3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

(*a*) *Subcutaneous administration*

Rat: Groups of 15 male and 15 female NIH Black rats, one to two months of age, received weekly subcutaneous injections of 12 mg of the total aqueous extract or 8 mg of the tannin fraction of Assam tea leaf alternately into each flank for 69-70 weeks (extract) or 45-77 weeks (fraction). A group of 15 male and 15 female controls received injections of saline. Whereas a high number of local tumours (malignant fibrous histiocytomas) developed in the rats receiving the tannin fraction (10/15 males and 11/15 females), a nonsignificant number of local tumours developed in rats treated with the aqueous extract (1/15 males and 1/15 females). No local tumour developed in the controls (Kapadia *et al.*, 1976).

(*b*) *Administration with known carcinogens*

(i) *Polycyclic aromatic hydrocarbons*

Mouse: A group of 15 young Swiss mice [sex unspecified] received a single skin application in the neck region of a 1% solution of benzo[*a*]pyrene in acetone,

followed by applications of black tea solution (1 g tea brewed for 5 min in 155 ml boiling water) on alternate days for 55 paintings. A control group of 15 mice received benzo[*a*]pyrene alone. [The duration of the study was not stated]. In the group treated with benzo[*a*]pyrene and tea, 6/15 mice developed epithelial-cell carcinomas in the neck region. Other mice in this group developed various preneoplastic lesions of the squamous epithelium. No skin lesion was observed in the group treated with benzo[*a*]pyrene alone (Kaiser, 1967). [The Working Group noted the absence of an appropriate control group and the inadequate reporting of histological findings.]

Two groups of 25 male and 25 female Charles River CD-1 random-bred albino mice, six weeks old, were treated with a single application of 50 µl of a 1% solution of benzo[*a*]pyrene (0.53-0.6 mg benzo[*a*]pyrene) in acetone on the shaved interscapular area. One group received no further treatment and served as controls. The other group received 80 applications three times per week of an infusion of black Chinese (Keemun) tea containing 1% tannin. Mice were observed for 567-580 days, at which time all survivors were killed. Survival was similar in both groups. The incidence of hepatomas was 10% in the group receiving benzo[*a*]pyrene alone and 6% in the group also given tea. Skin tumour occurrence in the interscapular area was similar in both groups: the incidences of benign and malignant (carcinomas) tumours in the group given benzo[*a*]pyrene were 15/50 and 2/50, respectively; those in animals also given tea were 15/50 and 3/50, respectively. In the group treated with benzo[*a*]pyrene plus tea, skin tumours occurred significantly earlier than in those given benzo[*a*]pyrene alone (Bogovksi *et al.*, 1977).

Eight groups of 20 female Sencar mice, six weeks old, were pretreated with plant phenols (tannic acid or quercetin; 3000 nmol), green tea polyphenols (24 mg/mouse) or acetone for seven days, after which they received a single topical application of 200 nmol (±)-7β,8α-dihydroxy-9α,10α-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene as the initiating agent or acetone. Beginning seven days after initiation, animals received applications of 3.24 nmol 12-*O*-tetradecanoylphorbol 13-acetate three times per week until termination of the experiment at 18 weeks. The formation of skin tumours [probably papillomas] > 1 mm in diameter and persisting for two weeks or more was recorded weekly and included in the cumulative total. Tannic acid and green tea phenols afforded significant protection ($p < 0.01$) against the induction of skin tumours; quercetin gave only moderate protection (Khan *et al.*, 1988).

Four groups of 20 female BALB/c mice, six weeks of age, were painted on shaved dorsal skin as follows: Group 1 received 0.2 ml acetone daily for seven days then 0.2 ml acetone twice weekly for 16 weeks; Group 2 received acetone daily for seven days and then 3-methylcholanthrene twice weekly for 16 weeks; Group 3 received 1.2 mg green tea polyphenols in acetone daily for seven days and then

3-methylcholanthrene in acetone 1 h following the green tea polyphenols twice weekly for 16 weeks; Group 4 received green tea polyphenols daily for seven days and then green tea polyphenols 1 h following acetone twice weekly for 16 weeks, at which time the experiment was terminated. The number of skin tumours > 1 mm in diameter and persisting for two weeks or more was 11.6 ± 0.5 in mice receiving 3-methylcholanthrene (Group 2) as compared with 5.8 ± 0.9 in those pretreated with green tea polyphenols followed by 3-methylcholanthrene (Group 3). In a parallel experiment, protection by green tea polyphenols was obtained in female Sencar mice pretreated by topical application or in the drinking-water against initiation by 7,12-dimethylbenz[*a*]anthracene or promotion by 12-*O*-tetradecanoyl phorbol 13-acetate; i.e., there was a longer latent period and 28.8 ± 1.7 or 29.1 ± 3.7 *versus* 51.3 ± 3.6 tumours per animals. Green tea polyphenols did not initiate skin tumours. Furthermore, when administered topically or orally, they significantly inhibited polycyclic aromatic hydrocarbon-DNA adduct formation in epidermis after topical administration of ^{3}H-7,12-dimethylbenz[*a*]anthracene or ^{3}H-benzo[*a*]-pyrene (Wang *et al.*, 1989a).

(ii) N-*Nitroso compounds*

Mouse: Thirty-one male C57Bl/6 mice, eight weeks of age, received 100 mg/l *N*-ethyl-*N'*-nitro-*N*-nitrosoguanidine in the drinking-water for four weeks; 15 animals subsequently received 0.005% epi-gallocatechin gallate (the main polyphenolic constituent of green tea infusion) in the drinking-water for 11 weeks; 16 animals received tap-water only for 11 weeks. All mice were sacrificed in the 16th week after the start of treatment with the nitrosamide. The incidences of duodenal tumours were 3/15 (20%) in the group receiving epi-gallocatechin gallate and 10/16 (63%; $p < 0.001$) in the group treated with the nitrosamide alone. Similar results were obtained when the experiment was repeated (Fujita *et al.*, 1989).

3.2 Other relevant data

(*a*) *Experimental systems*

(i) *Absorption, distribution, metabolism and excretion*

No data were available to the Working Group.

(ii) *Toxic effects*

Green and black teas have been reported to decrease significantly the activity of transketolase in whole blood of rats. The activity of liver transketolase was decreased by green tea only. Neither type of tea had any effect on the activity of intestinal transketolase. The activity of lactate dehydrogenase was not affected by the teas, while both green and black teas decreased the activity of lactate

dehydrogenase in whole blood. Neither tea had an effect on intestinal alkaline phosphatase, but thiamine diphosphatase activity was decreased by both teas (Ali *et al.*, 1989).

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects*

The genetic and related effects of tea have been reviewed (Sugimura, 1982; Sugimura & Sato, 1983; Nagao *et al.*, 1986).

Tea has been studied in experimental genetic and related systems following preparation by various methods (Nagao *et al.*, 1979; Uyeta *et al.*, 1981), including adding water at various temperatures to tea leaves, followed by decanting or filtering the solution. Variations included the use of different types of tea, water:leaf ratios and steeping times. The tea beverage was evaporated and the residue redissolved in a solvent (e.g., dimethylsulfoxide) for testing. The doses are expressed either as the original weight of tea leaves from which the extract was obtained or as the original volume of the tea beverage (infusion). Tea preparations were hydrolysed by various methods (e.g., acid, enzymes or bacteria), the hydrolysates extracted with organic solvents, the solvents evaporated and the residue redissolved in a solvent (e.g., dimethylsulfoxide) suitable for genetic assays.

Several studies addressed the nature of the components of green and black tea that are mutagenic to bacteria. Mutagenic activity suppressed by catalase may be attributed in part to hydrogen peroxide (Ariza *et al.*, 1988) and dicarbonyls present in tea (Nagao *et al.*, 1986). In addition, tea has been shown to contain precursors (flavonoid glycosides) of mutagenic flavonols (e.g., kaempferol, quercetin and myricetin) which are released when the tea is treated to produce hydrolysates. In these studies, treatment of dried teas with acid, glycosidase enzymes (e.g., hesperidinase) or bacteria (e.g., human intestinal bacteria) increased their mutagenic activity in *Salmonella typhimurium* TA98 and TA100, especially when an exogenous metabolic activation system was added (Nagao *et al.*, 1979; Uyeta *et al.*, 1981).

The results described in this section are listed at the end, in Table 19, with the evaluation of the Working Group, as positive, negative or inconclusive, as defined in the footnotes. The results are tabulated separately for the presence and absence of an exogenous metabolic system. The lowest effective dose (LED), in the case of positive results, or the highest ineffective dose (HID), in the case of negative results, are shown, together with the appropriate reference. The studies are summarized briefly below.

Black tea: Black teas were mutagenic to *S. typhimurium*. Oolong, Lapsang Souchong and jasmine teas inhibited DNA synthesis in cultured lymphocytes (Yang *et al.*, 1979).

Green tea: Green teas were mutagenic to *S. typhimurium*. An antioxidant fraction of green tea did not affect gap-junctional intercellular communication in cultured mouse hepatocytes and human keratinocytes.

Japanese green tea was found to contain a considerable amount of epi-gallocatechin gallate; this tannin effectively reduced the spontaneous mutation rate in NIG 1125 *Bacillus subtilis* carrying a mutation in DNA-polymerase III, but failed to lower the frequency of chemically or ultra-violet radiation-induced reverse mutations in *S. typhimurium* or *Escherichia coli* (Kada *et al.*, 1985).

Unspecified teas: Tea (Horniman's brand, puchased in Córdoba, Spain [unspecified as black or green, but probably black]) was mutagenic to *S. typhimurium* TA104 in the histidine reversion assay and to *S. typhimurium* BA13 in the arabinose-resistance forward mutation assay.

Tea in combination with other agents: Both green and black teas decreased the mutagenic activity of *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine in *E. coli* and *S. typhimurium* TA100, both *in vitro* and in an in-vivo/in-vitro assay in which the gastric contents of rats were sampled and tested 1 h after oral administration of the nitrosamide either alone or with tea extracts (Jain *et al.*, 1989a).

Green tea and black tea decreased the mutagenic activity of nitrosation products of methylurea and salted fish in *S. typhimurium* TA1535 (Stich *et al.*, 1982a,b) and decreased the mutagenic activity of benzo[*a*]pyrene in *S. typhimurium* TA100 (Joner & Dommarsnes, 1983). Both Oolong and green teas similarly decreased the mutagenicity induced by benzo[*a*]pyrene in *S. typhimurium*; and the frequency of chromosomal aberrations induced by benzo[*a*]pyrene in Chinese hamster lung (CHL) cells was decreased by the addition of Oolong tea (Kojima *et al.*, 1989). Oolong tea also decreased the mutagenicity induced in *S. typhimurium* by gasoline vehicle exhaust, cooked salmon, 1,6-dinitropyrene, 3-amino-1-methyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-2) and 2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ) (Kojima *et al.*, 1989).

The frequency of chromosomal aberrations in rat bone marrow following intraperitoneal injection of aflatoxin B_1 was reduced by hot-water extracts of green tea but not of black tea. This effect was observed when the teas were administered 24 h before the aflatoxin, and was attributed to green tea tannins (Ito *et al.*, 1989).

An antioxidant fraction from green tea containing catechins prevented the inhibition of gap-junctional intercellular communication induced by paraquat, glucose oxidase and phenobarbital in mouse hepatocytes, and by 12-*O*-tetradecanoylphorbol 13-acetate in human keratinocytes (Ruch *et al.*, 1989).

Green tea and polyphenols from green tea inhibited the mutagenicity of benzo[*a*]pyrene, aflatoxin B_1, 2-aminofluorene and coal-tar pitch in *S. typhimurium* TA100 and/or TA98. The polyphenols from green tea also inhibited aflatoxin B_1-induced mutations, decreased sister chromatid exchange and chromosomal aberrations in V79 cells and inhibited benzo[*a*]pyrene-induced mutations in V79 cells (Wang *et al.*, 1989b).

In one study, green tea and black tea reduced the induction of anchorage-independent growth of mouse epidermal JB6 cells by 12-*O*-tetradecanoylphorbol 13-acetate (Jain *et al.*, 1989b).

(*b*) *Humans*

(i) *Absorption, distribution, metabolism and excretion*

No data were available to the Working Group.

(ii) *Toxic effects*

In a number of studies in which coffee drinking was associated with increased serum cholesterol levels, participants who consumed tea showed either no association or a negative correlation with serum cholesterol levels (Arab *et al.*, 1983; Haffner *et al.*, 1985; Klatsky *et al.*, 1985; Curb *et al.*, 1986; Green & Jucha, 1986; Little *et al.*, 1986; Tuomilehto *et al.*, 1987).

Several studies, including the Boston Collaborative Drug Surveillance Program (1972), that showed a correlation between coffee consumption and the risk of coronary heart disease (see p. 104) showed no difference between patients and controls for tea drinking (Jick *et al.*, 1973; Rosenberg *et al.*, 1980).

Cases of asthma due to sensitivity to tea dust have been reported in workers who process tea in the tea industry (Lewis & Morgan, 1989).

A positive association between the consumption of tea and other caffeine-containing beverages and the premenstrual syndrome was suggested (Rossignol, 1985; Rossignol *et al.*, 1989). [The Working Group noted the limitation of the methodology and the small number of subjects.]

(iii) *Effects on reproduction and prenatal toxicity*

No association was found between tea consumption during pregnancy and the occurrence of malformations in offspring (Rosenberg *et al.*, 1982) (for a description of the study, see the monograph on coffee, p. 105).

In a study by Berkowitz *et al.* (1982), described on p. 109, tea drinking was compared among women who had had preterm infants and women who had had full-term infants. Drinking four or more cups daily was more frequent among cases than controls (odds ratios, 1.5-2.0 in the three trimesters), but these differences were

Table 19. Genetic and related effects of black, green and unspecified teas

Test system	Results		Dose[a] LED/HID	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
Black tea				
SA0, Salmonella typhimurium TA100, reverse mutation	+	-	7500.0000[b]	Nagao et al. (1979)
SA0, Salmonella typhimurium TA100, reverse mutation	-	+	0.0000 (hydrolysate)	Nagao et al. (1979)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	0.0000 (hydrolysate)	Uyeta et al. (1981)
SA9, Salmonella typhimurium TA98, reverse mutation	-	-	0.0000 (hydrolysate)	Nagao et al. (1979)
SA9, Salmonella typhimurium TA98, reverse mutation	+	+	0.0000 (hydrolysate)	Uyeta et al. (1981)
SA9, Salmonella typhimurium TA98, reverse mutation	-	+	0.0000 (hydrolysate)	Nagao et al. (1979)
Green tea				
SA0, Salmonella typhimurium TA100, reverse mutation	+	-	8000.0000[b]	Nagao et al. (1979)
SA0, Salmonella typhimurium TA100, reverse mutation	-	+	0.0000 (hydrolysate)	Nagao et al. (1979)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	0.0000 (hydrolysate)	Uyeta et al. (1981)
SA9, Salmonella typhimurium TA98, reverse mutation	-	-	0.0000 (hydrolysate)	Nagao et al. (1979)
SA9, Salmonella typhimurium TA98, reverse mutation	+	+	0.0000 (hydrolysate)	Uyeta et al. (1981)
SA9, Salmonella typhimurium TA98, reverse mutation	-	+	0.0000	Nagao et al. (1979)
ICR, Cell communication, mouse hepatocytes in vitro	-	0	50.0000[c]	Ruch et al. (1989)
ICH, Cell communication, human keratinocytes in vitro	-	0	50.0000[c]	Ruch et al. (1989)
Tea unspecified				
SAF, Salmonella typhimurium BA13, forward mutation ara^{R}	+	0	220.0000	Alejandre-Duran et al. (1987)
SA2, Salmonella typhimurium TA102, reverse mutation	-	0	880.0000	Alejandre-Duran et al. (1987)
SA4, Salmonella typhimurium TA104, reverse mutation	+	0	880.0000	Alejandre-Duran et al. (1987)
SA5, Salmonella typhimurium BA13, reverse mutation	-	0	880.0000	Alejandre-Duran et al. (1987)

[a] Expressed as dry weight of extract
[b] Weight of material from which extract was prepared
[c] Green tea antioxidant fraction

not significant. The odds ratio was 1.6 (95% confidence interval (CI), 0.7-3.7) after adjustment for smoking and alcohol and coffee consumption.

Brooke *et al.* (1989), in a study described on p. 110, found an association between tea consumption and low birth weight in their crude data. The birthweight ratios, adjusted to 40 weeks' gestation, were 1.050, 1.043, 1.034 and 1.012 in babies born to mothers drinking 0, 1-14, 15-43 and more than 43 cups of tea per week. While the difference among the groups and the linear trend were statistically significant, no significance remained when the data were additionally adjusted for smoking.

In the papers of Watkinson and Fried (1985) and Martin and Bracken (1987) tea drinkers were included but data were not given separately. The studies of Furuhashi *et al.* (1985) and Caan and Goldhaber (1989) showed no association between tea drinking and low birth weight. (These studies are discussed on pp. 109, 110, 106 and 111.)

In a study described on p. 111, late spontaneous abortions were studied by Srisuphan and Bracken (1986) in relation to caffeine intake from various beverages including tea. Tea was apparently not associated with spontaneous abortions (crude relative risk (RR), 1.1).

(iii) *Genetic and related effects*

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of cancer in humans

In comparison with coffee, less attention has been paid to the possible relationship between tea and cancer. No study has been specifically designed to study this issue, but data on tea have been published in several studies in which coffee and other possible risk factors for cancer were considered.

(*a*) *Descriptive epidemiology*

In the study of Phelps and Phelps (1988), described on p. 114, no association was found with breast cancer; no distinction was made between tea and coffee.

An ecological study examining the association between annual tea consumption, estimated from trade data, and age-adjusted cancer mortality rates for 1964-65 from 20 different countries (Stocks, 1970) noted that mean death rates from cancers at the following sites were significantly associated with tea consumption: intestine ($p < 0.01$), breast (women; $p < 0.01$), larynx (women; $0.01 < p < 0.05$), lung and bronchus (women; $0.01 < p < 0.05$). There was no association with oesophageal cancer.

A comprehensive examination of the correlation between cancer incidence (27 cancers in 23 countries) and mortality (14 cancers in 32 countries) and a variety of dietary and other environmental variables (Armstrong & Doll, 1975) showed weak positive correlations between tea consumption and cancers of the colon and rectum, although the adjusted correlation coefficients for tea were not noted. Lung cancer incidence in women was significantly associated with tea consumption ($p < 0.01$).

(i) *Pancreatic cancer*

In an early Japanese paper (Ishii *et al.*, 1973), information on diet, smoking and occupation was collected from a case series of 311 male patients with pancreatic cancer. A comparison group of the same age [but unspecified sex] was identified from a separate prospective study. In a ridit analysis, patients had a nonsignificantly higher prevalence of drinking hot tea.

(ii) *Oesophageal cancer*

A number of the studies investigating the association between oesophageal cancer and tea consumption have focused on the Caspian littoral of Iran, where oesophageal cancer rates are the highest in the world (Hormozdiari *et al.*, 1975; Joint Iran-IARC Study Group, 1977; Mahboubi & Aramesh, 1980; Ghadirian, 1987). Within this region, incidence rates for oesophageal cancer vary by 30 fold in women and by six fold in men (Hormozdiari *et al.*, 1975). A household survey showed that in the villages in the areas with the highest cancer rates there was higher tea consumption than in the lowest incidence villages, although the intermediate incidence region reported the highest tea consumption overall. These data were confirmed in a subsequent report (Joint Iran-IARC Study Group, 1977).

The effect of differences in the temperature at which the tea was consumed was reported (Ghadirian, 1987), and this was related to incidence rates in high- and low-risk regions of the littoral. In the low-risk region, tea was consumed at an average temperature of 50.1°C compared with an average temperature of 61.3°C ($p < 0.0001$) in the high incidence area.

In an ecological study by Segi (1975) in Japan, a geographical correlation was found between rates for cancer of the oesophagus and consumption of tea-gruel.

(*b*) *Cohort studies*

These studies are summarized in Table 20.

(i) *All sites*

In the study of Heilbrun *et al.* (1986), 7833 Hawaiian Japanese men were interviewed about their consumption of black tea in 1965-68, and incident cases of

cancer were identified. The RRs for rectal cancer, adjusted for age at examination and alcohol consumption, showed a significant dose-response relationship (p for trend = 0.0007) when the tea consumption category 'almost never' was used as the standard. The excess risk for rectal cancer was confined to men aged 58 years or over at examination. The authors also reported that none of the examined variables that were associated with tea intake (height, weight, pack-years of smoking and physical activity level) was associated with rectal cancer risk. Prostate cancer risk, adjusted for age at examination, showed a significant negative association with tea consumption, although there was no clear dose-response relationship. There was a nonsignificant, steady inverse association between the risk for liver cancer and tea consumption.

Kinlen *et al.* (1988) examined the relationship between tea consumption and rectal and other cancers in a mortality study of 14 453 men in London, UK, aged 45-60, who were administered a questionnaire about diet and smoking in 1967; 97% were traced to the end of 1986 (14 085 men). Only deaths that occurred after the first 18 months of follow-up were included in analyses. Expected numbers of deaths were calculated using age-specific mortality rates for men in England and Wales for the appropriate time periods. Rectal cancer showed no trend with tea consumption, while colon cancer showed a negative trend with increasing consumption; the risk associated with tea consumption was similar among older and younger men. The authors reported positive trends between increasing tea consumption and the risk for stomach, lung and kidney cancers. The association with stomach and lung cancer persisted after limited adjustment for social class and smoking. [The Working Group noted that there were inconsistencies in the paper in reporting the number of rectal cancer deaths.]

(ii) *Pancreatic cancer*

In the study by Hiatt *et al.* (1988; described on p. 117), cancer patients had drunk 0.32 cup of tea per day, while the controls from within the cohort had drunk 0.62 cup per day (p = 0.10). These figures were adjusted for age and smoking.

The nested case-control study of Whittemore *et al.* (1983; described on p. 116) found a RR of 0.6 for drinking ≥2 cups per day. The authors stated that adjustment for smoking at college did not alter the findings. The reduction remained after adjustment for coffee drinking.

Table 20. Summary of results of cohort studies on cancer and tea consumption

Reference, location, site	Subjects	Tea consumption	RR (95% CI)	Comments
Heilbrun *et al.* (1986)	7833 Japanese men			
Hawaii	76 cases	Almost never	1.0	*p* for trend = 0.0007;
Rectum		Twice/week	1.3	adjusted for age at
		2–4×/week	2.0	examination and
		Almost daily	2.1 significant	alcohol consumption
		>Once daily	4.2 significant	
Pancreas	30 cases	Almost never	1.0	*p* for trend = 0.87;
		Twice/week	0.6	adjusted for age at
		2–4×/week	1.4	examination and
		Almost daily >Once daily	0.9	pack-years of smoking
Prostate	149 cases	Almost never	1.0	*p* for trend = 0.02;
		Twice/week	0.8	adjusted for age at
		2–4×/week	0.4	examination
		Almost daily >Once daily	0.6	
Bladder	57 cases	Almost never	1.0	*p* for trend = 0.68;
		Twice/week	1.4	adjusted for age at
		2–4×/week	1.0	examination and
		Almost daily >Once daily	0.8	pack-years of smoking
Liver	25 cases	Almost never	1.0	*p* for trend =
		Twice/week	0.8	0.134; adjusted for
		2–4×/week Almost daily >Once daily	0.6	age at examination and alcohol consumption
Rectum	37 cases	Almost never	1.0	*p* for trend = 0.67; ad-
	<58 years old	Twice/week	1.4	justed for age at
	at examination	2–4×/week	1.4	examination and
		Almost daily	1.1	alcohol consumption
		>Once daily	1.4	
Rectum	39 cases	Almost never	1.0	*p* for trend < 0.0001;
	≥58 years old	Twice/week	1.0	adjusted for age at ex-
	at examination	2–4×/week	2.9	amination and alcohol
		Almost daily	3.5 significant	consumption
		>Once daily	8.7 significant	

Table 20 (contd)

Reference, location, site	Subjects	Tea consumption	RR (95% CI)	Comments
Kinlen *et al.* (1988) London, UK	14 085 men		Observed:expected ratios	Expected no. of deaths calculated using national age-specific data
Rectum	62 cases	0–3 cups/day	0.5	p for trend = 0.94
		4–6 cups/day	0.9	
		7–9 cups/day	0.8	
		≥10 cups/day	0.5	
Pancreas	70 cases	0–3 cups/day	0.6	p for trend = 0.28
		4–6 cups/day	0.8	
		7–9 cups/day	1.1	
		≥10 cups/day	0.9	
Prostate	88 cases	0–3 cups/day	0.6	p for trend = 0.30
		4–6 cups/day	0.8	
		7–9 cups/day	1.0	
		≥10 cups/day	0.8	
Bladder	71 cases	0–3 cups/day	1.0	p for trend < 0.13
		4–6 cups/day	0.7	
		7–9 cups/day	1.2	
		≥10 cups/day	1.4	
Stomach	172 cases	0–3 cups/day	0.6	p for trend < 0.0005
		4–6 cups/day	0.8	
		7–9 cups/day	1.2	
		≥10 cups/day	1.4	
Colon	79 cases	0–3 cups/day	1.0	p for trend = 0.066
		4–6 cups/day	0.8	
		7–9 cups/day	0.5	
		≥10 cups/day	0.7	
Lung	718 cases	0–3 cups/day	0.6	p for trend = 0.0001
		4–6 cups/day	0.8	
		7–9 cups/day	1.1	
		≥10 cups/day	1.4	
Kidney	26 cases	0–3 cups/day	0.4	p for trend = 0.04
		4–6 cups/day	0.7	
		7–9 cups/day	1.2	
		≥10 cups/day	1.8	

Table 20 (contd)

Reference, location, site	Subjects	Tea consumption	RR (95% CI)	Comments
Whittemore *et al.* (1983) USA	50 000 men			
Pancreas	126 cases	Nondrinkers	1.00	Adjusted for age, college and class year
		Drinkers	0.5 (0.3–0.9)	
		< 2 cups/day	1.0	Adjusted for age, college and class year
		≥2 cups/day	0.6 (0.3–1.1)	

(c) *Case-control studies*

(i) *Bladder and urinary tract*

These studies are summarized in Table 21, at the end of this section.

Bladder: In a Canadian case-control study of patients with histologically confirmed bladder cancer (Morgan & Jain, 1974; described on p. 122), there was no association with tea intake (overall RR for drinkers *versus* non-drinkers adjusted for sex, 0.7).

In the US study of Simon *et al.* (1975; described on p. 122), no relation between tea drinking and cancer of the lower urinary tract (renal pelvis, ureter, bladder and urethra) was revealed.

In the study by Miller *et al.* (1978; described on p. 123) of cases of bladder cancer in Ottawa, Canada, the RR for drinking tea (users *versus* nonusers) was close to unity for people of each sex. No quantitative data were provided on doses.

In the Canadian study of Howe *et al.* (1980; described on p. 123), the RRs for tea drinkers *versus* nondrinkers were 1.0 for men and 0.5 for women.

In the largest case-control study on bladder cancer carried out in the USA (Hartge *et al.*, 1983; described on p. 124), the relation between tea consumption and bladder cancer risk was examined among subjects who drank no more than seven cups of coffee per week. No evidence of an association was found for people of either sex, and the trends in risk with dose were nonsignificant.

In a case-control study conducted in 1976-78 in metropolitan Nagoya, Japan (Ohno *et al.*, 1985; described on p. 124), no relation was evident with consumption of black tea.

In the study by Jensen *et al.* (1986); described on p. 126) on bladder cancer in Denmark, a significant, direct relationship with dose of tea emerged among men, but not among women. The overall trend in risk associated with tea drinking in the

two sexes combined, adjusted for age, sex, smoking, coffee and soft drinks, was significant. The authors noted that the association with tea might be related to the unexpected finding of a positive association between total beverage consumption and bladder cancer risk in this study.

In a case-control study of bladder cancer in the Federal Republic of Germany (Claude *et al.*, 1986; described on p. 126), the estimated RRs for drinking black tea were above unity in men and women, but the trends in risk with dose were not significant. In this study, a positive association was found with total daily fluid intake, with a particularly high RR in men. [The Working Group noted the possible influence of the use of urological controls on these estimates.]

In the study by Iscovich *et al.* (1987; described on p. 127) in La Plata, Argentina, the RR for tea drinking was above unity. However, only four cases drank three or more cups per day, and the trend in risk with dose was not significant.

In a population-based case-control study from Utah, USA (Slattery *et al.*, 1988; described on p. 127), data for tea consumption were presented separately for people who had never smoked and those who had ever smoked. The authors stated that the risk increased in nonsmokers with number of cups of tea per week. [The Working Group noted that, when the data were examined globally, however, there was no appreciable association with tea. The RRs, as calculated by the Working Group, were 1.0 for one to three cups per week and 1.2 for more than three cups per week.]

In the study by Risch *et al.* (1988; described on p. 128), on bladder cancer in Canada, no association was found with various measures of tea consumption: the RR for 100 cup-years, derived from a multiple logistic model, was 1.0 for men and women.

In a study from northern Italy (La Vecchia *et al.*, 1989; described on p. 128), univariate analysis suggested a reduced bladder cancer risk among tea drinkers (RR, 0.5; [95%, 0.3-0.8]), but the risk rose to 0.8 (nonsignificant) after multivariate analysis.

Renal pelvis and ureter: The etiology and pathogenesis of transitional-cell cancer of the renal pelvis and ureter are in several aspects similar to those of bladder cancer, although the frequency of cancers at these sites is much lower and, hence, the studies are based on small data sets.

A matched hospital-based study of 33 cases of cancer of the renal pelvis and 33 controls in the UK (Amstrong *et al.*, 1976) found no association with tea drinking, although no risk estimate was reported.

Table 21. Summary of results of case–control studies of bladder cancer and tea consumption

Reference, location	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Morgan & Jain (1974) Canada	Men and women (232, 232)	0 < 1 cup/day 1–< 3 cups/day 3–< 5 cups/day ≥5 cups/day	1 [0.5] [0.6] [1.1] [1.0]	Nonsignificant; adjusted for sex only
Simon *et al.* (1975) USA	Men and women (132, 384)	Nonuser < 1 cup/day 1–2 cups/day ≥3 cups/day	1 1.0 1.3 0.8	Nonsignificant; unadjusted
Miller *et al.* (1978) Canada	Men (183, 366) Women (72, 144)	Users *versus* nonusers	1.1 0.9	Nonsignificant; unadjusted Nonsignificant
Howe *et al.* (1980) Canada	Discordant pairs[a] Men (80/79) Women (12/26)	Users *versus* nonusers	1.0 (0.7–1.4) 0.5 (0.2–1.0)	Nonsignificant; unadjusted estimates from matched analysis Nonsignificant
Hartge *et al.* (1983) USA	Men (455, 1106)	Nonuser < 7 cups/week 7–14 cups/week > 14 cups/week	1 1.1 1.1 1.0	Nonsignificant; adjusted for age, race, geographical area, tobacco and coffee
	Women (204, 452)	Nonuser < 7 cups/week 7–14 cups/week > 14 cups/week	1 1.1 1.7 1.2	Nonsignificant
Ohno *et al.* (1985) Japan	Men (227, 443) Women (65, 146)	Users *versus* nonusers	1.0 (0.7–1.3) 0.6 (0.3–1.0)	Nonsignificant; adjusted for age and smoking Nonsignificant
Jensen *et al.* (1986) Denmark	Men and women (371, 771)	0 < 0.5 l/day 0.5–0.99 l/day ≥1 l/day	1 0.8 2.0 1.5	$p = 0.03$; adjusted for age, sex, smoking (never/current and lifetime pack-years), coffee and soft drinks

Table 20 (contd)

Reference, location	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Claude *et al.* (1986) Federal Republic of Germany	Men (340, 340)	0 1–2 cups/day 3–4 cups/day >4 cups/day	1 1.0 1.5 1.9	Nonsignificant; adjusted for smoking (never/ever and lifetime packs)
	Women (91, 91)	0 1–2 cups/day 3–4 cups/day >4 cups/day	1 1.9 1.3 1.9	Nonsignificant
Iscovich *et al.* (1987) Argentina	Men and women (99, 99)	0 1 cup/day 2 cups/day ≥3 cups/day	1 1.5 1.2 1.4	Nonsignificant; adjusted for smoking
Slattery *et al.* (1988) USA	Men and women (413, 886)	0 1–3 cups/week ≥4 cups/week	1 [1.0] [1.2]	Nonsignificant; adjusted for smoking (never/ever) from published data; calculated by the Working Group
Risch *et al.* (1988) Canada	Men and women (826, 792)	Per 100 cup-years	1.0 (0.9–1.1) 1.0 (0.8–1.2)	Adjusted for smoking (cumulated pack-years) and history of diabetes
La Vecchia *et al.* (1989) Italy	Men and women (163, 181)	Users *versus* nonusers	0.8 [0.4–1.3]	Adjusted for age, area of residence, social class and selected indicator foods

[a]Patient ever used, control never used/patient never used, control ever used

A population-based case-control study of 74 cases (50 men and 24 women) of cancer of the renal pelvis and 697 controls from the USA (McLaughlin *et al.*, 1983) showed a positive trend with tea drinking in women only. The RRs, adjusted for smoking, were 2.6 for two cups per day, based on three cases, and 18.8 for three cups or more, based on nine cases. [The Working Group noted that the same control group was used in this study and in that on renal-cell cancer described below.]

Kidney: Among the studies in which tea was considered in the epidemiology of renal-cell cancers, four (Armstrong *et al.*, 1976; Goodman *et al.*, 1986, ≥2 cups/day; RR, 1.4 (0.9-2.2); Yu *et al.*, 1986, RR for daily consumption, 0.6; McCredie *et al.*, 1988) found no association, and one (McLaughlin *et al.*, 1984) found an association with drinking ≥3 cups/day in women only (RR, 3.4; 95% CI, 1.4-8.9), although the trend in risk was largely inconsistent.

(ii) *Pancreas* (see Table 22)

In the study of Kinlen and McPherson (1984), described on p. 136, a positive trend for tea consumption was found, which was not significant.

In several other case-control studies (MacMahon *et al.*, 1981; Mack *et al.*, 1986; La Vecchia *et al.*, 1987; Raymond *et al.*, 1987; Cuzik & Babiker, 1989; described on pp. 135, 137, 138, 139), no association was found between tea consumption and pancreatic cancer.

Table 22. Summary case–control studies of tea consumption and pancreatic cancer

Reference, location	Subjects (cases, controls)	Tea consumption (cups/day)	RR	Comments
MacMahon *et al.* (1981) USA	Men (216, 306)	0	1.0	$\chi^2 = 1.4$
		1–2	0.7	
		≥3	0.8	
	Women (150, 336)	0	1.0	$\chi^2 = 1.9$
		1–2	0.7	
		≥3	0.6	
Kinlen & McPherson (1984) UK	Men and women (216, 432)	0–2	1.0	
		3–4	2.2	Significant
		5–9	2.3	Significant
		≥10	2.5	
	Men and women	0–2	1.0	Adjusted for smoking and coffee
		3–4	2.3	Significant
		5–9	2.3	Significant
		≥10	2.6	
Mack *et al.* (1986) USA	Men and women (490, 490)	0	1.0	Crude odds ratio
		1–4	0.7	
		≥5	0.7	
La Vecchia *et al.* (1987) Italy	Men and women (150, 605)	0	1.0	
		1	0.9	
		≥2	1.3	
	Men and women	0	1.0	Adjusted for smoking and occupation
		1	0.8	
		≥2	1.1	

Table 22 (contd)

Reference, location	Subjects (cases, controls)	Tea consumption (cups/day)	RR	Comments
Raymond *et al.* (1987) Switzerland	Men and women (88, 336)	0 <910 ml/week >910 ml/week	1.0 2.2 (1.1–4.3) 1.0 (0.5–2.0)	90% CI
Cuzik & Babiker (1989) UK	Men and women (216, 279)	0–2 3–4 5–6 ≥7	1.0 0.8 0.9 0.9	Adjusted for smoking; χ^2 = 0.01
	Men and women	0–2 3–4 5–6 ≥7	1.0 1.2 1.1 1.5	Consumption ~10 years previously; adjusted for smoking; χ^2 = 1.0

(iii) *Breast*

Case-control studies of breast cancer and tea consumption are summarized in Table 23.

A study by Lawson *et al.* (1981), in which coffee and tea drinking were grouped, is described on p. 144.

In the hospital-based case-control study in Israel of Lubin *et al.* (1984, 1985; described on p. 144), no association between tea consumption and breast cancer risk was found.

In the study of Rosenberg *et al.* (1984, 1985; described on p. 145), using data from a case-control study in eastern USA, the consumption of tea was similar among all cases and controls and among those cases and controls who did not drink caffeine-containing coffee.

In the study by La Vecchia *et al.* (1986; described on p. 145), the RRs for drinkers of one and two or more cups per day were 1.3 and 1.0.

In the study by Schairer *et al.* (1987; described on p. 146), results were given on consumption of non-herbal tea: RRs were 0.9, 0.8, 1.3, 1.0 and 0.6 for increasing levels of consumption.

In the study of Mabuchi *et al.* (1985a; see p. 147), on risk factors for male breast cancer in a large number of hospitals in five US metropolitan areas, 42% of cases and 54% of controls drank one cup or more of tea per day; the difference was no significant.

Table 23. Summary of results of case–control studies of breast cancer and tea consumption

Reference, location	Subjects (cases, controls)	Tea consumption (cups/day)	Relative risk (95% confidence interval)	Comments
Lubin *et al.* (1984, 1985) Israel	Women (731, 731) surgical controls	0 1 2–3 ≥4	1.0 1.0 (0.6–1.4) 0.9 (0.5–1.2) 0.9 (0.4–1.8)	Matched for age, country of origin, length of residence in Israel
	(804, 804) neighbourhood controls	0 1 2–3 ≥4	1.0 0.8 (0.6–1.4) 0.8 (0.5–1.2) 0.8 (0.4–1.8)	
Rosenberg *et al.* (1985) USA	Women (2651, 1501) noncancer controls	0 1–2 3–4 ≥5	1.0 1.0 (0.8–1.1) 0.8 (0.6–1.0) 0.6 (0.5–0.9)	Adjusted for age within five years
	(2651, 385) cancer controls	0 1–2 3–4 ≥5	1.0 0.9 (0.7–1.2) 1.1 (0.7–1.6) 0.8 (0.5–1.4)	
La Vecchia *et al.* (1986) Italy	Women (616, 616)	0 1 ≥2	1.0 1.3 1.0	
Schairer *et al.* (1987) USA	Women (1510, 1882)	0 ≤1 2 3 4 ≥5	1.0 0.9 (0.8–1.1) 0.8 (0.6–1.1) 1.3 (0.8–2.1) 1.0 (0.5–2.3) 0.6 (0.2–1.9)	
Mabuchi *et al.* (1985a) USA	Men (52, 52)	<1 ≥1		42% *versus* 54%; nonsignificant; matched on age, race, marital status

(iv) *Ovary* (see Table 24)

In the study by Byers *et al.* (1983; described on p. 150), there was no significant association with any consumption category or dose trend of tea among ovarian cancer patients in Buffalo, NY, USA.

In the North American multicentre study of Miller *et al.* (1984, 1987; described on p. 150), no association was found between tea consumption and ovarian cancer.

Table 24. Summary of case–control studies of ovarian cancer (common epithelial tumours) and tea intake

Reference, location	Subjects (cases, controls)	Tea consumption (cups/day)	Relative risk (95% confidence interval)	Comment
Byers *et al.* (1983) USA	274, 1034	0	1.0	No significant association with any consumption category or trend
		<3	1.1	
		≥3	0.8	
Miller *et al.* (1984, 1987) Several cities in the USA and Canada	290 cases 480 noncancer controls	0	1.0	
		1–2	0.8 (0.6–1.2)	
		3–4	0.8 (0.5–1.4)	
		≥5	0.5 (0.2–1.0)	
	376 cancer controls	0	1.0	
		1–2	0.7 (0.5–1.0)	
		3–4	1.1 (0.6–2.1)	
		≥5	0.7 (0.3–1.6)	
	856 combined controls	0	1.0	
		1–2	[0.8]	
		3–4	[1.0]	
		≥5	[0.6]	

(v) *Cancers of the digestive tract*

Large bowel: Case-control studies on colorectal cancer and tea consumption are summarized in Table 25.

In the study of Higginson (1966; described on p. 152), no significant association was found between tea consumption and colorectal cancer in patients in Kansas City, USA.

In the study by Watanabe *et al.* (1984; described on p. 155), drinking black tea was negatively associated with the risk for rectal cancer in cases in Kyoto, Japan. There was a possible dose-response relationship (the RR for non-daily drinkers was 0.5 and for daily drinkers, 0.4). The positive association between rectal cancer and drinking green tea was not significant, nor were the associations between colon cancer and the consumption of black or green tea.

In the study of Tajima and Tominaga (1985; described on p. 155) in Nagoya, Japan, there was no significant association between black or green tea drinking and cancers of the colon or rectum.

In the large case-control study in Milan, Italy, conducted by La Vecchia *et al.* (1988; described on p. 156), subjects with a higher intake of tea had RRs of 1.4 for colon cancer [$p = 0.06$] and 1.5 for rectal cancer ($p < 0.05$).

Table 25. Summary of results of case–control studies on colorectal cancer and tea consumption

Reference, location, site	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Higginson (1966) USA Colon and rectum	Men and women (340, 1020)	Never/irregular	1.0	Nonsignificant
		< 1 cup/day	[1.0]	
		< 2 cups/day	[1.1]	
		≥3 cups/day	[0.5]	
Watanabe *et al.* (1984) Japan Rectum	Men and women (65, 65)	Green tea		Crude RR
		Nondrinkers	1.0	
		Drinkers	3.0 (0.4–25.8)	
		Black tea		
		Nondrinkers	1.0	
		Drinkers	0.5 (0.2–1.0)	
		Frequency		
		Never	1.0	
		Daily	0.4 (0.1–1.6)	
		Sometimes	0.5 (0.2–1.1)	
Colon	Men and women (138, 138)	Green tea		
		Nondrinkers	1.0	
		Drinkers	1.3 (0.3–5.9)	
		Black tea		
		Nondrinkers	1.0	
		Drinkers	1.1 (0.7–1.7)	
Tajima & Tominaga (1985) Japan Rectum	Men and women (51, 186)	Green tea		Adjusted for age and sex; nonsignificant
		0–3 times/day	1.0	
		≥4 times/day	0.9	
		Black tea		
		Nondrinkers	1.0	
		Drinkers	0.9	Nonsignificant
Colon	Men and women (42, 186)	Green tea		
		0–3 times/day	1.0	
		≥4 times/day	1.0	Nonsignificant
		Black tea		
		Nondrinkers	1.0	
		Drinkers	1.7	Nonsignificant
La Vecchia *et al.* (1988) Italy Rectum	Men and women (236, 778)	Low tertile	1.0	$p < 0.05$; adjusted for age, marital status, education, social class, smoking and alcohol consumption
		Intermediate/ high tertiles	1.5	

Table 25 (contd)

Reference, location, site	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Colon	Men and women (339, 778)	Low tertile	1.0	
		Intermediate/ high tertiles	1.4	Nonsignificant

Stomach: Case-control studies on stomach cancer and tea consumption are summarized in Table 26.

In the studies of Higginson (1966; see p. 152), in the Kansas City area, USA, of Graham *et al.* (1967; see p. 161) in Buffalo, NY, USA, of Tajima and Tominaga (1985; see p. 155) in Nagoya, Japan, and of Trichopoulos *et al.* (1985; see p. 161) in Piraeus, Greece, there was no significant association between drinking tea and cancer of the stomach.

Kono *et al.* (1988) studied 139 incident cases of gastric cancer in Kyushu, Japan. Two control groups were used: 2574 controls were subjects screened for gastrointestinal conditions but found to be healthy, and 278 (two per case) were population controls from ten neighbouring municipalities, matched to the cases by sex and year of birth. Individuals consuming ten or more cups of green tea per day tended to have a lower risk for gastric cancer. There was no difference, however, between individuals drinking none to four cups and five to nine cups per day.

Table 26. Summary of results of case–control studies on gastric cancer and tea consumption

Reference, location	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Higginson (1966) USA	Men and women (93, 279)	Never/irregular	1.0	Nonsignificant
		< 1 cup/day	[0.9]	
		< 2 cups/day	[1.3]	
		≥3 cups/day	[1.3]	
Graham *et al.* (1967) USA	Men and women (276, 2221)			No association
Tajima & Tominaga (1985) Japan	Men and women (93, 186)	Green tea		Nonsignificant; adjusted for age and sex
		0–4 times/day	1.0	
		≥5 times/day	0.6	
		Black tea		Nonsignificant
		Nondrinkers	1.0	
		Drinkers	0.8	

Table 26 (contd)

Reference, location	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Trichopoulos *et al.* (1985) Greece	Men and women (110, 100)	1 (low) 2 3 4 5 (high)	1.0 [1.7] [1.8] [2.7] [3.2]	Nonsignificant; adjusted for age, sex, years of schooling; p value based on chi-squared test for linear trend; coffee and tea intakes added
Kono *et al.* (1988) Japan	Men and women (139, 2574)	0–9 cups/day ≥10 cups/day	1.0 0.5 (0.3–1.1)	p = 0.10; hospital controls; adjusted for age, sex, smoking, consumption of oranges and other fruit
	Men and women (139, 278)	0–9 cups/day ≥10 cups/day	1.0 0.3 (0.1–0.7)	p = 0.007; population controls

Oesophagus: Case-control studies on oesophageal cancer and tea consumption are summarized in Table 27.

Kaufman *et al.* (1965) studied 82 cases of oesophageal cancer and 73 controls in Kazakhstan, USSR, and later added 51 cases from another area (effective numbers, 127 cases and 72 controls). Drinking very hot tea was associated with a three-fold higher risk of cancer.

In the same region, Bashirov *et al.* (1968) carried out a comparison of 301 cases of oesophageal cancer (142 men and 159 women) and 301 healthy population controls. Cases and controls had smoked for similar durations and used nass to the same extent. Oesophageal cancer was more common among those who reported drinking six or more cups of hot black tea at a single sitting than among those who did not.

In the study of de Jong *et al.* (1974; described on p. 163) among Singapore Chinese, there was no association between tea drinking and oesophageal cancer; however, drinking of 'burning hot' tea was associated with a three- to four-fold higher risk.

In northern Iran, Cook-Mozaffari *et al.* (1979) studied 344 patients with oesophageal cancer registered at the Caspian cancer registry between January 1975 and 1976. These comprised 54% of the patients registered during that period. Two population controls were chosen per case, matched for village of residence, age, sex and language group. A second group of 181 patients with other cancers (of whom

approximately 50% had stomach cancer) were also matched to two neighbourhood controls. Drinking hot tea was associated with a doubling in the risk of oesophageal cancer in males and females ($p < 0.01$). Hot-tea drinking was also associated with a three-fold higher risk of the other cancers studied among men, but with no excess among women.

In the study of Victora *et al.* (1987; see p. 280) in southern Brazil, cases and controls did not differ significantly in the frequency of tea intake, although no data were given.

Table 27. Summary of results of case–control studies on oesophageal cancer and tea consumption

Reference, location	Subjects (cases, controls)	Tea consumption	Relative risk	Comments
Kaufman *et al.* (1965) USSR	Men and women (127, 72)	Drinking of very hot tea		[$p < 0.001$]
		No	1.0	
		Yes	[3.2]	
Bashirov *et al.* (1968) USSR	Men (142, 142)	Glasses of hot tea at a time		[$p < 0.01$]
		<7	1.0	
		≥ 7	[2.6]	
	Women (159, 159)	Glasses of hot tea at a time		Nonsignificant
		<7	1.0	
		≥ 7	[3.0]	
de Jong *et al.* (1974) Singapore	Men (95, 465)	Not daily	1.0	Nonsignificant; adjusted for dialect group
		Daily	0.8	
		Burning hot	3.7	$p < 0.01$
	Women (36, 200)	Not daily	1.0	
		Daily	0.8	Nonsignificant
		Burning hot	3.5	$p < 0.05$
Cook-Mozaffari *et al.* (1979) Iran	Men (217, 434)	Drinking hot tea		
		No	1.0	$p < 0.01$
		Yes	1.7	
	Women (127, 254)	No	1.0	$p < 0.01$
		Yes	2.2	
Victora *et al.* (1987) Brazil	Men and women (171, 342)			No association

Other digestive tract (Table 28): In the study of Yen *et al.* (1987; described on p. 163) in eastern USA, subjects who consumed tea had half the risk for cancer of the extrahepatic bile ducts than people who had never drunk tea. This difference was marginally significant, but there was no suggestion of a dose-response relationship.

In the study of Franco *et al.* (1989; described on p. 164), in Brazil, no association was found between the frequency of tea drinking and oral cancer.

Table 28. Summary of results of case–control studies on other digestive tract cancers

Reference, location, site	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Yen *et al.* (1987) USA Extrahepatic bile duct	Men and women (67, 275)	0 Ever Occasionally 1–2 cups/day 3–4 cups/day ≥5 cups/day	1.0 0.5 (0.3–1.0) 0.4 (0.2–0.9) 0.6 (0.3–1.3) 0.5 (0.2–1.4) 0.8 (0.2–3.3)	Adjusted for age and sex
Franco *et al.* (1989) Brazil Oral cavity	Men and women (232, 464)	< 1 cup/month 1–30 cups/month > 30 cups/month	1.0 0.9 (0.6–1.3) 1.0 (0.6–1.7)	Nonsignificant; crude matched analysis; *p* level based on test for linear trend
		< 1 cup/month 1–30 cups/month > 30 cups/month	1.0 0.9 (0.6–1.3) 1.3 (0.7–2.3)	Nonsignificant; adjusted for tobacco and alcohol consumption

(vi) *Nasopharynx*

Case-control studies of nasopharyngeal cancers (NPC) and tea consumption are summarized in Table 29.

Lin *et al.* (1973) studied 343 patients with NPC and 1017 controls in Taiwan. No association was found between tea drinking and NPC, but no data were given.

In the study of Henderson *et al.* (1976; described on p. 165), tea drinking was associated with a significantly decreased risk for NPC ($p = 0.02$). Cases with other pharyngeal cancers, however, were not more likely to drink tea (RR, 1.4; $p = 0.3$).

Shanmugaratnam *et al.* (1978) investigated the association between tea drinking and NPC in Singapore. The case series consisted of 379 Chinese patients (266 men, 113 women) with histologically confirmed NPC in Singapore between 1966 and 1968. Two control groups were recruited: the first were 595 Chinese patients from the ear, nose and throat department at the same hospital, and the

second were 1044 Chinese patients in the medical, surgical and orthopaedic wards of another hospital. No difference was found regarding the frequency of consumption of Chinese tea between cases and ear, nose and throat controls; the comparison with other hospital controls showed no consistent association.

Table 29. Summary of results of case–control studies on nasopharyngeal cancers and tea consumption

Reference, location	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Henderson *et al.* (1976) USA	Men and women (156, 267)	0 Drinkers	1.0 0.5 [0.3–1.0]	$p = 0.02$; adjusted for age, sex, race, socio-economic status and place of residence
Shanmugaratnam *et al.* (1978) Singapore	Men and women (379, 595)	< once/month < once/day Daily	0.9 0.9 1.2	Nonsignificant; ear, nose and throat controls; adjusted for sex, age and interviewer
	Men and women (379, 1044)	< once/month < once/day Daily	1.1 0.7 1.3	$p < 0.05$; other hospital controls

(vii) *Other sites*

Case-control studies of cancers at other sites and tea consumption are summarized in Table 30.

In the study of Mabuchi *et al.* (1985b; described on p. 166) of carcinoma of the vulva in five US metropolitan areas, no association was found between the consumption of tea and cancer of the vulva.

Bunin *et al* (1987) studied tea drinking during pregnancy and Wilms' tumour in the offspring. Cases were white children under 15 years of age identified through the registries of the three main childhood cancer hospitals in Philadelphia, PA, during 1970-83. About 30% of eligible cases could not be interviewed. Tea consumption during pregnancy was associated with a doubling of the risk for Wilms' tumour in the offspring ($p < 0.05$).

[The Working Group noted that, unless otherwise specified, the studies did not distinguish different types of tea (green, black or herbal). Furthermore, the effect of the consumption of other hot beverages was not considered in most of the studies. Consequently, non-drinkers of tea could represent drinkers of other hot beverages, including coffee.]

Table 30. Summary of results of case–control studies on other cancers and tea consumption

Reference, location, site	Subjects (cases, controls)	Tea consumption	Relative risk (95% CI)	Comments
Mabuchi *et al.* (1985b) USA Vulva	Women (149, 149)	< 1 cup/day	1.0	Nonsignificant; unmatched analysis
		1–2 cups/day	0.8	
		3–4 cups/day	1.1	
		≥5 cups/day	1.1	
Bunin *et al.* (1987) USA Wilms' tumour	Boys and girls (88, 88)	Tea intake of mother during pregnancy		Matched analysis
		0	1.0	
		Drinkers	2.2 (1.0–4.7)	$p < 0.05$