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Epidemiologic Studies on Possible Health Effects of Intake of Pyrolyzates of Foods, with Reference to Mortality among Japanese Seventh-Day Adventists

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To elucidate the effect of intake of mutagenic and/or carcinogenic pyrolysis products of proteins and amino acids on carcinogenesis in man, we have undertaken two epidemiologic cohort studies: one concerning the possible association of broiled fish consumption with cancer and the other concerning the cancer mortality among Japanese Seventh-Day Adventists. The main findings of these studies are described.

To elucidate the effect of the mutagenic and/or carcinogenic pyrolysis products of proteins and amino acids on producing cancer in man (*1*), we have undertaken two epidemiologic cohort studies: one concerning the possible association of broiled fish consumption with cancer (*2*); and another concerning cancer mortality among the Japanese Seventh-Day Adventists, which is still in progress. The main findings of these studies will be described, although results of the second study are preliminary in nature.

Cohort Sudy on Association of Broiled Fish Intake and Cancer Death

Broiled fish is a very common dish in Japan and is considered to be one of the major sources of mutagenic pyrolyzates of proteins ingested by the Japanese. The Radiation Effects Research Foundation in Hiroshima examined the dietary habits of a group of adult persons in 1968, inquiring about the frequency of intake of six food items, including broiled fish, dried fish, milk, salted pickles, fruits, and rice, together with other personal characteristics, such as date of birth, sex, school career, smoking habit, and radiation dose from the atomic bomb. For a total of 7553 subjects, consisting of 2746 males and 4807 females, complete records were available for the above 11 personal characteristics (independent variables) as well as for vital status. Therefore, we followed this cohort, aged 50.1 years on the average, from January 1, 1968, up to the end of 1978. Deaths seen during the observation period were periodically checked by utilizing the so-called "ko-seki" system, confirming the vital status of all of the cohort members. Causes of death were classified by the International Classification of Diseases, 8th Revision.

The relative risk, that is, mortality, among those consuming broiled fish twice or more weekly per mortality among those consuming broiled fish less frequently, as calculated by the Mantel-Haenszel method (*3*), was 1.33 ($p < 0.05$) and 1.67 ($p < 0.05$) for all cancer and for stomach cancer, respectively. A similar excess mortality from liver cancer was also observed among frequent consumers of broiled fish, but with no statistical significance. Mortality rates during the observation period for cancer at all sites and cancer of the stomach were calculated by sex and age and by frequency of intake of broiled fish and examined by stepwise linear multiple regression analysis (*4*) for possible association with various variables, without considering interaction effects of the variables tested, using a linear model. It was revealed that intake of broiled fish makes the fourth largest contribution to deaths from cancer at all sites, being surpassed only by age, sex, and radiation dose (Table 1). It was also shown that intake of broiled fish makes the third largest contribution to deaths from stomach cancer.

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Table 5. Comparison of Seventh-Day Adventists with general population in regard to exposure to environmental mutagens.

Population	Tobacco	Alcohol	Coffee	Tea	Meat	Fish	Group
General population	+	+	+	+	+	+	A
	−	−	−	−	+	+	B
SDA	−	−	+	+	+	+	C
	−	−	−	−	+	+	D
	−	−	+	+	−	−	E
	−	−	−	−	−	−	F

lation, allowing us a more refined and precise analysis of the risk of diseases which might be associated with different dietary habits. As shown in Table 5, if we could compare the risk of diseases between group B and group F consisting of the most devoted Adventists who compose about a half of the Adventists in the United States (*5,6*), or between group D which consists of Adventists not strictly abstaining from meat, poultry, and fish, and group F, it might be possible to elucidate the possible effects of the intake of mutagenic pyrolyzates of foods. Unfortunately, such an epidemiologic study cannot readily be done in Japan because the number of Adventists is limited there, while it may be possible in the United States.

If the second difficulty could be overcome in the future, the epidemiologic elucidation of the present question will become far more precise and efficient. In order to clarify epidemiologically the possible health effects of the intake of a specific mutagenic compound formed by cooking, we, of course, have to know the individual exposure to such compound. This is very important in view of the fact that quite a few different mutagens have been isolated from food pyrolyzates. Good cooperation with chemical analysts seems particularly important for the epidemiologic study.

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