Cancer Causes and Control, 1998, **9**, pp. 209-216

Tea and coffee consumption and the risk of digestive tract cancers: data from a comparative case-referent study in Japan

M. Inoue, K. Tajima, K. Hirose, N. Hamajima, T. Takezaki, T. Kuroishi, and S. Tominaga

(Received 8 September 1997; accepted in revised form 8 December 1997)

Objectives: **The purpose of this study was to examine the hypothesis that tea and coffee consumption have a protective effect against development of digestive tract cancers.**
***Methods*: A comparative case-referent study was conducted using Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC) data from 1990 to 1995 in Nagoya, Japan. This study comprised 1,706 histologically diagnosed cases of digestive tract cancers (185 esophagus, 893 stomach, 362 colon, 266 rectum) and a total of 21,128 non-cancer outpatients aged 40 years and over. Logistic regression was used to analyze the data, adjusting for gender; age; year and season at hospital-visit; habitual smoking and alcohol drinking; regular physical exercise; fruit, rice, and beef intake; and beverage intake.**
***Results*: The odds ratio (OR) of stomach cancer decreased to 0.69 (95 percent confidence interval [CI] = 0.48-1.00) with high intake of green tea (seven cups or more per day). A decreased risk was also observed for rectal cancer with three cups or more daily intake of coffee (OR = 0.46, CI = 0.26-0.81).**
***Conclusions*: The results suggest the potential for protective effect against site-specific digestive tract cancer by consumption of green tea and coffee, although most associations are limited only to the upper category of intake and have no clear explanation for site-specificity.** *Cancer Causes and Control* 1998, **9**, 209-216

Key words: Coffee, digestive tract cancer, Japan, tea.

Introduction

Tea and coffee drinking are common worldwide, despite the internationally wide variety of drinking habits, *e.g.*, type, frequency of intake, temperature, strength, *etc.* These beverages are widely consumed by the Japanese; Of the three beverages – green tea, black tea, and coffee – green tea is most commonly consumed, followed by coffee,[1] and it is usual that two or more types of these beverages are drunk by Japanese consumers.

For both tea and coffee, experimental studies suggest inhibition of digestive tract carcinogenesis through some biologic mechanisms.[2] However, the results from the epidemiologic studies on the association between tea and coffee consumption and the risk modification of those cancers are inconsistent, and the effect of these beverages on human digestive tract cancers is still unclear.

To gain further epidemiologic evidence on this issue,

Drs Inoue and Tajima, Ms Hirose, and Drs Hamajima, Takezaki, and Kuroishi are with the Division of Epidemiology, Aichi Cancer Center Research Institute, Nagoya, Japan. Authors are also affiliated with the Aichi Cancer Center Research Institute, Nagoya, Japan (Dr Tominaga). Address correspondence to Dr Inoue, Division of Epidemiology, Aichi Cancer Center Research Institute, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681 Japan. *This work was funded partially by Grant-in-Aid for Cancer Research (9-4) from the Ministry of Health and Welfare, Japan, and a grant from the Foundation of All Japan Coffee Association.*

we conducted a case-referent study, using a hospital outpatient population in Japan. The purpose of this study was to examine and compare the relative risk of digestive tract cancers by site, in relation to the consumption of tea and coffee, on the hypothesis that these beverages have the potential to protect against development of digestive tract cancers, particularly among the Japanese population, which is characterized by the widespread intake of green tea and coffee.

Materials and methods

The Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC) was started in Nagoya, Japan in 1988 and information on lifestyles has been collected routinely from all first-visit outpatients, using a self-administered questionnaire checked by a trained interviewer. Each patient is asked about his or her general lifestyle when healthy or before current symptoms developed. Details of the questionnaire and data procedures are described elsewhere.[3-5] The present study is based on data collected from June 1990 to June 1995.

Among all first-visit outpatients in this period (n = 38,773), the questionnaire was administered to 35,497 (91.6 percent). The remaining 3,276 (8.4 percent) were excluded for one of the following reasons: young age (under 18 years old) (420 patients); missed by the interviewer (2,261 patients); or because someone other than the patient discussed the patient's condition with the physician (595 patients). Of the 35,497 outpatients, 34,661 (97.1 percent) provided an adequate response to the questionnaire. Among them, 5,225 newly diagnosed cancer patients (15.1 percent) were identified through the hospital cancer registry system.

In the present study, subjects who were under 40 years old at the time of first hospital-visit were excluded, because those cancers which occur in humans under 40 years of age were suggested to be more affected by host-related factors than environmental factors. Consequently, the referent group comprised 21,128 non-cancer outpatients aged 40 years and over (6,307 males and 14,821 females) who had their first hospital-visit during this period (June 1990-June 1995) and were confirmed to be cancer-free by diagnostic procedure at Aichi Cancer Center Hospital (ACCH), and had no history of cancer. We assessed the clinical diagnosis among non-cancer outpatients in the previous study[4] and confirmed that 44 percent presented with no abnormal findings by examination and 35 percent presented with non-specific diseases.

All patients with incident digestive tract cancer were identified *via* the hospital cancer registry system using ICD-9[6] code (esophagus, code 150; stomach, code 151; colon, code 153; rectum, code 154), and in which each case was confirmed on the basis of both clinical and pathologic examination at ACCH between June 1990 and June 1995. Consequently, 185 patients with esophageal cancer (161 males and 24 females), 893 with stomach cancer (613 males and 280 females), 362 with colon cancer (213 males and 149 females), and 266 with rectal cancer (173 males and 93 females) were recruited as cases in the present study.

The questionnaire included items on demographic characteristics, medical history, family history, habitual smoking and alcohol drinking, regular physical exercise, reproductive history (females only), bowel habits, health screenings, and dietary habits. Information on green tea, coffee, and black tea consumption was obtained in terms of frequency and amount of intake (everyday [number of cups/day], occasionally, rarely).

All analyses were conducted separately by each site of digestive tract cancers. Odds ratios (OR) and their 95 percent confidence intervals (CI) were estimated using unconditional logistic regression. To control for potential confounding factors for each site of digestive tract cancers, we carried out multivariate analyses. Demographic and lifestyle features were compared for referent subjects across the categories of each beverage consumption, to consider possible confounding factors, as well as the factors reported to predict the risk of digestive tract cancers. All three beverage types are entered in the model to estimate independent risks, using categories as follows, according to the distribution of each beverages; green tea intake (rarely, occasional, everyday [1-3 cups, 4-6 cups, 7+ cups]), coffee intake (rarely, occasional, everyday [1-2 cups, 3+ cups]), and black tea intake (rarely, occasional, everyday). These beverage categories were entered as scored variables in the logistic model when testing for linear trend. All models further adjusted for following variables, because these variables substantially altered the risk estimates of the beverages in the logistic model: gender (male, female); age at first hospital-visit (years, continuous); year (continuous) and season (spring [March-May], summer [June-August], autumn [September-November], winter [December-February]) at first hospital-visit; habitual smoking (nonsmoker, current smoker, ex-smoker); habitual alcohol drinking (non-drinker, current drinker, ex-drinker); regular physical exercise (< 2×/week, 2+×/week); fruit intake (< everyday, ≥ everyday); rice intake (< 3 bowls/day, 3+ bowls/day), beef intake (< 3-4×/week, 3-4+×/week). Procedure LOGISTIC from SAS[7] was used to perform the calculation.

Results

Table 1 shows mean age and distribution of green tea, black tea, and coffee consumption among cases by each

Table 1. Age (yrs) at first hospital-visit, and distribution (percent[a]) of green tea, coffee, and black tea consumption among cases of esophageal, stomach, colon, and rectal cancer and referent groups by gender; Japan

Variable	Males					Females				
	Referent group (*n* = 6,307)	Cases				Referent group (*n* = 14,821)	Cases			
		Esophagus (*n* = 161)	Stomach (*n* = 613)	Colon (*n* = 213)	Rectum (*n* = 173)		Esophagus (*n* = 24)	Stomach (*n* = 280)	Colon (*n* = 149)	Rectum (*n* = 93)
Age (yrs) at first hospital-visit (mean ± SD)	55.8 (± 9.9)	61.1 (± 9.5)	61.7 (± 9.6)	62.1 (± 9.0)	59.1 (± 9.8)	52.0 (± 9.1)	62.1 (± 9.8)	59.6 (± 10.2)	60.0 (± 10.1)	60.9 (± 9.1)
Beverage consumption										
Green tea (Japanese tea)										
Rarely	5.5	6.8	5.5	7.0	3.5	5.9	8.3	6.8	7.4	5.4
Occasional	11.7	12.4	11.9	9.4	9.8	11.3	8.3	9.3	8.1	15.1
Daily	82.9	80.7	82.4	83.6	86.1	82.6	83.3	83.9	83.9	79.6
1-3 cups/day	40.1	41.0	38.7	33.3	33.5	36.2	45.8	33.6	32.2	29.0
4-6 cups/day	31.4	28.0	34.7	37.1	39.9	34.9	20.8	38.9	37.6	37.6
7+ cups/day	11.4	11.8	9.0	13.1	12.7	11.5	16.7	11.4	14.1	12.9
Status unknown	0.2	0.0	0.2	0.0	0.6	0.1	0.0	0.0	0.7	0.0
Coffee										
Rarely	20.2	28.0	24.3	29.1	24.3	23.8	37.5	35.0	34.2	38.7
Occasional	17.7	14.9	18.4	17.8	18.5	20.7	25.0	21.8	20.8	19.4
Daily	61.9	57.1	57.1	53.1	56.6	55.4	37.5	43.2	45.0	41.9
1-2 cups/day	44.7	43.5	43.4	43.7	46.8	44.5	25.0	33.9	37.6	40.9
3+ cups/day	17.2	13.7	13.7	9.4	9.8	10.9	12.5	9.3	7.4	1.1
Status unknown	0.1	0.0	0.2	0.0	0.6	0.1	0.0	0.0	0.0	0.0
Black tea (English tea)										
Rarely	74.0	85.1	76.0	71.8	72.3	63.2	79.2	71.1	59.7	58.1
Occasional	20.6	7.5	17.5	22.1	23.7	29.3	20.8	23.6	28.9	29.0
Daily	5.0	6.2	5.7	5.6	3.5	7.2	0.0	5.4	11.4	9.7
1-2 cups/day	4.7	5.6	5.5	4.7	2.9	6.7	0.0	5.4	10.1	9.7
3+ cups/day	0.3	0.6	0.2	0.9	0.6	0.4	0.0	0.0	1.3	0.0
Status unknown	0.4	1.2	0.8	0.5	0.6	0.4	0.0	0.0	0.0	3.2

[a] All percent values were rounded to one decimal place.

Table 2. Distribution (percent) of selected demographic and lifestyle factors by green tea, coffee, and black tea consumption among referent groups, Japan

Variable	Green tea (Japanese tea)					Coffee				Black tea (English tea)			
	Rarely	Occasional	Daily (cups/day)			Rarely	Occasional	Daily (cups/day)		Rarely	Occasional	Daily (cups/day)	
			1-3	4-6	7+			1-2	3+			1-2	3+
Males (*n* = 6,307)													
Age (yrs)													
40-49	41.6	39.1	35.8	25.1	21.9	18.8	22.3	33.0	52.2	30.2	35.2	35.5	55.0
50-59	25.6	31.5	31.2	34.4	34.7	28.3	32.5	33.4	34.1	33.0	31.4	28.4	20.0
60+	32.8	29.4	33.0	40.5	43.4	52.9	45.2	33.6	13.7	36.8	33.4	36.1	25.0
Habitual smoking													
Current smoker	42.3	44.7	45.3	40.5	45.6	26.2	31.2	46.6	68.9	45.9	37.9	32.8	30.0
Ex-smoker	38.2	32.3	33.4	37.3	36.1	43.8	40.6	34.6	20.5	34.6	34.6	42.9	45.0
Habitual alcohol drinking													
Current drinker	59.0	66.3	67.9	62.7	59.4	60.2	64.3	68.3	60.9	64.6	65.8	61.2	45.0
Ex-drinker	10.2	7.1	5.8	6.0	6.3	10.2	6.5	4.8	5.4	6.7	4.9	5.7	15.0
Physical exercise													
2+/week	16.0	17.2	17.3	19.4	17.7	20.8	21.7	17.5	12.1	17.7	18.2	21.4	20.0
Fruit intake													
Every day	44.5	51.8	60.3	65.2	64.5	67.8	63.6	61.1	51.1	57.2	69.2	73.7	75.0
Rice intake													
3+ bowls/day	49.4	50.6	58.6	68.2	72.4	63.8	66.2	59.7	60.1	63.3	58.2	48.7	65.0
Beef intake													
3-4+ times/week	11.7	9.7	8.2	9.4	9.2	6.5	8.6	9.4	11.5	8.5	9.8	14.2	20.0
Females (*n* = 14,821)													
Age (yrs)													
40-49	55.5	54.4	53.4	42.4	36.5	30.6	40.2	54.2	73.7	45.2	51.8	55.0	58.5
50-59	27.0	27.6	29.0	33.0	35.7	31.9	34.9	30.9	21.4	31.3	30.9	27.6	27.7
60+	17.5	18.0	17.6	24.6	27.8	37.5	24.9	14.9	4.9	23.5	17.3	17.4	13.8
Habitual smoking													
Current smoker	24.0	15.4	10.1	6.6	11.1	3.7	4.5	11.6	31.3	12.3	7.3	6.0	14.1
Ex-smoker	4.9	4.7	3.4	2.9	2.8	2.3	3.1	3.9	4.3	3.5	3.1	3.1	6.3
Habitual alcohol drinking													
Current drinker	31.1	32.2	27.7	20.9	22.4	13.7	21.4	30.4	38.9	25.0	26.3	25.6	21.5
Ex-drinker	2.8	2.2	1.1	1.2	1.6	1.9	1.6	1.1	1.7	1.5	1.2	1.7	0.0
Physical exercise													
2+/week	16.8	13.8	15.6	16.1	15.2	16.9	16.0	15.3	13.3	15.4	15.9	16.1	18.8
Fruit intake													
Every day	66.9	69.2	77.9	82.0	80.8	79.5	82.0	77.8	68.3	75.4	82.2	83.9	83.1
Rice intake													
3+ bowls/day	30.6	35.1	37.9	48.8	53.0	54.1	46.9	36.0	33.6	45.3	39.8	26.8	26.2
Beef intake													
3-4+ times/week	11.4	10.3	9.8	10.3	12.1	8.5	10.2	10.8	13.1	9.3	12.1	12.4	7.8

Table 3. Estimated odds ratio (OR) and 95% confidence intervals (CI) for the association between green tea (Japanese tea), coffee, and black tea (English tea) consumption and risk of esophageal, stomach, colon, and rectal cancer;[a] Japan

	Esophagus		Stomach		Colon		Rectum	
	OR	(CI)	OR	(CI)	OR	(CI)	OR	(CI)
Green tea (Japanese tea)								
Rarely	1.00	—	1.00	—	1.00	—	1.00	—
Occasional	1.02	(0.50-2.10)	1.00	(0.77-1.44)	0.62	(0.36-1.05)	1.41	(0.70-2.83)
Daily								
1-3 cups/day	1.07	(0.58-2.00)	0.96	(0.70-1.32)	0.64	(0.42-1.00)	1.04	(0.55-1.98)
4-6 cups/day	0.96	(0.50-1.83)	1.01	(0.74-1.39)	0.76	(0.49-1.17)	1.42	(0.75-2.69)
7+ cups/day	1.14	(0.55-2.34)	0.69[b]	(0.48-1.00)	0.77	(0.47-1.26)	1.25	(0.62-2.51)
Coffee								
Rarely	1.00	—	1.00	—	1.00	—	1.00	—
Occasional	0.82	(0.51-1.31)	0.91	(0.74-1.13)	0.83	(0.61-1.14)	0.77	(0.53-1.11)
Daily								
1-2 cups/day	0.77	(0.52-1.12)	0.88	(0.73-1.05)	0.97	(0.74-1.27)	0.91	(0.67-1.24)
3+ cups/day	0.79	(0.46-1.36)	0.93	(0.72-1.21)	0.87	(0.56-1.35)	0.46[b]	(0.26-0.81)
Black tea (English tea)								
Rarely	1.00	—	1.00	—	1.00	—	1.00	—
Occasional	0.44[b]	(0.26-0.74)	0.92	(0.76-1.10)	1.21	(0.94-1.57)	1.26	(0.94-1.69)
Daily	1.03	(0.53-2.00)	1.09	(0.80-1.49)	1.59[b]	(1.06-2.37)	1.16	(0.67-1.98)

[a] Model includes green tea intake, coffee intake, black tea intake, gender, age, year and season at first hospital-visit, habitual smoking, habitual alcohol drinking, regular physical exercise, fruit intake, rice intake, and beef intake.
[b] $P < 0.05$.

site and referent group. More than 80 percent of referent subjects and cases of each site consume green tea every day; however, less than 10 percent of these same subjects consume black tea everyday. Approximately 60 percent of subjects consume coffee everyday, and the percentage of everyday drinkers of coffee tended to be higher in males than in females. Because of the small number of subjects who drink black tea everyday, we did not conduct an analysis by daily intake of black tea.

Table 2 shows distribution of demographic and lifestyle factors across the categories of each beverage consumption among referent group. The subjects who consume high quantities of green tea tended to be older and take fruit and rice more frequently than the subjects who consume low quantities. On the other hand, the subjects who consume high quantities of coffee tended to be younger, be more current smokers, exercise and take fruit and rice less frequently, and take beef more frequently than the subjects who consume low quantities of coffee. The subjects with black tea tended to be younger, be more nonsmokers, and take fruit and beef more frequently than the subjects with low intake of black tea.

Table 3 shows the adjusted ORs and CIs of the association between green tea, coffee, and black tea consumption, and risk by site of digestive tract cancers – controlling for gender; age; year and season at first hospital-visit; habitual smoking and alcohol drinking; regular physical exercise; fruit, rice, and beef intake; and consumption of each beverage. For all types of beverage, the category 'rarely' is used as the reference category. The OR of stomach cancer decreased statistically significantly among those who drank seven or more cups of green tea per day (OR = 0.69, CI = 0.48-1.00). Slightly decreased risk was observed for esophageal and stomach cancer, and OR of rectal cancer decreased only among those who drank three or more cups of coffee daily (OR = 0.46, CI = 0.26-0.81). The OR of esophageal cancer decreased statistically significantly among occasional black-tea drinkers (OR = 0.44, CI = 0.26-0.74). Daily intake of black tea moderately increased the risk of colon cancer (OR = 1.59, CI = 1.06-2.37). Regarding confounding factors, increased risk was observed for esophageal and stomach cancer in both current and ex-smoking categories, esophageal cancer in current and ex-alcohol drinking categories, and stomach and colon cancer in the ex-alcohol drinking category, and a decreased risk was observed for cancer at all sites with regular physical exercise and fruit intake.

Discussion

Tea, especially green tea, is one of the most common beverages in Japan. Experimental studies have demonstrated inhibitory effects on carcinogenesis by tea polyphenols, which suggest the protective effect of tea consumption against human digestive tract cancers.[2]

Association between tea drinking and esophageal cancer differs with tea drinking habits. A positive association was observed between tea drinking and esophageal cancer when tea was consumed in very hot temperature.[8-11] These studies suggest that consumption of tea of high temperature rather than tea itself increases the risk of esophageal cancer, and that tea itself still has an inhibitory effect on carcinogenesis of the esophagus. There was no association between the drinking of green tea and esophageal cancer in the present study. We did not take into account the temperature of the tea consumed due to the lack of information in the questionnaire. It is, therefore, possible that the estimated ORs are attenuated by these opposite effects of tea. On the other hand, the present study showed decreased risk of esophageal cancer by occasional black tea intake. The difference of the effect of black tea between rarely and occasional intake does not seem to be considerable, and the result may be partly due to chance.

An inverse association between tea and stomach cancer has been observed in previous studies, especially in large quantity consumption.[12-17] The present study also shows only lowered risk with fairly high consumption of green tea (7+ cups/day), and not in lower green tea intake or in daily intake of black tea. These results are consistent with a study in Japan[15] which utilized a study population with similar characteristics in terms of stomach cancer incidence and tea consumption. Inconsistency in the results of other studies seems to be partly due to the difference in the definition of tea drinker in each study.

The association between tea consumption and colorectal cancers has been examined in previous studies, but the results are inconsistent thus far.[14,18-22] Like two previous studies in Japan,[14,20] the present study shows no increased or decreased risk of colon and rectal cancers by green tea intake, but only an increased risk of colon cancer among drinkers of black tea. It is true that there are not enough black-tea drinkers among Japanese population compared with green-tea drinkers to examine whether it is related to cancer risk. One possibility is that drinkers of black tea in our study population have more Westernized lifestyles, such as diet, which increases the risk of colon and rectal cancers which occurs more in Western countries.

The association between coffee consumption and digestive tract cancers has been discussed mainly in Western countries. Coffee drinking is not as popular as green tea drinking in Japan, although about 85 percent of Japanese[1] and 60 percent of our study population aged 40 years and over drink coffee daily, but in lesser quantities than green tea. Thus far, no association has been found between coffee consumption and stomach cancer[14,23,24] and/or esophageal cancer except in a study documenting a population which drinks coffee at very high temperatures.[10] In this study, we found a decreased risk of rectal cancer with no increased or decreased risk of colon cancer in those who consumed high quantities of coffee (3+ cups/day). There are contradictory findings in previous studies.[14,20,23-29] The biologic mechanism of the protective effects of coffee has been explained in the anti-oxidants, reduction of the excretion of bile acid by increasing serum cholesterol level in the bowel,[30,31] and the inhibition of carcinogenesis by caffeine.[32,33] Yet, the effect of coffee on the digestive tract is still unclear, to say nothing of the site-specificity of the effect.

An important methodologic issue may be selection bias derived from discrepant characteristics between the general population and outpatients. We performed a validation study to evaluate this issue[3] and confirmed that lifestyle differences were small between outpatients and the general population after adjustment for age, gender, and season. Also, there were no meaningful differences between outpatients and the general population in tea and coffee consumption. In this study, therefore, we controlled those potential confounding factors by statistical modeling at the analysis stage. Another aspect of selection bias derived from the low response rate followed by selection bias among outpatients. Among the eligible outpatient subjects, response rate of the questionnaire was 97 percent, reducing the possibility of this bias. Unfortunately, we did not include questions on socioeconomic status in our questionnaire, because Japanese are rather reluctant to answer such questions. It generally is acknowledged that majority of Japanese are socioeconomically middle-class.

Another methodologic issue may be information bias. Questionnaires were administered and checked by a single trained interviewer in order to exclude inter-interviewer variation. Further, we conducted the questionnaire study before the patients' diseases were identified, and thus were able to keep recall bias low between cases and referent group.

Even reducing these biases as much as possible, the most crucial issue in conducting case-referent studies using the Japanese population, and regarding exposure to such habits as tea and coffee drinking, is that a substantially high proportion of Japanese are already exposed to these beverages, especially green tea. This common ecologic feature in the study base leads us to underestimate the strength of association and thus the effect might not be marked even if it exists. Further, it is quite common in Japan that two or more types of these beverages are consumed by each person, and, in fact, the beverage drunk can easily alternate on every occasion. This condition made it more difficult for us to deal with the interaction of each beverage and to perform appropriate analyses to control for the effect of each beverage intake, even if we obtained the precise information on them.

We could not estimate the ORs by further detail of

drinking habits such as temperature and strength, because of the lack of information in the questionnaire; this was a limitation of the present study. Temperature of the beverage taken especially affects the risk to the upper part of the digestive tract, and a detailed study suggests the possible effect of the strength of these beverages.[16] The analyses of the above aspects of drinking habits might give us clearer results for understanding the effects of tea and coffee on digestive tract carcinogenesis.

In summary, we observed site-specific risk modification by each beverage: risk reduction of stomach cancer by high consumption of green tea (7+ cups/day) and of rectal cancer by coffee (3+ cups/day), and increased risk of colon cancer by the daily consumption of black tea. However, these associations are limited only to the upper category of intake, and we have no clear explanation for site-specificity. Our results provide some epidemiologic clue for understanding the effect of tea and coffee on digestive tract cancers, but further studies are needed to clarify the plausible effect of these beverages on human cancer.

Acknowledgments — The authors are grateful to all the doctors, nurses, technical staff, and hospital business staff of ACCH for their daily administration of the HERPACC study. They also thank Mss Hiroko Fujikura, Yukiko Yamauchi, Takako Kuno, Etsuko Kimura, and Michiyo Takasaki for their technical assistance, and Mr Erick C. Ubels for his linguistic support.

References

1. International Agency for Research on Cancer. Coffee, tea, mate, methylxanthines, and methylgloxyal. Lyon, France: IARC, 1991; *IARC Monogor Eval Carcinog Risk Hum*, **51**: 41-271.
2. Yang CS, Wang ZY. Tea and cancer. *J Natl Cancer Inst* 1993; **85**: 1038-49.
3. Inoue M, Tajima K, Hirose K, *et al*. Epidemiological features of first-visit outpatients in Japan: Comparison with general population and variation by sex, age, and season. *J Clin Epidemiol* 1997; **50**: 69-77.
4. Inoue M, Tajima K, Hirose K, *et al*. Subsite-specific risk factors for colorectal cancers: a hospital-based case-control study in Japan. *Cancer Causes Control* 1995; **6**: 14-22.
5. Inoue M., Tajima K, Hirose K, Kuroishi T, Gao CM, Kito T. Life-style and subsite of gastric cancer – joint effect of smoking and drinking habit. *Int J Cancer* 1994; **56**: 494-9.
6. World Health Organization. *International Classification of Diseases, 9th Revision*. Geneva, Switzerland: WHO, 1977.
7. SAS Institute Inc. *SAS/STAT User's Guide, Version 6*. Cary, NC (USA): SAS Inst Inc, 1990.
8. Gao YT, McLaughlin JK, Blot WJ, Ji BT, Dai Q, Fraumeni Jr JF. Reduced risk of esophageal cancer associated with green tea consumption. *J Natl Cancer Inst* 1994; **86**: 855-8.
9. Ghadirian P. Thermal irritation and esophageal cancer in northern Iran. *Cancer* 1987; **60**: 1909-14.
10. De Jong UW, Breslow N, Goh Ewe Hong J, Sridharan M, Shanmugaratnam K. Aetiological factors in oesophageal cancer in Singapore Chinese. *Int J Cancer* 1974; **13**: 291-303.
11. Segi M. Tea-gruel as a possible factor for cancer of the esophagus. *Gann* 1975; **66**: 199-202.
12. Yu GP, Hsieh C-c. Risk factors for stomach cancer: a population-based case-control study in Shanghai. *Cancer Causes Control* 1991; **2**: 169-74.
13. Ji BT, Chow WH, Yang G, *et al.* The influence of cigarette smoking, alcohol, and green tea consumption on the risk of carcinoma of the cardia and distal stomach in Shanghai, China. *Cancer* 1996; **77**: 2449-57.
14. Tajima K, Tominaga S. Dietary habits and gastro-intestinal cancers: a comparative case-control study of stomach and large intestinal cancers in Nagoya, Japan. *Jpn J Cancer Res* 1985; **76**: 705-16.
15. Kono S, Ikeda M, Tokudome S, Kuratsune MA. Case-control study of gastric cancer and diet in Northern Kyushu, Japan. *Jpn J Cancer Res* 1988; **79**: 1067-74.
16. Yu GP, Hsieh C-c, Wang LY, Yu SZ, Li XL, Jin TH. Green tea consumption and risk of stomach cancer: a population-based case-control study in Shanghai, China. *Cancer Causes Control* 1995; **6**: 532-8.
17. Hansson LE, Nyren O, Bergstrom R, Lindgrem A, Baron J, Adami HO. Diet and risk of gastric cancer. A population-based case-control study in Sweden. *Int J Cancer* 1993; **55**: 181-9.
18. Heilbrum LK, Nomura A, Stemmermann GN. Black tea consumption and cancer risk: a prospective study. *Br J Cancer* 1986; **54**: 677-83.
19. Kinlen LJ, Willows AN, Goldblatt P, Yudkin J. Tea consumption and cancer. *Br J Cancer* 1988; **58**: 397-401.
20. Kato I, Tominaga S, Matsuura A, Yoshii Y, Shirai M, Kobayashi S. A comparative case-control study of colorectal cancer and adenoma. *Jpn J Cancer Res* 1990; **81**: 1101-8.
21. Baron JA, Gerhardsson de Verdier M, Ekbom A. Coffee, tea, and cancer of the large bowel. *Cancer Epidemiol Biomarkers Prev* 1994; **3**: 565-70.
22. Ji BT, Chow WH, Hsing AW, *et al.* Green tea consumption and the risk of pancreatic and colorectal cancers. *Int J Cancer* 1997; **70**: 255-8.
23. Nomura A, Heilbrum LK, Stemmermann GN. Prospective study of coffee consumption and the risk of cancer. *J Natl Cancer Inst* 1986; **76**: 587-90.
24. La Vecchia C, Ferraroni M, Negri E, *et al.* Coffee consumption and digestive tract cancers. *Cancer Res* 1989; **49**: 1049-51.
25. La Vecchia C, Negri E, Decarli A, *et al*. Case-control study of diet and colo-rectal cancer in Northern Italy. *Int J Cancer* 1988; **41**: 492-8.
26. Benito E, Obrado A, Stiggelbout A, *et al*. Population-based case-control study of colorectal cancer in Majorca. I. Dietary factors. *Int J Cancer* 1990; **45**: 69-76.
27. Jarebinski M, Adanja B, Vlajinac H. Case-control study of relationship of some biosocial correlates to rectal cancer patients in Belgrade, Yugoslavia. *Neoplasma* 1989; **36**: 369-74.
28. Slattery ML, West DW, Robison LM, *et al.* Tobacco, alcohol, coffee and caffeine as risk factors for colon cancer in a low-risk population. *Epidemiology* 1990; **1**: 141-5.
29. Kotake K, Koyama Y, Nasu J, Fukutomi T, Yamagushi N. Relation of family history of cancer and environmental factors to the risk of colorectal cancer: a case-control study.

Jpn J Clin Oncol 1995, **25**: 195-202.

30. Rosenberg L. Coffee and tea consumption in relation to the risk of large bowel cancer: a review of epidemiologic studies. *Cancer Lett* 1990, **52**: 163-71.
31. Jacobsen B, Thelle, DS. Coffee, cholesterol, and colon cancer: is there a link? *Br Med J* 1987; **294**: 4-5.
32. Nomura T. Diminution of tumorigenesis initiated by 4-nitro-quinoline-1-oxide by post treatment with caffeine in mice. *Nature* 1976; **260**: 547-9.
33. Petrek JA, Sanberg WA, Cole MN, Silberman MS, Collins DC. The inhibitory effect of caffeine on hormone-induced rat breast cancer. *Cancer* 1985; **56**: 1977-81.