RESEARCH COMMUNICATION

The Risk of Helicobacter Pylori Infection and Atrophic Gastritis from Food and Drink Intake: a Cross-sectional Study in Hokkaido, Japan

Yoshinori Ito[1], Koji Suzuki[1], Naohiro Ichino[1], Hideo Imai[2], Hiroshi Sakaguchi[2], Masaki Hokama[2], Masatoshi Nishii[2], Hiroshi Nakano[2]

Abstract

One-hundred and fifteen subjects were diagnosed with Helicobacter pylori (HP) infection and 93 subjects with atrophic gastritis (AG) from tests of HP antibodies or serum levels of pepsinogen I and pepsinogen II involving 210 inhabitants, who participated in the health check-up program. Logistic regression analysis found that refreshing (isotonic) beverages significantly reduced the risk of HP infection (odds ratio: 0.767, 95%C.I.: 0.616-0.956). A higher frequency of intake for margarine (odds ratio: 1.413, 95%C.I.: 1.080-1.848), cheese (odds ratio: 1.416, 95%C.I.: 1.044-1.920), Tsukemono (odds ratio: 1.277, 95%C.I.: 1.000-1.631) or Cola-beverages (odds ratio: 1.471, 95%C.I.: 1.051-1.239) showed a significantly increased risk of AG. In addition, high serum values of β-carotene (odds ratio: 0.691, 95%C.I.: 0.498-0.958), linoleic acid (odds ratio: 0.594, 95%C.I.: 0.382-0.924), and γ-linolenic acid (odds: 0.987, 95%C.I.: 0.976-0.998) were found to reduce the risk of AG, but not HP infection. Furthermore, these results suggest that a more frequent intake of margarine, Tsukemono (pickled vegetables), or Cola-beverages may be a risk factor for AG, while foods rich in carotenes, such as, β-carotene and n-6PUFAs, such as γ-linolenic acid, may reduce the risk of AG.

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Introduction

Recent studies have reported a close relationship between Helicobacter pylori (HP) infection and atrophic gastritis (AG), a precancerous condition of gastric cancer, and HP infection is a known risk factor of AG (Correa, 1983; Kato et al., 1992; Kuipers et al., 1995; Kawaguchi et al., 1996; Watanabe et al., 1997). The incidence of both HP infection and AG increase with age (Kawaguchi et al., 1996), and AG is prevalent in countries with a high incidence of HP infection (Tsugane et al., 1999). The morbidity of AG was previously determined by serological tests for low serum levels of pepsinogen I and low serum ratios of pepsinogen I and pepsinogen II in the general population (Miki et al., 1989; Kabuto et al., 1993).

Numerous epidemiological studies have shown that the intake of common Japanese foods such as Tsukemono (pickled vegetables) is a significant risk factor for gastric cancer (Hirayama, 1971; Haenszel, et al., 1976; Tajima and Tominaga, 1985; Kato et al., 1992), while the consumption of large quantities of fruit and vegetables is associated with a reduced risk of gastric cancer (Hirayama, 1971; Hirayama, 1975; Haenszel et al., 1976; Tajima and Tominaga, 1985; Correa et al., 1985; Ziegler, 1991; Kato et al., 1992; Kim et al., 1996). A large number of potentially anti-carcinogenic substances including carotenoids, which protect against reactive oxygen metabolites and enhance immune response are present in such foods (Bendich and Olsen, 1989; Bendich, 1990; Hwang et al., 1994). In addition, certain reports showed that HP-associated gastritis is related to a high content of polyunsaturated fatty acids in gastric mucosal (Wakabayashi et al., 1998) and that unsaturated fatty acids, such as oleic

[1]Departments of Public Health and Clinical Physiology, Fujita Health University School of Health Sciences, Toyoake, Japan
[2]Department of Internal Medicine, Fujita Health University School of Medicine, Toyoake, Japan Department of Public Health, Fujita Health University School of Health Sciences, Dengakugakubo, Kutsukake-cho, Toyoake City, Aichi Prefecture, 470-1192, Japan@ Fax: 81-562-93-9405, Email yoshiito@fujita-hu.ac. jp

acid, contribute to the inhibition of HP growth (Khulisi et al., 1995).

In the present study, we investigated whether the intake frequencies of some common Japanese foods and beverages are related to the risk of HP infection or AG in the general population in Hokkaido, Japan.

Subjects and Methods

Subjects

A total of 210 subjects (80 males and 130 females), living in a rural area of Hokkaido, Japan, were recruited from 986 residents who attended the health check-up program in August 1997. All subjects were over 40 years of age and worked primarily in fishing, dairy farming or commerce.

Trained health nurses administered a questionnaire on health and daily lifestyle including food intake at the time of the health examination. Inquiries about lifestyle habits included smoking (current smoker, former smoker, never smoked), alcohol consumption (regular drinker, occasional drinker, and non-drinker) and dietary intake of major foods and drinks. The habitual intake of major foods and drinks was classified by frequency into five categories: rarely, 1-2 times/month, 1-2 times/ week, 3-4 times/ week, and daily.

Methods

Fasting serum samples were taken at the time of the health check and the sera were separated from blood cells by centrifugation within one hour. Biochemical analysis of the sampled sera was performed using an autoanalyzer (JCA-RX20, Nihon Denshi Co. Ltd.).

Serum concentrations of b-carotene (BC), a-carotene (AC), lycopene (LY), cryptoxanthin (CR), zeaxanthin & lutein (ZL), retinol (RE), and a-tocopherol (AT) were measured separately by high-performance liquid chromatography (HPLC) as reported previously (Ito, et al., 1991). Serum values of total carotenoids were estimated the sum of BC, AC, LY, CR, ZL and canthaxanthin values. Serum values of thiobarbituric acid-reactive substance (TBARS) were determined using the thiobarbituric acid reaction method (Yagi, 1976). Serum values of NO and NO_3 were determined using an HPLC method (Green, et al., 1982), while those of fatty acids were separately determined using gas chromatography (Ozawa, et al., 1982). Serum concentrations of fatty acids were determined as follows: total saturated fatty acids (TSFAs) from the sum of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid and lignoceric acid values; monounsaturated fatty acids (MUFAs) from the sum of myristoleic acid, palmitoleic acid, oleic acid (OLA), isosenoic acid, ersinic acid and nervonic acid values; n-3 polyunsaturated fatty acids (n-3PUFAs) from the sum of linolenic acid (LLA), eicosapentaenoic acid (EPA), docosapentaenoic acid and docosahexaenoic acid (DHA) values; n-6 poly- unsaturated fatty acids (n-6PUFAs) from the sum of linoleic acid (LNA), g-linolenic acid (GLA), icosadienoic acid, dihomo-g-linolenic acid, arachidonic acid (ADA) and docosatetraenoic acid values; n-9 unsaturated fatty acids (n-9UFAs) from the sum of oleic acid, icosaenoic acid, icosatrienoic acid, ersinic acid and nervonic acid values; and total unsaturated fatty acids (TUFAs) from the sum of myristric acid, palmitoleic acid, n-3PUFAs, n-6PUFAs and n-9UFAs values.

Serum values of pepsinogen I (Pep I) and II (Pep II) were estimated using the Pepsinogen RIA Kit (Dainabot Co. Ltd.) based on the RIA method (Samloff et al., 1982) and the HP antibody was detected by the HP Determiner Kit (Kyowa Medics Co. Ltd.) based on the ELISA method (Evans et al., 1989). AG was serologically diagnosed using the serum cut-off values of PepÅÖ 70 ng /ml and Pep I/ Pep II ratio ÅÖ3.0 (Kabuto et al., 1993). HP infection (HP-antibody positive) was diagnosed using the serum cut-off values of HP antibody ÅÜ2.3 ELISA Value (EV) (Tani et al., 1997).

All statistical analyses were performed using a logistic regression analysis (statistical package: StatView 5.0, Power Macintosh) after controlling for gender, age, and lifestyle habits, smoking and alcohol consumption. The analysis of covariance (ANCOVA) adjusting for sex, age, smoking and alcohol consumption was performed using the StatView 5.0 statistical package.

Results

The odd ratios of foods and drinks consumed among the subjects with Helicobacter pylori or atrophic gastritis

Table 1 shows the subject characteristics in the present study. The percentage of subjects 70 years of age or older was low, compared to other age groups. Current smokers or regular alcohol drinkers accounted for 37.5% or 51.2% of all males and 10.0% or 13.8% of all females, respectively. The percentages of individuals with HP infection or those with AG were 67.5% or 46.3% of all males and were 46.9% or 44.6% of all females, respectively. The percentages of the subjects with HP infection and AG, aged above 70 years old, were not always high, compared to other age groups.

Table 2 illustrates the breakdown of odds ratios for food and drinks consumed. In the HP infection group, the odds ratio was significantly lower on a frequent intake of Kamaboko (processed fish) and refreshing (isotonic) beverages, whereas that of green tea or oolong tea was not associated with a reduced risk of HP infection. No significant risk of HP infection due to the intake frequency of any other foods was found. The odds ratios of AG was significantly higher for more frequent intakes of margarine, cheese, Tsukemono (pickled vegetables), and Cola-beverages. In addition, the odds ratios of meats (liver) and tofu rich in protein, and Chinese cabbage, other vegetables and Sansai (wild plants) rich in lutein tended to be associated with the risk of AG. In contrast, the odds ratios of higher intake frequencies of potatoes, yogurt, Kamaboko, tomato juice, and fruit juice appeared to be protective, but not significantly. The odds ratios for AG with HP infection was also higher

Table 1. Subject Characteristics

Item		Males (%)	Females (%)
Age	Total	80 (100)	130 (100)
	39-49	19 (23.8)	43 (33.1)
	50-59	23 (28.7)	45 (34.6)
	60-69	26 (32.5)	35 (26.9)
	70+	12 (15.0)	7 (5.4)
Smoking status	Never smoked	28 (35.0)	115 (88.5)
	Former smoker	22 (27.5)	2 (1.5)
	Current smoker	30 (37.5)	13 (10.0)
Alcohol consumption	Non drinker	33 (41.3)	110 (84.6)
	Occasional drinker	6 (7.5)	2 (1.5)
	Regular drinker	41 (51.2)	18 (13.8)
Helicobacter pylori infection#	Total	54 (67.5)	61 (46.9)
	39-49	11 (57.9)	18 (41.9)
	50-59	17 (73.9)	23 (51.1)
	60-69	19 (73.1)	17 (48.6)
	70+	7 (58.3)	3 (42.9)
Atrophic gastritis##	Total	35 (46.3)	58 (44.6)
	39-49	7 (36.8)	19 (44.2)
	50-59	10 (43.5)	25 (55.6)
	60-69	13 (50.0)	11 (31.4)
	70+	5 (41.7)	3 (42.9)
Atrophic gastritis & Helicobacter pylori infection	Total	30 (37.5)	39 (30.0)
	39-49	6 (31.6)	13 (30.2)
	50-59	10 (43.5)	18 (40.0)
	60-69	11 (42.3)	6 (17.1)
	70+	3 (25.0)	2 (28.6)

#: Helicobacter pylori antibody≥2.3 ELISA Value
##: Pepsinogen I ≤70 ng/ml and pepsinogen I/II ratio ≤3.0
Data represented are number and percentages of totals in parenthesis, and percentages of each age group in bracket.
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for margarine, Tsukemono and Cola-beverages, but were lower for Kamaboko intake. The intake frequency of other foods was not found to be significantly associated with an increased or decreased risk of AG.

Comparison of serum component levels among subjects with Helicobacter pylori infection or atrophic gastritis

Mean values of serum components, such as protein, glucose, lipids, carotenoids, were compared between the individuals with and without HP infection or AG (Table 3). Subjects with HP infection and those with AG and HP infection had significantly lower serum values of total carotenoids and BC. Those of n-6PUFAs, such as LNA and GLA also tended to be lower for subjects with AG and HP infection, whereas those of n-3PUFAs, such as EPA and DHA, were higher. In contrast, differences in the serum values of TBARS, NO_x, and other components did not show significantly between subjects with and without AG or HP infection.

The odds ratios of serum components among subjects with Helicobacter pylori or atrophic gastritis

The odds ratios of serum component values did not correlate significantly with HP infection (Table 4). Serum values of carotenoids, such as AC, BC, LY, and CR, and n-6 PUFAs, such as GLA and DLA, were associated with a reduced, but not significant, risk of HP infection. In addition, the odds ratios of serum values of TBARS and NO_x did not correlate with the risk of HP infection. Serum values of n-6 PUFAs, such as LNA and GLA, and carotenoids, AC, BC, LY and CR, also were associated with a reduced risk of AG, while those of ZL, RE and AT did not always correlate with a reduced risk of AG. Furthermore, the odds ratios of serum values of potassium, calcium, sodium and SOD activity tended to be linked with a reduced risk of AG and HP. In contrast, those of TBARS and n-3PUFAs, such as EPA and DHA with the exception of LLA, correlated with an increased risk of AG, a trend also observed with HP infection.

Table 2-1. Odds Ratios of Food Intake Frequency for Healthy Subjects to Helicobacter pylori Infection, Atrophic Gastritis, or Atrophic Gastritis with Helicobacter Pylori Infection

Food intake (Frequency: five categories)	Helicobacter pylori infection (Non-infection: Infection))			Atrophic gastritis (Non-gastritis: Gastritis)			Atrophic gastritis with Helicobacter pylori infection (Non-gastritis: Gastritis)		
	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability
Beef	0.905	(0.620, 1.323)	0.610	0.932	(0.642, 1.352)	0.710	0.863	(0.541, 1.379)	0.540
Pork	0.894	(0.639, 1.250)	0.510	1.208	(0.867, 1.683)	0.270	1.073	(0.717, 1.606)	0.730
Chicken	0.999	(0.720, 1.385)	0.990	1.022	(0.741, 1.409)	0.900	1.302	(0.705, 1.512)	0.870
Liver	1.066	(0.631, 1.798)	0.810	1.553	(0.899, 2.681)	0.114	1.419	(0.766, 2.626)	0.270
Ham	0.910	(0.678, 1.223)	0.530	1.126	(0.842, 1.505)	0.424	1.028	(0.723, 1.463)	0.880
Eggs	0.989	(0.754, 1.297)	0.940	1.114	(0.852, 1.457)	0.430	1.049	(0.754, 1.460)	0.780
Tofu (Bean paste)	1.267	(0.893, 1.797)	0.190	1.295	(0.919, 1.824)	0.140	1.390	(0.885, 2.184)	0.153
Potatoes	0.876	(0.645, 1.196)	0.410	0.863	(0.639, 1.165)	0.340	0.777	(0.547, 1.147)	0.210
Butter	0.750	(0.558, 1.008)	0.056	1.161	(0.873, 1.544)	0.310	0.916	(0.646, 1.299)	0.620
Margarine	1.309	(0.995, 1.724)	0.055	1.413	(1.080, 1.848)	0.012	1.671	(1.166, 2.396)	0.005
Milk	1.043	(0.860, 1.266)	0.670	1.024	(0.846, 1.239)	0.810	1.052	(0.822, 1.347)	0.690
Cheese	0.915	(0.676, 1.238)	0.560	1.416	(1.044, 1.920)	0.025	1.187	(0.821, 1.718)	0.360
Yogurt	0.837	(0.657, 1.066)	0.150	0.893	(0.702, 1.135)	0.353	0.800	(0.587, 1.090)	0.158
Fresh fish	1.157	(0.823, 1.626)	0.403	1.137	(0.814, 1.589)	0.450	1.241	(0.822, 1.883)	0.302
Dried fish	1.041	(0.767, 1.413)	0.800	1.057	(0.784, 1.425)	0.720	1.040	(0.728, 1.484)	0.830
Kamaboko (Processed fish)	0.679	(0.484, 0.951)	0.024	0.868	(0.629, 1.197)	0.390	0.618	(0.396, 0.963)	0.033
Counts		210			210			140	

Odds ratios and 95% confidence intervals (C.I.) in parenthesis were calculated by logistic regression analysis after adjusting for sex, age and habits of smoking and alcohol consumption.
Helicobacter pylori infection : ≥2.3 ELISA Value. Atrophic gastritis: pepsinogen I≤70 ng/ml and Pepsinogen I/II ratio ≤ 3.0.

Table 2-2. Odds Ratios of Food and Drink Intake Frequency for Healthy Subjects to Helicobacter pylori Infection, Atrophic Gastritis, or Atrophic Gastritis with Helicobacter Pylori Infection

Food and drink intake (Frequency: five categories)	Helicobacter pylori infection (Non-infection: Infection)			Atrophic gastritis (Non-gastritis: Gastritis)			Atrophic gastritis with Helicobacter pylori infection (Non-gastritis: Gastritis)		
	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability
Green leaf vegetables	1.039	(0.777, 1.389)	0.800	1.054	(0.793, 1.402)	0.720	1.042	(0.722, 1.505)	0.820
Carrot & Pumpkin	0.920	(0.659, 1.283)	0.621	0.969	(0.701, 1.339)	0.850	0.906	(0.612, 1.343)	0.620
Tomato	1.020	(0.770, 1.350)	0.892	1.091	(0.825, 1.442)	0.541	1.088	(0.780, 1.519)	0.620
Tomato juice	0.831	(0.619, 1.116)	0.220	0.848	(0.633, 1.137)	0.271	0.720	(0.479, 1.081)	0.113
Cabbage	0.940	(0.652, 1.355)	0.741	1.007	(0.705, 1.441)	0.970	0.935	(0.597, 1.464)	0.770
Chinese cabbage	0.894	(0.650, 1.231)	0.492	1.266	(0.921, 1.739)	0.146	1.104	(0.744, 1.638)	0.620
Seaweed	1.125	(0.816, 1.552)	0.470	1.101	(0.805, 1.506)	0.550	1.112	(0.740, 1.669)	0.610
Sansai(wild plants)	0.976	(0.704, 1.351)	0.880	1.372	(0.990, 1.901)	0.057	1.175	(0.794, 1.738)	0.420
Other vegetables	0.950	(0.711, 1.270)	0.730	1.219	(0.914, 1.626)	0.178	1.086	(0.755, 1.561)	0.660
Tsukemono (pickled veg)	1.163	(0.913, 1.490)	0.221	1.277	(1.000, 1.631)	0.050	1.381	(1.012, 1.883)	0.042
Tsukudani (boiled in soy)	0.980	(0.750, 1.284)	0.890	1.286	(0.982, 1.674)	0.068	1.218	(0.868, 1.711)	0.254
Oranges	0.961	(0.716, 1.290)	0.792	1.032	(0.772, 1.379)	0.830	0.987	(0.693, 1.407)	0.940
Other fruits	1.031	(0.784, 1.355)	0.830	0.988	(0.755, 1.293)	0.930	1.012	(0.726, 1.410)	0.940
Fruit juice	0.857	(0.655, 1.121)	0.260	0.804	(0.613, 1.054)	0.115	0.767	(0.546, 1.077)	0.126
Cola-beverages	1.284	(0.907, 1.819)	0.160	1.471	(1.051, 2.058)	0.024	1.620	(1.057, 2.495)	0.027
Refreshing beverages	0.767	(0.616, 0.956)	0.018	1.005	(0.815, 1.239)	0.960	0.826	(0.628, 1.087)	0.173
Green tea (Macha)	1.011	(0.832, 1.230)	0.910	1.073	(0.884, 1.302)	0.480	1.067	(0.831, 1.370)	0.610
Coffee	1.104	(0.920, 1.324)	0.290	1.165	(0.973, 1.393)	0.096	1.215	(0.973, 1.518)	0.085
Oolong tea	0.953	(0.785, 1.156)	0.630	0.910	(0.752, 1.102)	0.330	0.929	(0.735, 1.173)	0.536
Counts		210			210			140	

Odds ratios and 95% confidence intervals (C.I.) in parenthesis were calculated by logistic regression analysis after adjusting for sex, age and habits of smoking and alcohol consumption.
Helicobacter pylori infection : ≥2.3 ELISA Value. Atrophic gastritis: pepsinogen ≤70 ng/ml and Pepsinogen I/II ratio ≤ 3.0.

Table 3-1. Comparison of Serum Component Values between Subjects with and without Helicobacter pylori Infection, Atrophic Gastritis, or Atrophic Gastritis with Helicobacter pylori Infection.

Serum components		Helicobacter pylori infection			Atrophic gastritis			Atrophic gastritis with Helicobacter pylori infection		
		Non-infection	Infection	probability	Non-gastritis	Gastritis	probability	Non-gastritis	Gastritis	probability
Albumin	(g/dl)	4.7 (0.2)	4.6 (0.2)	0.200	4.6 (0.2)	4.7 (0.2)	0.370	4.7 (0.2)	4.7 (0.2)	0.810
Glucose	(mg/dl)	97.7 (0.27)	94.2 (16.7)	0.250	97.0 (27.4)	94.3 (12.3)	0.600	97.6 (29.6)	93.0 (9.4)	0.210
Fructosamine	(μg/ml)	263 (35)	255 (26)	0.540	259 (34)	258 (2)	0.630	262 (35)	255 (21)	0.120
Total cholesterol	(mg/dl)	219 (38)	219 (36)	0.930	222 (39)	215 (35)	0.130	221 (40)	215 (35)	0.320
Triglyceride	(mg/dl)	118 (80)	127 (125)	0.540	124 (84)	120 (130)	0.780	120 (86)	124 (147)	0.860
SOD activity	(μg/ml)	0.28 (0.12)	0.28 (0.12)	0.920	0.28 (0.12)	0.27 (0.12)	0.569	0.28 (0.12)	0.27 (0.11)	0.670
TBARS	(μmol/L)	2.64 (0.52)	2.62 (0.50)	0.780	2.61 (0.49)	2.66 (0.52)	0.580	2.59 (0.51)	2.61 (0.52)	0.870
Sodium	(mEq/L)	142.4 (2.4)	142.2 (2.4)	0.470	142.4 (2.5)	142.1 (2.3)	0.240	142.5 (2.4)	142.1 (2.3)	0.240
Potassium	(mEq/L)	4.1 (0.3)	4.1 (0.3)	0.200	4.1 (0.3)	4.1 (0.3)	0.210	4.1 (0.3)	4.0 (0.3)	0.103
Calcium	(mg/dl)	9.2 (0.3)	9.1 (0.3)	0.310	9.2 (0.3)	9.1 (0.3)	0.270	9.2 (0.3)	9.1 (0.3)	0.190
NO	(μmol/l)	4.04 (2.69)	4.14 (2.02)	0.215	3.96 (1.77)	4.27 (2.92)	0.348	3.84 (1.64)	4.14 (2.07)	0.340
NO3	(μmol/l)	35.3 (20.3)	39.5 (25.6)	0.215	38.0 (24.5)	36.9 (22.0)	0.730	33.5 (1.1)	35.5 (19.7)	0.520
All carotenoids	(μmol/L)	3.98 (3.12)	3.36 (1.74)	0.044	3.89 (2.19)	3.52 (1.85)	0.164	3.98 (2.12)	3.36 (1.74)	0.044
β-Carotene	(μmol/L)	1.53 (1.06)	1.26 (0.97)	0.044	1.50 (1.05)	1.24 (0.96)	0.053	1.59 (1.10)	1.20 (0.97)	0.019
β-Carotene	(μmol/L)	0.15 (0.09)	0.14 (0.10)	0.610	0.15 (0.09)	0.13 (0.09)	0.144	0.15 (0.09)	0.13 (0.09)	0.210
Lycopene	(μmol/L)	0.70 (0.52)	0.61 (0.38)	0.113	0.69 (0.50)	0.60 (0.37)	0.128	0.72 (0.54)	0.58 (0.34)	0.063
Cryptoxanthin	(μmol/L)	0.37 (0.26)	0.33 (0.25)	0.200	0.36 (0.26)	0.33 (0.25)	0.351	0.37 (0.25)	0.31 (0.24)	0.160
Zeaxanthin&lutein	(μmol/L)	1.19 (0.65)	1.15 (0.79)	0.730	0.12 (0.77)	1.18 (0.68)	0.831	1.12 (0.54)	1.11 (0.58)	0.800
Retinol	(μmol/L)	2.47 (0.66)	2.71 (0.91)	0.029	2.63 (0.75)	2.57 (0.88)	0.579	2.43 (0.60)	2.60 (0.91)	0.300
α-Tocopherol	(μmol/L)	22.2 (6.1)	21.9 (9.6)	0.780	22.6 (9.9)	21.3 (5.4)	0.244	22.2 (6.3)	21.0 (5.2)	0.210
Counts	95	115			117	93		71	69	

Data are represented as the mean values, with S.D. in parentheses.
Mean differences were calculated by ANOVA analysis (statistical package: StatView 5.0) after controlling for sex, age, and habits of smoking and alcohol consumption.

Table 3-2. Comparison of Serum Values for Fatty Acids between Subjects with and without Helicobacter pylori Infection, Atrophic Gastritis, or Atrophic Gastritis with Helicobacter pylori Infection.

Serum fatty acids (mmol/L)	Helicobacter pylori infection			Atrophic gastritis			Atrophic gastritis with Helicobacter pylori infection		
	Non-infection	Infection	probability	Non-gastritis	Gastritis	probability	Non-gastritis	Gastritis	probability
Total saturated fatty acids	3.95 (1.37)	4.00 (1.80)	0.840	3.98 (1.33)	3.97 (1.92)	0.981	3.96 (1.44)	4.00 (2.13)	0.920
Palmitic acid	2.88 (1.08)	2.92 (1.38)	0.840	2.90 (1.05)	1.90 (1.48)	0.999	2.89 (1.13)	2.92 (1.64)	0.920
Stearic acid	0.80 (0.21)	0.81 (0.29)	0.920	0.81 (0.22)	0.80 (0.30)	0.820	0.81 (0.22)	0.80 (0.34)	0.940
Total unsaturated fatty acids	7.10 (1.48)	7.15 (2.02)	0.853	7.24 (1.38)	6.98 (2.02)	0.332	7.18 (1.50)	7.03 (2.20)	0.650
Monounsaturated fatty acids	2.52 (0.87)	2.56 (1.21)	0.820	2.57 (1.88)	2.51 (1.27)	0.686	2.54 (0.86)	2.52 (1.38)	0.920
n-9 unsaturated fatty acids	2.21 (0.71)	2.24 (0.82)	0.830	2.26 (0.74)	2.18 (1.08)	0.515	2.23 (0.70)	2.19 (1.09)	0.810
Oleic acid	2.07 (0.71)	2.10 (0.97)	0.820	2.12 (0.73)	2.04 (1.00)	0.530	2.09 (0.70)	2.05 (1.08)	0.820
n-3 polyunsaturated fatty acids	1.09 (0.39)	1.13 (0.46)	0.520	1.09 (0.39)	1.15 (0.48)	0.296	1.07 (0.38)	1.14 (0.50)	0.310
Linolenic acid	0.08 (0.03)	0.09 (0.05)	0.403	0.09 (0.04)	0.08 (0.03)	0.088	0.08 (0.03)	0.08 (0.04)	0.530
Eicosapentaenoic acid	0.40 (0.20)	0.42 (0.25)	0.474	0.40 (0.21)	0.44 (0.25)	0.194	0.39 (0.19)	0.43 (0.25)	0.195
Docosahexaenoic acid	0.51 (0.17)	0.52 (0.19)	0.730	0.51 (0.16)	0.53 (0.19)	0.298	0.51 (0.17)	0.53 (0.21)	0.410
n-6 polyunsaturated fatty acids	3.48 (0.67)	3.46 (0.84)	0.840	3.58 (0.78)	3.33 (0.74)	0.022	3.56 (0.70)	3.36 (0.80)	0.119
Linoleic acid	2.87 (0.61)	2.86 (0.74)	0.910	2.96 (0.70)	2.74 (0.65)	0.021	2.95 (0.63)	2.78 (0.70)	0.122
α-Linolenic acid	0.05 (0.03)	0.04 (0.03)	0.374	0.05 (0.03	0.04 (0.02)	0.029	0.05 (0.03)	0.04 (0.03)	0.062
DimonoÉ¡-linolenic acid	0.10 (0.03)	0.09 (0.05)	0.840	0.10 (0.04)	0.09 (0.04)	0.791	0.10 (0.03)	0.09 (0.05)	0.725
Arachidonic acid	0.44 (0.11)	0.43 (0.10)	0.590	0.44 (0.11)	0.43 (0.10)	0.367	0.44 (0.12)	0.42 (0.10)	0.370
Counts	95	115		117	93		71	69	

Data are represented as mean values, with S.D. in parentheses.
Mean differences were calculated by ANOVA analysis (statistical package: StatView 5.0) after controlling for sex, age, and habits of smoking and alcohol consumption.

Table 4-1. Odds Ratios for Serum Components in Helicobacter pylori infection, atrophic gastritis, and atrophic gastritis with Helicobacter pylori infection

Serum components	Helicobacter pylori infection (Non-infection: Infection)			Atrophic gastritis (Non-gastritis: Gastritis)			Atrophic gastritis with Helicobacter pylori infection (Non-gastritis:Gastritis)		
	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability
Albumin g/dl	0.407	(0.102, 1.615)	0.200	1.886	(0.493, 7.211)	0.354	0.855	(0.170, 4.299)	0.850
Glucose mg/dl	0.990	(0.975, 1.004)	0.151	0.994	(0.979, 1.009)	0.431	0.987	(0.966, 1.008)	0.230
Fructosamine mg/dl	0.989	(0.979, 0.999)	0.038	0.997	(0.988, 1.007)	0.550	0.987	(0.974, 1.001)	0.069
Total cholesterol mg/dl	1.001	(0.993, 1.009)	0.810	0.994	(0.986, 1.001)	0.100	0.997	(0.988, 1.006)	0.500
Triglyceride mg/dl	1.001	(0.998, 1.004)	0.500	1.000	(0.997, 1.002)	0.900	1.000	(0.998, 1.003)	0.730
TBARS μ mol/L	0.849	(0.452, 1.594)	0.610	1.137	(0.614, 2.107)	0.680	1.032	(0.494, 2.154)	0.930
SOD activity unit	1.517	(0.096, 23.86)	0.770	0.378	(0.024, 5.929)	0.490	0.671	(0.019, 24.10)	0.830
Sodium mEq/L	0.945	(0.840, 1.063)	0.340	0.930	(0.829, 1.045)	0.222	0.876	(0.751, 1.022)	0.092
Potasium mEq/L	0.384	(0.139, 1.060)	0.065	0.514	(0.190, 1.392)	0.191	0.237	(0.061, 0.922)	0.038
Calcium mg/dl	0.667	(0.284, 1.566)	0.353	0.613	(0.267, 1.407)	0.249	0.546	(0.195, 1.529)	0.250
NO μ mol/L	0.992	(0.879, 1.120)	0.900	1.061	(0.935, 1.203)	0.360	1.037	(0.853, 1.262)	0.715
NO_3 μ mol/L	1.006	(0.993, 1.019)	0.396	0.998	(0.986, 1.011)	0.770	1.005	(0.985, 1.024)	0.631
Total carotenoids μ mol/L	0.918	(0.790, 1.067)	0.266	0.876	(0.751, 1.021)	0.090	0.831	(0.679, 1.017)	0.072
b-Carotene μ mol/L	0.838	(0.615, 1.141)	0.262	0.691	(0.498, 0.958)	0.027	0.668	(0.448, 0.995)	0.047
b-Carotene μ mol/L	0.809	(0.036, 18.24)	0.890	0.056	(0.002, 1.535)	0.088	0.086	(0.001, 5.673)	0.251
Lycopene μ mol/L	0.640	(0.335, 1.234)	0.183	0.579	(0.296, 1.131)	0.110	0.485	(0.204, 1.153)	0.101
Cryptoxanthin μ mol/L	0.775	(0.241, 2.501)	0.670	0.517	(0.157, 1.704)	0.278	0.474	(0.100, 2.256)	0.350
Zeaxanthin&lutein μ mol/L	0.896	(0.556, 1.346)	0.596	0.984	(0.666, 1.464)	0.949	0.855	(0.451, 1.623)	0.633
Retinol μ mol/L	1.325	(0.879, 1.998)	0.179	0.842	(0.580, 1.223)	0.367	1.082	(0.659, 1.776)	0.756
a-Tocopherol μ mol/L	1.003	(0.969, 1.038)	0.860	0.974	(0.930, 1.017)	0.222	0.970	(0.900, 1.034)	0.350
Counts		210			210			140	

Odds ratios and 95% confidence intervals (C.I.) were calculated by logistic regression analysis (statistical package: StatView 5.0) after adjusting for sex, age, and habits of smoking and alcohol consumption.
Hericobacter pylori infection: ≥2.3 ELISA Value. Atrophic gastritis: pepsinogen I ≤70 ng/ml and pepsinogen I/II ratio ≤ 3.0.

Table 4-2. Odds Ratios for Serum Values of Fatty Acids in Helicobacter pylori Infection, Atrophic Gastritis, and Atrophic Gastritis with Helicobacter pylori Infection

Serum fatty Acids	Helicobacter pylori infection (Non-infection: Infection)			Atrophic gastritis (Non-gastritis: Gastritis)			Atrophic gastritis with Helicobacter pylori infection (Non-gastritis:Gastritis)		
	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability	Odds ratio	95% C.I.	probability
Total saturated fatty acids mmol/L	1.035	(0.868, 1.227)	0.720	1.000	(0.843, 1.187)	0.990	1.036	(0.850, 1.238)	0.790
Palmitic acid mmol/L	1.036	(0.083, 1.274)	0.750	1.005	(0.806, 1.253)	0.967	1.033	(0.811, 1.315)	0.790
Stearic acid mmol/L	1.263	(0.423, 3.771)	0.680	0.855	(0.285, 2.571)	0.780	1.119	(0.332, 3.765)	0.860
Total unsaturated fatty acids mmol/L	1.025	(0.878, 1.197)	0.750	0.919	(0.776, 1.089)	0.330	0.972	(0.807, 1.171)	0.860
Monounsaturated fatty acids mmol/L	1.041	(0.801, 1.354)	0.760	0.957	(0.733, 1.249)	0.750	1.006	(0.747, 1.354)	0.970
n-9 Unsaturated fatty acids mmol/L	1.049	(0.759, 1.450)	0.770	0.909	(0.649, 1.272)	0.576	0.981	(0.674, 1.428)	0.920
Oleic acid mmol/L	1.049	(0.757, 1.455)	0.770	0.912	(0.651, 1.2179)	0.594	0.983	(0.674, 1.434)	0.930
n-3 Polyunsaturated fatty acids mmol/L	1.232	(0.624, 2.431)	0.550	1.347	(0.696, 2.610)	0.380	1.577	(0.697, 3.568)	0.270
Linolenic acid μ mol/L	1.004	(0.996, 1.011)	0.310	0.993	(0.986, 1.001)	0.104	0.998	(0.997, 1.008)	0.673
Eicosapentaenoic acid mmol/L	1.391	(0.380, 5.085)	0.620	2.008	(0.573, 7.033)	0.276	2.589	(0.514, 13.04)	0.250
Docosahexaenoic acid mmol/L	1.466	(0.289, 7.436)	0.640	2.116	(0.429, 10.44)	0.358	2.747	(0.409, 18.47)	0.299
n-6 Polyunsaturated fatty acids mmol/L	1.049	(0.759, 1.450)	0.770	0.909	(0.649, 1.272)	0.576	0.981	(0.674, 1.428)	0.920
Linoleic acid mmol/L	1.019	(0.674, 1.540)	0.930	0.594	(0.382, 0.924)	0.021	0.681	(0.396, 1.169)	0.165
a-Linolenic acid μ mol/L	0.997	(0.988, 1.006)	0.514	0.987	(0.976, 0.998)	0.024	0.986	(0.972, 1.001)	0.061
Dihomo-linolenic acid μ mol/L	1.001	(0.994, 1.008)	0.743	0.998	(0.991, 1.005)	0.580	0.999	(0.991, 1.008)	0.882
Arachidoic acid	0.468	(0.033, 6.667)	0.580	0.248	(0.017, 3.532)	0.304	0.238	(0.009, 6.405)	0.390
Counts		210			210			140	

Odds ratios and 95% confidence intervals (C.I.) were calculated by logistic regression analysis (statistical package: StatView 5.0) after adjusting for sex, age, and habits of smoking and alcohol consumption.
Hericobacter pylori infection: ≥2.3 ELISA Value. Atrophic gastritis: pepsinogen I ≤70 ng/ml and pepsinogen I/II ratio ≤ 3.0.

Table 5. Differences of Serum Levels of Lipids, Fatty Acids and Carotenoids among the Same Persons who Attended Health Screening on August, 1996 and 1999, which were Compared to the Data Determined in March, 2000.

Component		1996y sample	1999y sample	probability
SOD activity	unit	3.24 (3.90)	3.57 (3.69)	0.74
TBARS	μ mol/L	2.74 (0.46)	2.80 (0.73)	0.72
Total Carotenoids	μmol/L	1.665 (0.913)	1.852 (1.113)	0.48
β-Carotene	μ mol/L	0.518 (0.457)	0.583 (0.581)	0.63
α-Carotene	μ mol/L	0.091 (0.050)	0.108 (0.085)	0.33
Lycopene	μ mol/L	0.130 (0.138)	0.122 (0.096)	0.8
β-Cryptoxanthin	μ mol/L	0.218 (0.144)	0.209 (0.138)	0.79
Zeaxanthin&lutein	μ mol/L	0.678 (0.348)	0.799 (0.354)	0.19
Retinol	μ mol/L	1.662 (0.432)	2.072 (0.549)	0.002
α-Tocopherol	μ mol/L	16.61 (4.02)	19.86 (4.60)	0.005
Tota saturated fatty acids	mmol/L	4.092 (0.886)	4.179 (0.913)	0.71
Palmitic acid	mmol/L	2.945 (0.698)	3.029 (0.723)	0.65
Stearic acid	mmol/L	0.866 (0.139)	0.868 (0.151)	0.95
Total unsaturated fatty acids	mmol/L	7.356 (1.400)	7.506 (1.354)	0.68
n-3 Polyunsaturated fatty acids	mmol/L	1.245 (0.348)	1.200 (0.376)	0.64
Linolenic acid	μ mol/L	89.1 (29.7)	90.1 (35.4)	0.9
Eicosapentaenoic acid	μ mol/L	471.3 (200.8)	394.3 (174.7)	0.12
Docosahexaenoic acid	μ mol/L	589.4 (147.6)	619.5 (195.5)	0.5
n-6 Polyunsaturated fatty acids	mmol/L	3.676 (0.752)	3.622 (0.570)	0.76
Linoleic acid	mmol/L	3.005 (0.678)	2.937 (0.468)	0.66
γ-Linolenic acid	μ mol/L	33.1 (17.5)	36.5 (23.0)	0.52
Dihomo-γ-linolenic acid	μ mol/L	102.3 (35.4)	110.2 (37.9)	0.41
Arachinonic acid	μ mol/L	505.4 (99.9)	505.1 (111.8)	0.99
Mono unsaturated fatty acids	mmol/L	3.436 (0.669)	2.684 (0.753)	0.18
n-9 Unsaturated fatty acids	mmol/L	2.148 (0.568)	2.376 (0.641)	0.15
Oleic acid	mmol/L	1.995 (0.561)	2.228 (0.638)	0.14
Number		30	30	

Data represented are mean values and S.D. in parenthesis.
Probability are calculated by Student t-test.

Table 6-1. Comparison of Serum Levels of Carotenoids, Retinol, α-tocopherol, and Lipids among Japanese Inhabitants, Aged more than 50 Years Old

Component		Males			Females		
		Present inhabitant	Other inhabitant	Mean difference	Present inhabitant	Other inhabitant	Mean difference
Total cholesterol	(mmol/l)	5.39 (0.886)	4.75 (0.81)	***	5.92 (0.970)	5.213 (0.946)	***
Triglyceride	(mmol/l)	13.71 (6.48)	18.10 (12.37)	*	15.14 (16.46)	18.05 (11.44)	
TBARS	(μ mol/l)	2.72 (0.52)	3.91 (1.19)	***	2.64 (0.49)	3.74 (1.12)	***
SOD activity	(unit)	0.26 (0.10)	0.31 (0.22)		0.31 (0.14)	0.44 (0.37)	**
β-Carotene	(μ mol/l	0.531 (0.371)	0.491 (0.469)		1.098 (0.665)	1.167 (0.764)	
α-Carotene	(μ mol/l)	0.108 (0.075)	0.112 (0.128)		0.152 (0.103)	0.205 (0.231)	
Lycopene	(μ mol/l)	0.333 (0.230)	0.167 (0.136)	***	0.397 (0.285)	0.253 (0.173)	***
Cryptoxanthin	(μ mol/l)	0.245 (0.212)	0.245 (0.213)		0.411 (0.257)	0.473 (0.279)	
Zeaxanthin&lutein	(μ mol/l)	1.178 (0.696)	1.330 (0.754)	**	1.285 (0.882)	1.622 (0.764)	**
ProvitaminA	(μ mol/l)	0884 (0.615)	0.848 (0.665)		1.661 (0.958)	1.844 (1.067)	
Retinol	(μ mol/l)	2.200 (0.681)	2.552 (0.658)	**	2.004 (0.518)	2.205 (0.562)	*
α-Tocopherol	(μ mol/l	19.81 (3.68)	20.17 (7.84)		24.21 (11.26)	23.48 (7.82)	
Number		61	108		85	109	

Data represented are mean values and S.D. in parentheses.
*p<0.05,**p<0.01,***p<0.001(mean differences, Student t-test)

Table 6-2. Comparison of Serum Levels of Fatty Acids among Japanese Inhabitants, Aged more than 50Years Old

Fatty acids (mM/L)	Males			Females		
	Present inhabitant	Other inhabitant	Mean difference	Present inhabitant	Other inhabitant	Mean difference
Total saturated fatty acids	3.846 (0.807)	4.160 (1.780)		4.253 (2.226)	3.799 (1.448)	
Palmitic acid	2.825 (0.616)	2.996 (1.377)	*	3.099 (1.730)	2.684 (1.078)	
Stearic acid	0.758 (0.145)	0.863 (0.270)	*	0.863 (0.342)	0.841 (0.264)	
Total unsaturated fatty acids	6.882 (1.097)	6.792 (2.144)		7.414 (2.300)	6.528 (2.037)	*
n-3 unsaturated fatty acids	1.110 (0.457)	1.045 (0.416)		1.190 (0.409)	0.961 (0.409)	**
Linolenic acid	0.081 (0.033)	0.083 (0.054)		0.089 (0.045)	0.093 (0.051)	
Eicosapentaenoic acid	0.423 (0.253)	0.406 (0.204)		0.441 (0.196)	0.370 (0.216)	*
Docosahexaenoic acid	0.510 (0.182)	0.497 (0.195)		0.555 (0.183)	0.446 (0.175)	***
n-6 unsaturated fatty acids	3.279 (0.627)	3.055 (0.840)		3.541 (0.842)	3.196 (0.833)	*
Linoleic acid	2.703 (0.568)	2.350 (0.753)	**	2.920 (0.729)	2.485 (0.709)	***
γ-Linolenic acid	0.040 (0.024)	0.035 (0.018)		0.050 (0.038)	0.037 (0.019)	
Dihomo γ-linolenic acid	0.040 (0.024)	0.105 (0.028)	***	0.050 (0.038)	0.111 (0.037)	***
Arachidonic acid	0.421 (0.102)	0.530 (0.122)	***	0.436 (0.108)	0.527 (0.139)	***
Mono unsaturated fatty acids	2.488 (0.685)	2.686 (1.235)		2.677 (1.385)	2.368 (1.042)	
n-9 unsaturated fatty acids	2.175 (0.577)	2.299 (0.945)		2.316 (1.097)	2.074 (0.909)	
Oleic acid	2.037 (0.574)	2.175 (0.935)		2.174 (1.089)	1.950 (0.894)	
Nervonic acid	0.099 (0.022)	0.095 (0.019)		0.103 (0.021)	0.100 (0.022)	
n-6PUFA/n-3PUFA	3.603 (2.127)	3.339 (1.631)		3.247 (1.112)	3.783 (1.504)	*
Age	63.2 (8.5)	60.2 (6.6)	*	60.6 (6.7)	59.9 (6.3)	
Number	61	58		85	55	

Data are represented as the mean values and S.D. in parenthesis.
*p<0.05,**p<0.01,***p<0.001 (mean differences, Student t-test)

Discussion

In the residential areas covered in the present study, the health check-up program has been running for inhabitants over 40 years of age every August for the past 15 years. Prior history of disease, dietary habits and other lifestyle habits in this residential area did not apparently differ between the present study population and other Japanese population (Research group, 1996). In our preliminary study, individual variations of carotenoids and fatty acids in stored sera determined by the same method at March, 2000, in which were collected from the same inhabitants between August, 1996 and 1999, showed no significant differences, in exception of RE and AT, as shown in Table5. However, it was obtained that serum values of carotenoids (LY and ZL), RE, TC, TBARS, fatty acids (LNA, DGA, and ADA), which were easy to depend on lifestyle, such as habit of food intake, appeared significant differences between present subjects and other Japanese inhabitants (Table 6) (Ito et al., 1999).

Subjects with HP infection or with AG were diagnosed using the available cut-off values used in previous studies involving Japanese subjects (Miki et al., 1989; Kabuto et al., 1993). Although sensitivity was more than 85% for HP (Tani et al., 1997) and 90% for AG (Samloff et al., 1982), we accepted the RIA method to diagnose HP and the ELISA for AG in this study. In the present study, the distribution of HP infection and AG was similar to that previously reported for Japanese subjects (Miki et al., 1989; Tsugane et al., 1993: Watanabe et al., 1997).

In the present study, no significant relationship between the food intake and HP infection was found, with the exception of the intake of refreshing (isotonic) beverages and processed fish. However, the intake of fruit juice tended to reduce the risk of HP infection. It appears that a high intake of these beverages and processed fish might play a role in the eradication of HP by washing out or by some antiseptic substances added into processed fish.

AG is the precancerous condition of gastric cancer (Watanabe et al., 1997) and HP infection also carries a significant risk of gastric cancer (Ma et al., 1998). Numerous studies reported that the food intakes of pickled foods (Hirayama 1971; Haenszel et al., 1976; Tajima and Tominaga, 1985; Kato et al., 1992), meats such as pork and ham (Higginson, 1966; Vecchia, 1987), and fish (Graham et al., 1972) increases the risk of gastric cancer, whereas those of green-yellow vegetables (Hirayama, 1971; Tajima and Tominaga, 1985; Correa et al., 1985, Ziegler, 1991; Kim et al., 1996) and milk (Hirayama, 1981; Tajima and Tominaga, 1985; Correa et al., 1985) reduces its risk. In the present study, the results of an increased intake of Tsukemono (pickled vegetables), cheese and margarine presented a significant risk of AG supports the findings of these studies. Intake of dairy products did not consistently reduce the risk of gastric cancer, as most dairy products, usually contain a lot of salt. Margarine generally contains many PUFAs, compared to butter. We also found that high serum levels of n-3 PUFAs, such as EPA and DHA, tend to increase the risk of AG. Moreover, fish oil, taken by the majority of present

subjects, is usually rich in EPA and DHA. These n-3 PUFAs levels in Japanese were strongly associated with serum levels of lipid peroxides, such as TBARS, which are produced more by lipid peroxidation, when compared to n-6 PUFAs levels (Ito et al., 1999). Lipid peroxidation correlates with an increased risk of AG, as the odds ratio of serum TBARS values tended to be higher and serum BC values showed a reduced risk of AG. Some studies found that green-yellow vegetables rich in BC reduced the risk both of AG and HP infection (Kato, et al., 1992; Tsugane et al., 1993). AG with HP infection might have been due in part to the oxidative reaction since BC acts as an antioxidant (Burton and Ingold, 1984; Bendich and Olsen, 1989; Farinati et al., 1994; Sanjose et al., 1996).

Moreover, GLA is found in abundance in plant seed oils, such as evening primrose, blackcurrant and borage, and is metabolized from LNA to DLA (Das, 1990; Fan and Chapkin, 1998). In the present study, serum GLA values were associated with a reduced risk of AG, especially in HP-infected individuals. Furthermore, n-6PUFAs, such as LNA also correlated with a reduced, but not significant, risk of AG.

The consumption of borage rich in GLA is reported to reduce the risk of gastric cancer (Gonzalez et al., 1993) and inhibits cell growth in colon cancer (Johnson et al., 1997). GLA exerts an anti-inflammatory effect and inhibits both motility and invasiveness of colon cancer cells by increasing the expression of E-cadherin (a suppressor of metastasis) (Jiang et al., 1995). Moreover, GLA reduces tumor-endothelium adhesion and suppresses the tumor growth in vivo (Hrelia et al., 1996). Although further research is needed to clarify the detailed protective mechanism against AG, especially in HP infection, the results in the present study support the notion that a high intake of foods rich in n6-PUFAs such as GLA might play a role in the reducing the risk of AG concomitant with HP infection. These results suggest that high incidence of gastric cancer for Japanese population, comparing to that for Caucasians may due in a part to lifestyle, such as high intake of fish oil and salted foods.

We also found that intakes of Cola-beverages and coffee appeared to increase the risk of AG, whereas intakes of fruit juices and oolong tea tended to reduce the risk. It appears that Cola-beverages may exert some potential physical stress, compared to fruit juices and oolong tea. Numerous reports state that alcohol consumption increases the risk of gastric cancer (Haenszel et al., 1976; Tajima and Tominaga, 1985) and the present study found that an increased consumption of alcohol, as well as coffee and heavy smoking, increased the risk of HP infection (Brenner et al., 1997). It appears that possibility of potential physical stress to stomach mucosa, may increase the risk of gastric cancer.

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personal profile: **Yoshinori Ito**