.65-3.22)	1.67 (0.81-3.44)
Distilled spirits	1.46 (0.73-2.90)	0.61 (0.33-1.12)
Coffee	0.92 (0.46-1.85)	0.63 (0.34-1.17)
Tea	0.99 (0.51-1.96)	0.65 (0.35-1.22)
Soft drinks	1.02 (0.52-2.0)	1.15 (0.47-2.85)

[a] Adjusted for age (continuous) and sex.
[b] $P<.05$.
[c] $P<.01$.

TABLE 4.—*Estimated relative risk of gastric cancer precursor lesions associated with pack-year history of cigarette smoking*

Specification	Pack-year category[a]					
	0	1	2	3	4	
Cases	16	10	16	21	24	
Control group I	22	22	14	11	7	$\chi^2_4 = 14.72$, $P<.01$
Adjusted OR[b]	1.0	0.89	1.90	2.50	4.44[c]	Test for trend:
95% CI	—	0.31-2.57	0.68-5.30	0.91-6.83	1.34-14.67	$\chi^2_1 = 13.52$, $P<.001$
	0	1	2	3	4	
Cases	16	16	18	21	16	
Control group II	30	18	18	15	18	$\chi^2_4 = 3.78$
Adjusted OR[b]	1.0	1.30	1.52	2.45	2.38	Test for trend:
95% CI	—	0.49-3.44	0.60-3.85	0.93-6.42	0.87-6.52	$\chi^2_1 = 2.24$

[a] 0=nonsmoker; 1=1-25% tile; 2=26-50% tile; 3=51-75% tile; 4=76-100% tile.
[b] Adjusted for age (continuous) and sex.
[c] $P<.05$.

group, a twofold elevated risk was noted for current, but not ex-, smokers, and this was statistically significant with the hospital control comparison, 2.29 (1.14-4.60). A positive trend of increasing risk with pack-year history of cigarette use was found to be significant ($P<.001$) for case-control comparison with the use of the clinic controls and of smaller magnitude with the hospital controls (table 4). Less than 10% of the study population ever smoked pipes or cigars.

Use of certain medications and dietary supplements was examined for possible etiologic associations. A large proportion (65%) of the clinic study population reported use of antacids, but the proportion was not significantly different in cases versus controls. Neither were there differences in vitamin supplementation, laxative use, use of cimetidine, or use of pain relievers.

Results of the analysis of gastric juice by histologic classification are presented in table 5. The results of the gastric juice analysis for a high-risk cohort currently being studied by the authors in Colombia are also presented, and the age- and sex-adjusted parameters from the two regions are compared. The distribution of values for both nitrate and nitrite were non-normal and accordingly transformed to common logarithms. The antilog of the mean log estimates and 95% CI are shown.

In Louisiana mean pH increased with increasing severity of the lesion, 5.0 for persons with dysplasia compared to 3.1 for persons with normal gastric mucosa. Nitrate levels were highest in persons with normal mucosa (254.8 μM) and decreased to a low of 118.3 μM in persons with dysplasia. Level of pH and concentration of nitrite were significantly correlated, $r=0.59$

TABLE 5.—*Mean[a] levels of gastric juice pH, nitrate, nitrite in two populations: New Orleans, Louisiana, and Nariño, Colombia*

Specification	Normal	Superficial gastritis	Intestinal metaplasia	Dysplasia
pH				
Louisiana	3.1	3.5	4.2[b]	5.0[b]
	(2.13, 4.13)	(2.83, 4.25)	(3.63, 4.83)	(3.92, 6.0)
Colombia	3.2	4.0	6.0[b]	7.0[b]
	(2.94, 3.42)	(3.64, 4.18)	(5.59, 6.26)	(6.55, 7.55)
Nitrate, μM				
Louisiana	254.79	185.10[c]	146.95[b]	118.25[b]
	(214.88, 302.12)	(120.39, 284.61)	(95.17, 226.91)	(58.41, 239.39)
Colombia	368.19	475.79[c]	554.03[b]	855.96[b]
	(310.51, 436.58)	(403.73, 560.70)	(435.73, 704.45)	(609.35, 1,202.40)
Nitrite, μM, pH<5.0				
Louisiana	1.16[b]	1.79[b]	1.29[b]	1.16
	(1.10, 1.21)	(1.51, 2.12)	(1.16, 1.44)	(0.84, 1.59)
Colombia	1.0[b]	1.05[b]	1.0[b]	1.05
	(0.99, 1.01)	(0.98, 1.12)	(0.93, 1.08)	(0.77, 1.44)
Nitrite, μM, pH ≥5.0				
Louisiana	—	4.72	4.08[b]	4.96
	—	(0.91, 24.33)	(1.70, 9.80)	(1.07, 23.06)
Colombia	6.92	8.71	14.91[b]	18.06
	(3.51, 13.64)	(5.33, 14.24)	(10.29, 21.62)	(9.77, 33.38)

[a] Adjusted for age and sex.
[b] Significant difference between regions, $P<.01$. *Numbers in parentheses* are 95% confidence limits.
[c] Significant difference between regions, $P<.05$.

($P<.0005$). There were only minimal differences in nitrite level by histopathology, but large differences in the nitrite concentration in gastric juice related to pH, above and below 5.

Relative comparisons within each area indicate a consistent finding of increasing pH with increasing severity of histopathology; however, the contrast in pH between persons with dysplasia and with normal mucosa is more striking in the Colombian population. Similarly, in both areas the nitrite levels are elevated in persons with elevated pH (≥5.0). In Colombia, but not in Louisiana, there is a nonsignificant trend of increasing nitrite concentration associated with severity of the lesion. In all histologic categories, nitrite levels are higher in Colombia than in Louisiana. Divergent findings for gastric juice nitrate concentration are seen. In New Orleans nitrate concentration decreases with increasing severity; in Colombia overall values in all categories are higher than in New Orleans, and the levels increase with the progression of the lesion. The values shown in the table are consistent with earlier published data on the Colombian population (*10*), but these values have been converted from parts per million to micromoles.

DISCUSSION

Two studies that utilized premalignant lesions of the gastric mucosa as a means of investigating the etiology of stomach cancer have been reported, one conducted in Colombia (*5*) and one in Japan (*11*). Both of these studies were designed as endoscopic surveys in populations at very high risk of stomach cancer. Gastroscopic examination and a dietary questionnaire were offered to apparently well volunteers who responded in large numbers, reflecting an awareness of stomach cancer as a leading cause of death. The findings of these two studies were consistent with established risk factors for gastric cancer, and each suggested a possible protective effect related to consumption of fruits and/or vegetables.

The present study was also designed to identify factors that influence the risk of gastric cancer prior to development of cancer by linking these factors to lesions that presumably are forerunners of invasive disease. It was of interest to determine whether the factors operating in populations with the highest rates for gastric cancer internationally were also determinants in a high-risk U.S. population where the risk is of much smaller magnitude. A population-based endoscopic survey was not feasible. Instead, persons with and without precursor lesions were identified from a group of individuals scheduled for diagnostic endoscopy at the gastroenterology service. The ideal control group would be a random sample of the general population, who upon gastroscopy and biopsy are found to be free of atrophic gastritis. However, risks associated with the diagnostic procedures precluded use of a population-based series of cases and controls and were balanced by use of persons scheduled by a physician to undergo these procedures. This group proved to be an excellent source of cases; approximately one-third of the persons undergoing gastroscopy had histologically confirmed atrophic gastritis. As noted, unlike endoscopic surveys in a representative sample of the population, our subjects were referrals for endoscopy and therefore selected on the basis of signs and/or symptoms related to the gastrointestinal system. Although our gastroscopy clinic controls (control group I) are known to be free of the precursor lesions, they have some abnormality resulting in gastrointestinal referral and as such do not represent the general population of persons free of these lesions, particularly with respect to diet. The persons comprising the second comparison series, control group II, were not referrals to the gastrointestinal clinic, did not undergo gastroscopy and biopsy, and therefore do not have histologic confirmation of their "disease-free" status. While a small proportion of these controls may actually have chronic atrophic gastritis, which would minimize case-control differences, this group provides a more meaningful comparison for a number of life-style parameters, particularly with regard to diet because these controls were hospitalized with a broad range of conditions not related to diet. We were not able to compare levels of pH, nitrate, and nitrite in cases and control group II because no gastric juice could be obtained. Hence, while neither control group I nor II provides the ideal comparison series, each contributes relevant contrasts.

The case-control comparisons utilizing the general hospital admission control series show a protective effect associated with the fruit and vegetable food group as well as dietary vitamin C. These findings are consistent with both the findings of numerous studies that have demonstrated the positive association between gastric cancer risk and diets deficient in fresh fruits and vegetables (*12–15*) as well as with the two reported studies of gastric cancer precursor lesions (*5, 9*). The findings also give support to the hypothesis of intragastric nitrosation as a source of carcinogens. This step has been shown to be effectively blocked by vitamin C (*16*). Multiple comparisons were made, increasing the probability of a statistically significant result due to chance alone. For example, the diet section contained 59 food items. However, a number of dietary factors were selected a priori because of previous work on stomach cancer and precursor lesions, and these include fruits, vegetables, and dietary vitamin C.

The risk elevation associated with milk consumption in our series runs contrary to findings of case-control studies of gastric cancer in Japan that indicate a protective effect of milk (*17*). The positive association in our study with milk consumption may well reflect its use to relieve symptoms of gastric discomfort. This is consistent with findings of Modan et al. (*18*) who reported no long-term differences in milk consumption between gastric cancer patients and controls, but they did find higher recent consumption of milk by cases presumably related to a change in diet after symptom onset. The elevated risk associated with bread consumption may also reflect its consumption to relieve symptoms of gastric discomfort or may be related to the high sodium content of breads. We examined the starches as a

group composed of rice, potatoes, corn, noodles (pasta), cereals, bread, and cornbread, but we found no increased risk associated with total intake using either control group as a comparison, unlike Modan et al. (*18*). Hence it seems unlikely that in this population the increased risk associated with bread intake is related solely to its starch content.

The finding of a twofold increased risk of gastric cancer precursor lesions among cigarette smokers is similar to risk estimates from both prospective and retrospective studies of gastric cancer (*14, 19-20*). Because no consistent dose response has been found in these studies, the etiologic significance is unclear. In the present study a strong trend is seen when cases and clinic controls are compared, but not when hospital controls serve as the comparison. Recent changes in smoking habits related to disease symptoms are unlikely to account for the elevated risks with pack-year consumption in the clinic series. The composition of the second control group, which included a large proportion of subjects with smoking-related diseases such as coronary heart disease and stroke, may have minimized case-control differences. It may be that the findings for both smoking and salt use, each associated with increased risk of CAG, are related to their roles as irritants of the gastric mucosa and stimulators of gastric secretion. Irritants, while ubiquitous, are likely to differ from population to population. Thus the finding of increased risk of gastric cancer or its precursors associated with different irritants in different study populations is not surprising. Our finding of a threefold increase in risk associated with reported heavy salt consumption while not significant was suggestive of a possible role for salt in the development of chronic atrophic gastritis. Correlations between reported patterns of salt use and actual salt intake have been shown to be quite good ($r=.63$, $P<.001$) and strengthen the use of this crude estimate of salt intake (*21, 22*).

An interesting pattern emerges when comparisons are made between the gastric juice parameters of subjects from Nariño (Colombia) and New Orleans blacks. Both populations are at high risk of gastric cancer. The Nariño population under study displays one of the highest incidence rates, estimated at 150/100,000 (adjusted to world population) (*5*). The correspondent rate for New Orleans blacks is 22.4, considered high when compared to the New Orleans whites whose rate is 7.5 (*3*), but certainly not of the magnitude of the Colombian rates. In addition, the two populations differ greatly with respect to racial and cultural composition. The New Orleans population is black and urban, whereas the Colombian study subjects are primarily rural mestizos. Both groups represent the lower socioeconomic stratum that is at high risk worldwide, but the conditions of poverty in the two regions differ. Because diet is intimately related to gastric physiology and pathology and is diverse from culture to culture, differences in gastric juice chemistry are not unexpected. The gastric juice nitrite values are much higher in Nariño than in New Orleans blacks and may play a role in their much higher cancer rates. Gastric juice nitrite presumably results mostly from reduction of gastric juice nitrate, again present at substantially higher levels in the Nariño population than in New Orleans blacks. The gastric juice nitrate gradient, however, runs in different directions in the 2 populations. In Nariño more severe lesions display increasingly higher concentrations, whereas in New Orleans blacks the nitrate level decreases as the severity of lesions increases. The most probable explanation of this phenomenon is that the source of nitrates is different. In Nariño, nitrate comes mostly from drinking water and from grains and vegetable roots that have been associated with increased risk (*23*). In New Orleans, nitrate comes mostly from fresh fruits and fresh green, leafy vegetables, which apparently exert a protective effect (*24*). New Orleans blacks who eat less fruits and vegetables have a higher frequency of dysplasia, but the nitrate that reaches their stomachs is reduced to nitrite in greater proportion than in normal subjects, thereby increasing the potential formation of N-nitroso compounds. Nitrate in fresh fruits and vegetables is mixed with vitamin C and other protective factors, whereas nitrate in fava beans is mixed with mutagenic precursors of N-nitroso compounds (*25, 26*).

REFERENCES

(*1*) Correa P, Tannenbaum SR. The microecology of gastric cancer. In: Scanlan RS, Tannenbaum SR, eds. N-nitroso compounds. ACS symposium series 1174. Washington, DC: Am Chem Soc, 1981:319-329.

(*2*) Correa P. The gastric precancerous process. Cancer Surveys 1983; 2:437-450.

(*3*) Young JL Jr, Percy CL, Asire AJ, eds. Surveillance, epidemiology and end results: Incidence and mortality data: 1973-77. Natl Cancer Inst Monogr 1981; 57:1-1082.

(*4*) Pickle LW, Hartman AH. Indicator foods for vitamin A assessment. Nutr Cancer 1985; 7:3-23.

(*5*) Correa P, Cuello C, Duque E, et al. Gastric cancer in Colombia. III. Natural history of precursor lesions. J Natl Cancer Inst 1976; 57:1027-1035.

(*6*) Green LC, Wagner DA, Glogowski J, et al. Analysis of nitrate, nitrite and [^{15}N]nitrate in biologic fluids. Anal Biochem 1982; 126:131-138.

(*7*) Mantel N. Chi square tests with one-degree of freedom: Extensions of the Mantel-Haenszel procedure. J Am Stat Assoc 1963; 58:690-700.

(*8*) Harrell F. The LOGIST procedure. In: SAS supplemental library users' guide. 1979:83-102.

(*9*) The GLM procedure. In: SAS user's guide: Statistics. 1982: 139-199.

(*10*) Tannenbaum SR, Moran D, Rand W, et al. Gastric cancer in Colombia. IV. Nitrite and other ions in gastric contents of residents from a high-risk region. JNCI 1979; 62:9-12.

(*11*) Nomura A, Yamakawa H, Ishidate T, et al. Intestinal metaplasia in Japan: Association with diet. JNCI 1982; 68:401-405.

(*12*) Bjelke E. Epidemiologic studies of cancer of the stomach, colon, and rectum. Scand J Gastroenterol 1974; 9 (suppl 31):1-235.

(*13*) Graham S, Schotz W, Martino P. Alimentary factors in the epidemiology of gastric cancer. Cancer 1972; 30:927-938.

(*14*) Haenszel W, Kurihara M, Segi M, et al. Stomach cancer among Japanese in Hawaii. J Natl Cancer Inst 1972; 49:969-988.

(*15*) Joosens JV, Geboors J. Nutrition and gastric cancer. Nutr Cancer 1981; 2:250-261.

(*16*) Mirvish SS. The etiology of gastric cancer. JNCI 1983; 71: 629-647.

(*17*) Hirayama T. The epidemiology of cancer of the stomach in

Japan with special reference to the role of diet. Unio Intern Contre Cancrum Monogr 1967; 10:37-48.

(18) MODAN B, LUBIN F, BARELL V, et al. The role of starches in the etiology of gastric cancer. Cancer 1974; 34:2087-2092.

(19) KAHN HA. The Dorn study of smoking and mortality among U.S. veterans: Report on 8½ years of observation. Natl Cancer Inst Monogr 1966; 19:1-25.

(20) HAMMOND EC. Smoking in relation to the death rates of 1 million men and women. Natl Cancer Inst Monogr 1966; 19:127-204.

(21) KUMANYIKA S, ROE DA. Blood pressure and table salt use in black and white normotensive college males. Clin Res 1977; 25:329.

(22) KUMANYIKA S, JONES DY. Patterns of week to week table salt use by men and women consuming constant diets. Hum Nutr 1983; 37A:348-356.

(23) HAENSZEL W, CORREA P, CUELLO C, et al. Gastric cancer in Colombia. II. Case-control epidemiologic study of precursor lesions. J Natl Cancer Inst 1976; 57:1021-1026.

(24) Assembly of Life Sciences Committee. The health effects of nitrate, nitrite, and N-nitroso compounds. Washington, DC: National Acad Press, 1981:5.26-5.51.

(25) YANG D, TANNENBAUM SR, BUCHI G, et al. 4-Chloro-6-methoxy-indole is the precursor of a potent mutagen (4-chloro-6-methoxy-2-hydroxy-1-nitroso-indolin-3-one oxime) that forms during nitrosation of the fava bean (*Vicia faba*). Carcinogenesis 1984; 5:1219-1224.

(26) MONTES G, CUELLO C, CORREA P, et al. Mutagenic activity of nitrosated foods in an area of high risk for stomach cancer. Nutr Cancer 1984; 6:191-195.