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Caffeine Consumption and Benign Breast Disease: A Case-Control Comparison

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Abstract: In this case-control comparison of 323 women with benign breast disease and 1,458 controls, no differences were noted in the coffee and tea consumption patterns of the cases and controls. These findings do not support the recent suggestion of Minton, *et al*, that methylxanthine ingestion is causally related to benign breast disease or breast cancer. *Am J Public Health* 1982; 72:610–613.)

Interest has recently been directed toward the potential role of methylxanthine ingestion as a factor in benign breast disease. Finding elevated levels of cyclic adenosine monophosphate (AMP) and guanosine monophosphate (GMP) in biopsy tissue of women with benign breast disease, Minton has suggested that methylxanthine ingestion, by facilitating an intracellular accumulation of AMP and GMP, may be causally related to benign breast disease and perhaps breast cancer.[1,2] Common foods containing methylxanthines include coffee, tea, cola, and chocolate. This case-control study is designed to address the possible role of coffee and tea consumption as factors in benign breast disease.

Material and Methods

Between 1957 and 1965 all patients admitted to Roswell Park Memorial Institute completed a detailed questionnaire immediately prior to presenting at the hospital. At admission, they were interviewed in detail about their dietary habits in the period up to one year before they first observed the symptoms leading them to seek admission. A section of this interview dealt with coffee and tea consumption. Coffee and tea consumption data were collected for 323 women whose diagnosis, after admission, indicated fibrocystic breast disease. The coffee and tea consumption patterns of these women were compared to the coffee and tea consumption patterns of 1,458 women who were diagnosed as having a variety of non-neoplastic diseases of sites other than the breast. Breast history and examination were included as part of the admission examination of controls as well as cases. The most prevalent sites of the control diseases were the reproductive system, gastrointestinal tract, and skin.

The data were analyzed by the computation of risk ratios[3] and chi-square trend statistics.[4]

Results

Table 1 presents the distribution of cases and controls by age and by reported daily coffee consumption. There is no evidence that those with higher levels of coffee consumption are at elevated risk of benign breast disease.

In Table 2, risk is analyzed according to reported daily tea consumption. The data suggest that a decrease in risk accompanies higher levels of tea consumption. None of the comparisons in Tables 1 and 2 is significant at the .05 level.

Table 3 contains estimates of the risks of coffee and tea consumption, adjusted for the consumption of the other beverage. The data have been collapsed to increase the stability of the estimates. Low coffee and tea consumption is defined as one cup per day or less. High consumption is

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TABLE 1—Case-Control Distribution by Age and Reported Daily Coffee Consumption

Reported Daily Coffee Consumption	Age 20–29				Age 30–39				Age 40–49				Age 50 +					
	Case	Control	RR_1	RR_2	Case	Control	RR_1	RR_2	Case	Control	RR_1	RR_2	Case	Control	RR_1	RR_2	RR_1*	RR_2*
None	3	4	1.1	1.0	6	15	0.9	1.0	6	15	1.0	1.0	7	73	1.2	1.0	1.0	1.0
<1	5	5	1.5	1.3	2	7	0.7	0.7	5	8	1.5	1.6	1	41	0.3	0.3	0.9	0.8
1	3	10	0.5	0.4	9	19	1.1	1.2	16	33	1.2	1.2	17	199	1.0	0.9	1.0	1.0
2	6	13	0.7	0.6	12	24	1.2	1.3	20	47	1.1	1.1	13	212	0.7	0.6	0.9	0.9
3	3	8	0.6	0.5	19	35	1.3	1.4	12	36	0.8	0.8	18	139	1.6	1.4	1.1	1.1
>3	27	31	1.3	1.2	44	114	0.9	1.0	50	130	0.9	1.0	19	240	1.0	0.8	1.0	0.9
Total	47	71	1.0		92	214	1.0		109	269	1.0		75	904	1.0		1.0	
Chi-Square for trend			.5				.0				.5				.2		.0	

*Mantel-Haenszel age-weighted risk ratio.
RR_1: Risk is relative to sample population risk of one.
RR_2: Risk is relative to risk among individuals who do not drink coffee.

defined as more than one cup per day. The Table also displays the risks associated with the consumption of different possible combinations of tea and coffee levels.

The Table does not show that high coffee consumption, if adjusted for tea consumption, increases risk. There is a slight, statistically significant decrease in the risk associated with high tea consumption adjusted for coffee consumption levels. Individuals who consume greater amounts of coffee and tea are not at higher risk than individuals whose consumption of coffee and tea is minimal.

Discussion

These findings should be regarded with considerable caution. These data are based upon reports which describe a general consumption pattern in the period prior to the recognition of disease. It is assumed by the use of such data that a basic consistency of use over time obtains for patterns of substance ingestion, i.e., that coffee and tea consumption in the past year distinguish benign breast disease patients from controls in regard to coffee and tea consumption in the period prior to the appearance of disease. There are no data on the latent period for benign breast disease.

Doubtless, a few of the women who reported that they never drank coffee or tea actually did so. The converse is probably also true. Nevertheless, there is little reason to believe that a substantial proportion of the women who never drink coffee or tea would have reported that they actually drink three or more cups per day. There is no reason to suspect that cases would have been more or less likely than controls to understate or overstate the level of their exposure. As recent studies have shown, such error as probably inheres in retrospective diet histories is unlikely to obscure substantial risks actually present in the data.[5,6]

The cases in this study initially suspected that they might have breast cancer. These cases, and the controls, received a thorough physical examination upon admission. Nevertheless, some nonclinical fibrocystic disease among controls might have gone undetected. Any such misclassification of cases and controls would tend to depress the appearance of any association between methylxanthine ex-

TABLE 2—Case-Control Distribution by Age and Reported Daily Tea Consumption

Reported Daily Coffee Consumption	Age 20–29				Age 30–39				Age 40–49				Age 50 +					
	Case	Control	RR_1	RR_2	Case	Control	RR_1	RR_2	Case	Control	RR_1	RR_2	Case	Control	RR_1	RR_2	RR_1*	RR_2*
None	10	11	1.4	1.0	15	30	1.2	1.0	15	32	1.2	1.0	15	118	1.5	1.0	1.3	1.0
<1	28	38	1.1	0.8	49	113	1.0	0.9	47	119	1.0	0.8	29	291	1.2	0.8	1.0	0.8
1	6	8	1.1	0.8	16	23	1.6	1.4	19	47	1.0	0.9	10	191	0.6	0.4	1.0	0.8
2	2	7	0.4	0.3	5	14	0.8	0.7	11	46	0.6	0.5	10	184	0.7	0.4	0.7	0.5
3	0	2	—	—	1	10	0.2	0.2	4	12	0.8	0.7	5	44	1.4	0.9	0.8	0.6
>3	1	5	0.3	0.2	6	23	0.6	0.5	13	13	2.5	2.1	5	75	0.8	0.5	1.0	0.8
Total	47	71	1.0		92	213	1.0		109	269	1.0		74	903	1.0		1.0	
Chi-Square for trend			3.7				2.1				.4				2.9		3.7	

*Mantel-Haenszel age-weighted risk ratio.
RR_1: Risk is relative to sample population risk of one.
RR_2: Risk is relative to risk among individuals who do not drink coffee.

TABLE 3—Adjusted Risks due Separately to Coffee and Tea Consumption, by Age*

		Age 20–29			Age 30–39			Age 40–49			Age 50 +			
Coffee	Tea	Case	Control	RR	Case	Control	RR	Case	Control	RR	Case	Control	RR	RR**
Low	Low	8	10	1.00	12	25	1.00	11	30	1.00	13	158	1.00	1.00
Low	High	3	9	.42	5	15	.69	16	26	1.68	11	153	.87	.95
High	Low	36	47	.96	68	141	1.00	70	168	1.14	41	441	1.13	1.07
High	High	0	5	—	7	32	.46	12	45	.73	9	149	.72	.58
Total		47	71		92	213		109	269		74	901		
Mantel-Haenszel Estimate: Risk due to high coffee consumption adjusted for tea consumption				.77			.91			.77			1.02	.88
Mantel-Haenszel Estimate: Risk due to high tea consumption adjusted for coffee consumption				.22			.52			.89			.74	.68+

*Low coffee consumption is defined as one cup per day or less. High consumption is more than one cup per day. Low tea consumption is defined as one cup per day or less. High consumption is more than one cup per day. Risks defined as relative to low exposure risk of one.
**Mantel-Haenszel Risk, adjusted for age.
+$p < .05$

posure and breast disease. It is unlikely, however, that this could have happened with sufficient frequency to obscure a pattern of substantial risk enhancement.

Some of the control diagnoses involved the gastrointestinal tract. Severe gastrointestinal distress, by altering the controls' caffeine consumption patterns, could have distorted the appearance of risk. However, analyses from which gastrointestinal controls were excluded revealed the same pattern of risk non-enhancement presented in Tables 1–3.

Obesity has been suggested as a risk factor in fibrocystic breast disease.[7] Obesity adjusted relative risk estimates were essentially the same as those presented. Unfortunately, data describing such potential confounders as age at first live birth, parity, family history, and oral contraceptive use were not available. Since our data were collected on an age group of women who were fertile before there was widespread use of oral contraceptives, it is unlikely that our results are distorted by patterns of oral contraceptive intake. Future investigations, however, should also consider the role of each of these possible risk factors.

This study should be replicated with other, larger populations; one of its weaknesses is that only two of the many common substances containing methylxanthines are considered. Future studies should also note the consumption of cola and chocolate and the use of medications containing phenothiazines.

Minton, *et al*,[1,2] reported that the level of methylxanthine consumption among patients was not related to the extent of their disease, although the rate of symptom resolution among patients who stopped consuming foods containing methylxanthines was higher than among patients who continued to consume such foods. We have no evidence about whether coffee or tea consumption is related to either the extent of disease or symptom resolution. In a recent randomized trial Ernster, *et al*,[8] found that abstention from methylxanthine-containing substances had little impact upon the course of fibrocystic breast disease.

Coffee, tea, chocolate, and cola consumption are common throughout the United States. If they do generate a risk of disease, it is important that it be recognized. Definitive answers regarding the role of methylxanthine ingestion in benign breast disease await data from retrospective and prospective field studies and controlled clinical investigation.

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