Cantongese-style Salted Fish as a Cause of Nasopharyngeal Carcinoma: Report of a Case-Control Study in Hong Kong

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ABSTRACT

Two hundred fifty incident cases of nasopharyngeal carcinoma under age 35 years in Hong Kong Chinese and an equal number of age- and sex-matched friend controls were interviewed. Mothers of cases and controls were interviewed also, if available, to obtain information on childhood events concerning the study subjects. Consumption of Cantonese-style salted fish during all time periods was significantly associated with nasopharyngeal carcinoma; the association was especially strong during childhood. The relative risk for having Cantonese-style salted fish as one of the first solid foods during weaning was 7.5 (95% confidence limits, 3.9, 14.8), and the relative risk for consuming the food at least once a week compared to none, 3.1 (95% confidence limits, 14.1, 100.4). It is estimated that over 90% of young nasopharyngeal carcinoma cases in Hong Kong Chinese can be attributed to consumption of this food during childhood.

INTRODUCTION

NPC is a rare cancer among whites in Europe and North America; the age-standardized incidence rates in these populations are considerably less than 1 per 100,000 (1). In contrast, NPC is one of the most common cancers among Chinese residing in the southeastern provinces of China, particularly the province of Guangdong (of which Hong Kong is a part geographically); the age-standardized incidence rate in males is greater than 50 per 100,000 in certain parts of the province (2, 3). Southern Chinese who migrated to intermediate-risk areas such as southeast Asia or low-risk areas such as Canada and the United States continue to show a high rate of NPC (4-8). However, succeeding generations of Chinese-Americans in California (3, 6) and Hawaii (8) and Chinese in Australia (9) who are more likely to give up their traditional ways of life than their southeast Asian counterparts display a decrease in risk for NPC. This suggests that environmental factors inherent in the traditional culture of south China are responsible for the extraordinarily high rates of this disease in southern Chinese.

Inhalation of carcinogens containing smoke or dust as a risk factor for NPC in Chinese has been investigated in many studies. Results suggest that domestic exposure to smoke or dust is not an important risk factor for NPC in high-risk Chinese even though such exposure in an occupational setting may explain some cases of NPC (3, 10, 11).

Thirteen years ago, Ho (12, 13) first suggested that ingestion of Cantonese-style salted fish, a favorite food item among southern Chinese, might be a risk factor for NPC. Since then, three case-control studies conducted among southern Chinese populations have investigated such an hypothesis. All three studies are supportive of the hypothesis. In Los Angeles, significantly more Chinese patients reported current consumption of Cantonese-style salted fish compared to controls (RR for more than once a week consumption compared to none, 3.1) (10). In Hong Kong, Cantonese-style salted fish was fed to infants during weaning significantly more often in households with a NPC case than in control households (RR = 2.6) (14). In Malaysia, histories of Cantonese-style salted fish intake in childhood and adolescence were significant risk factors for NPC in Chinese; daily consumption of this food item in childhood carried a RR of 17.4 (11). There are supportive experimental findings as well: mutagenic activity (15) and volatile nitrosamines (16, 17) were found in Cantonese-style salted fish extracts; Wistar albino rats fed Cantonese-style salted fish were found to pass mutagenic urine (18); and in an experiment in which 20 Wistar albino rats were fed Cantonese-style salted fish, 4 subsequently developed carcinomas in the nasal or paranasal regions while none of the 6 control rats did (19).

The southern Chinese diet contains a variety of salt-preserved foods and one which is rich in salted fish tends also to be rich in other preserved foods. Therefore, it is important to investigate if other food items that are associated with Cantonese-style salted fish intake could also be important in the etiology of NPC. In the present study, we examined the relationship of lifetime dietary habits to the development of NPC in Chinese patients under age 35 years in Hong Kong (NPC is the most common cancer in Hong Kong Chinese ages 15-34 years (20)). Other factors under study were prior ear and nose disease, domestic and occupational exposure to inhalants, use of nasal oil, and cigarette smoking.

MATERIALS AND METHODS

Cases were incident cases of NPC under age 35 years among Chinese residents of Hong Kong. Cases were identified from the files of four

Received 7/29/85; revised 10/15/85; accepted 10/29/85.

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1 Supported in part by Grants CA00884 from the National Cancer Institute and SIG-2 from the American Cancer Society; donations from Mr. Wong Hoo Chuen of Hong Kong, and the Hong Kong Anti-Cancer Society.

2 To whom requests for reprints should be addressed.

3 The abbreviations used are: NPC, nasopharyngeal carcinoma; RR, relative risk; CL, confidence limits.
cases and the controls. The questionnaire for mothers contained detailed questionnaire for all cases and controls and a separate standard ques to together identify over 90% of all new cases of NPC in Hong Kong.

data collected by the Hong Kong Cancer Registry, these four hospitals in Hong Kong; Queen Mary Hospital; Queen Elizabeth Hospital; Hong Kong Sanatorium and Hospital; and Baptist Hospital. According to

data or in the study design.) At the end of each case interview, the patient was asked to provide the name of a close friend (excluding blood relatives) who met the matching criteria. In two instances, the first identified “close” friend refused to participate and a second “close” friend was interviewed.

We attempted to interview all mothers of cases and controls who resided in Hong Kong. Thirty-eight case-mothers had died and 24 did not reside in Hong Kong; of the 188 case-mothers contacted, 6 refused to be interviewed. For the control-mothers, 27 had died, 50 did not reside in Hong Kong, and 18 refused to be interviewed. In all, we interviewed 182 case-mothers and 155 control-mothers; there were 127 matched case-mother-control-mother pair interviews.

All interviews were conducted in person by S. Lai using a standard questionnaire for all cases and controls and a separate standard question-naire for their mothers. The questionnaire for cases and controls requested information on place of birth; ethnic origin; dietary habits (3 years prior to diagnosis and at age 10 years); occupational exposure to smoke, dust, or fumes; exposure to insecticide, antimosquito coils, and other domestic inhalants (3 years prior to diagnosis and at age 10); cigarette smoking; use of nasal oils; lifetime history on type of cooking fuel used; prior ear or nose disease; and history of NPC in first degree relatives. Mothers were asked about childhood events concerning the cases and the controls. The questionnaire for mothers contained detailed questions on weaning habits; dietary habits during childhood (between ages 1 and 2 years and at age 10 years); exposure to smoke, dust, or fumes at home; chronic illnesses of the ear or nose; and use of nasal oils. Information on diet included frequency of consumption on all preserved foods eaten by southern Chinese. Also included in our food list were the various sauces and condiment pastes used by Chinese in their cooking and the cooling soup, a type of medicinal drink unique to the southern Chinese (Table 1). Other food items were fresh meats and fish, milk, bread, oranges and other fruits, carrots, tomatoes, and fresh leafy green vegetables.

We used matched-pair methods (21) to analyze the interview data. Study variables were examined singly and then jointly for confounding and interaction effects. We used the exact binomial test on individual dichotomous variables and the multivariate logistic regression method for multivariate analysis and individual variables with more than two possible outcomes. We also analyzed the data on all mothers, stratifying by the sex of their child (21). Results of the stratified analysis were similar to those obtained from the matched analysis. All statistics presented in this paper were based on the matched analysis. Pairs in which either the case or the control had a missing value were eliminated from the corresponding analysis. For factors with prevalence rates in the general population between 25 and 75% (all of our primary variables fall within this range), the expected power of this study to detect a RR of 2.0 with a one-sided significance level of 0.05 is greater than 90%.

RESULTS

One hundred sixty male and 90 female cases were interviewed; their mean age at diagnosis was 29.2 years. The diagnoses of all but five cases were confirmed histologically. Controls had a mean age of 28.6 years at date of diagnosis of the index case. One hundred seventy-nine (72%) cases were born in Hong Kong compared to 151 (60%) controls. Only 9 cases and 10 controls were born outside of Guangdong Province. Cases and controls were similar with respect to ethnic origin (Cantonese, Sze Yap, Chiu Chau, elsewhere in Guangdong, Fukien/Taiwan, elsewhere in China), marital status, and level of education.

Table 2 shows the self-reported frequencies of Cantonese-style salted fish consumption among cases and controls during childhood (at age 10 years) and as an adult (3 years prior to diagnosis). Consumption during both time periods was significantly associated with NPC; the association was especially strong for childhood consumption. For weekly consumers of salted fish at age 10 years, the RR of NPC compared to those who never or rarely ate this food item was 37.7 (95% CL = 14.1, 100.4).

The mothers also were asked about their child’s consumption pattern of Cantonese-style salted fish at age 10 years. There was again a very strong positive association between frequency of consumption of salted fish and NPC. Only one of the responses between the mothers and their offspring (a case) differed by more than one frequency category (the categories were rarely, once a month to less than once a week, and one or more times a week).

Table 2 also shows the frequencies of Cantonese-style salted fish intake among cases and controls during other times in their childhood as reported by their mothers. Significantly more case-mothers reported feeding salted fish, salted fish head soup, and broth from steamed salted fish to their offspring between ages 1 and 2 years compared to control mothers. Foods that were considered as typical meals for the subject when he or she was between ages 1 and 2 years were coded as eaten “often” by the subject. Compared to individuals who never ate salted fish between ages 1 and 2 years, those who were fed this food “often” had a RR for NPC of 20.2 (95% CL = 6.8, 60.2). Similarly, more cases than controls were given salted fish as one of their first four solid foods during weaning (RR = 7.5, 95% CL = 3.9, 14.8).

Table 3 presents the salted fish intake frequencies for male and female cases and controls. The consumption patterns between male and female controls were very similar, and the risk ratios for corresponding levels of consumption are quite comparable between the two sexes.

Cases and controls who ate Cantonese-style salted fish regularly were similar with respect to the current usual kind of salted...
fish eaten ("soft meat" versus "tough meat") and the current
usual method of cooking it (over 90% of both case and control
groups reported steaming the fish over rice). As expected,
consumption patterns during the different time periods were
highly correlated. Logistic regression analysis was used to study
the joint effect of consumption of salted fish in the various time
periods. Consumption during weaning and at age 10 years were
independent significant risk factors for NPC; each remained
significant after adjustment was made for the other factor. There
was no significant residual effect for the remaining salted fish
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highly correlated. Logistic regression analysis was used to study
the joint effect of consumption of salted fish in the various time
periods. Consumption during weaning and at age 10 years were
independent significant risk factors for NPC; each remained
significant after adjustment was made for the other factor. There
was no significant residual effect for the remaining salted fish
variables.

Besides Cantonese-style salted fish, consumption (3 years
prior to diagnosis or at age 10 years) of a number of preserved
foods including moldy bean curd, salted pork, pork sausage,
lemon sausage, salted mustard green (mui choy), dried shrimp,
dried red date, cooling soup, and dried fruits at least once a week at age
10 years. Moldy bean curd and salted mustard green were
consumed at least weekly by 18 and 25% of cases, respectively,
at age 10 years. On the other hand, 46% of cases ate Cantonese-
style salted fish at least once a week at age 10 years.

A history of NPC among first degree relatives (parents and
siblings) was a significant risk factor for NPC; 18 cases compared
to 4 controls reported such a history. Eight case-mothers, 1
case-father, and 9 case-siblings had NPC; among controls there
were 1 father and 3 siblings who had NPC. All except one of
these 18 cases (and 2 of the 4 controls) ate Cantonese-style
salted fish at least once a week at age 10 years.

Table 3 presents the RRs for domestic exposure to smoke,
dust, or fumes among cases and controls. A significantly in-
creased risk (RR = 1.7) was observed for ever use of wood as
cooking fuel. The association was not statistically significant
after adjusting for Cantonese-style salted fish intake. All remain-
ing RRs in Table 4 (either unadjusted or after adjusting for salted
fish intake) remained highly significant after these other signifi-
cant risks to NPC were observed for occupational exposure to smoke,
dust, or fumes (Table 5). However, after taking consumption of
salted fish into account, none of the adjusted RRs was signifi-
cantly different from one. On the other hand, the RRs for salted
fish intake remained highly significant after these other significant
factors were taken into account.

Cases and controls were similar in their cigarette smoking
habits and in prior ear or nose disease. Very few cases and
controls were exposed to nasal oil at age 10 years. However, signifi-
cantly more cases used nasal oil 3 years prior to diagnosis
compared to controls; reasons given for the use indicate that
such use was probably related to the onset of their disease.

DISCUSSION

This study strongly suggests that consumption of Cantonese-
style salted fish is the primary cause of NPC in young Hong
Kong Chinese. Due to the possibility of bias in every observa-

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Frequency of salted fish consumption among cases and controls during various time periods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
</tr>
<tr>
<td>3 yr ago</td>
<td></td>
</tr>
<tr>
<td>Salted fish</td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>107</td>
</tr>
<tr>
<td>1/mo to less than 1/wk</td>
<td>100</td>
</tr>
<tr>
<td>1+/wk but less than daily</td>
<td>37</td>
</tr>
<tr>
<td>Daily</td>
<td>6</td>
</tr>
<tr>
<td>Salted fish head soup</td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>227</td>
</tr>
<tr>
<td>1+/mo</td>
<td>23</td>
</tr>
<tr>
<td>At age 10 yr</td>
<td></td>
</tr>
<tr>
<td>Salted fish</td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>10</td>
</tr>
<tr>
<td>1/mo to less than 1/wk</td>
<td>125</td>
</tr>
<tr>
<td>1+/wk</td>
<td>113</td>
</tr>
<tr>
<td>Salted fish head soup</td>
<td></td>
</tr>
<tr>
<td>Rarely</td>
<td>190</td>
</tr>
<tr>
<td>1+/mo</td>
<td>57</td>
</tr>
<tr>
<td>Between ages 1 and 2 yr (reported by mother)</td>
<td></td>
</tr>
<tr>
<td>Salted fish</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>19</td>
</tr>
<tr>
<td>Sometimes</td>
<td>65</td>
</tr>
<tr>
<td>Often</td>
<td>41</td>
</tr>
<tr>
<td>Salted fish head soup</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>99</td>
</tr>
<tr>
<td>Ever</td>
<td>25</td>
</tr>
<tr>
<td>Salted fish broth</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>27</td>
</tr>
<tr>
<td>Sometimes</td>
<td>58</td>
</tr>
<tr>
<td>Often</td>
<td>39</td>
</tr>
<tr>
<td>During weaning (reported by mother)</td>
<td></td>
</tr>
<tr>
<td>Salted fish</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>25</td>
</tr>
<tr>
<td>Ever</td>
<td>102</td>
</tr>
</tbody>
</table>

* Total may not add up to 250 case-control pairs or 127 case-mother/control-
mother pairs due to missing values.
tional study, we shall discuss in some detail the alternative explanations to our findings.

Case Selection. Misleading findings from a case-control study can be the result of inclusion of a nonrepresentative or even a wrong sample of cases. In the present study, all but five cases (98%) were confirmed histologically, and none of the tumors were incidental pathological findings. The 266 cases we contacted represent over 90% of all new cases of NPC in Hong Kong and only 16 of them (6%) refused to participate in the study. The distributions of cases by sex, age, or histological classification are similar to the population-based Hong Kong cancer registry data.

Table 4
Domestic exposure to smoke, dust, or fumes among cases and controls

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Unadjusted RR</th>
<th>Adjusted(a) RR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wood as cooking fuel</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>67</td>
<td>89</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>183</td>
<td>161</td>
<td>1.7(^b)</td>
<td>1.4</td>
</tr>
<tr>
<td>3 yr ago Incense</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>64</td>
<td>80</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>186</td>
<td>170</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Antimosquito coils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>189</td>
<td>192</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>61</td>
<td>58</td>
<td>1.1</td>
<td>2.4</td>
</tr>
<tr>
<td>At age 10 yr Incense</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>42</td>
<td>57</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>208</td>
<td>193</td>
<td>1.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Antimosquito coils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>172</td>
<td>174</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>78</td>
<td>76</td>
<td>1.0</td>
<td>1.8</td>
</tr>
<tr>
<td>At birth (reported by mother) Incense</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>19</td>
<td>20</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>108</td>
<td>107</td>
<td>1.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Antimosquito coils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>98</td>
<td>90</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>29</td>
<td>37</td>
<td>0.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Carried subject while cooking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>35</td>
<td>23</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Occasionally</td>
<td>52</td>
<td>63</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Often</td>
<td>40</td>
<td>41</td>
<td>0.6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

\(a\) Adjusted for salted fish intake during weaning and at age 10 years.
\(b\) Lower 95% confidence limit >1.0.

Table 5
Occupational exposure to smoke, dust, or fumes among cases and controls

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Unadjusted RR</th>
<th>Adjusted(a) RR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>240</td>
<td>247</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>10</td>
<td>3</td>
<td>4.5(^b)</td>
<td>0.6</td>
</tr>
<tr>
<td>Dust</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>191</td>
<td>209</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>59</td>
<td>41</td>
<td>1.8(^b)</td>
<td>1.2</td>
</tr>
<tr>
<td>Chemical fumes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>175</td>
<td>201</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ever</td>
<td>75</td>
<td>49</td>
<td>2.0(^b)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

\(a\) Adjusted for salted fish intake during weaning and at age 10 years.
\(b\) Lower 95% confidence limit >1.0.

Control Selection. A comparison group nonrepresentative of the population at risk can lead to a spurious association or mask a real association. The controls in this study are healthy individuals explicitly comparable to the cases in confounding variables such as age, sex, and socioeconomic status. Friend controls pose the risk of being too similar to the cases; they are unlikely to produce spurious associations.

More case-mothers (182/250 = 73%) than control-mothers (155/250 = 62%) were available for interview. There is no evidence, however, to indicate that these mothers were not representative of the source population. Comparisons of all case-mothers to all control-mothers were very similar to those between pairs of mothers of cases and their matched controls.

Since the interviewer was aware of the case status of the respondent and the interview took place after the diagnosis of NPC, we had taken special precautions against possible interviewer bias and recall bias on the part of the cases and their mothers. All questions were in closed form, were highly structured, and did not require probing by the interviewer. Salted fish was included with other food items in a long list with specific frequencies for each food as the only requested response. The respondent was asked to choose one from among two, three, or four frequency categories depending on whether the time period of interest was early or late childhood or adulthood. There was close correlation between the subject's chosen category of salted fish consumption frequency at age 10 years and his or her mother's response. Only one of 337 pairs of subject versus mother responses differed by more than one frequency category. Thus, it is unlikely that systematic bias from the interviewer or the respondent could completely account for the dramatic difference in salted fish consumption frequency between cases and controls.

Could salted fish be a confounder for some etiological variable not measured in this study? We think it is highly unlikely. If an observed association is not causal but simply the reflection of a causal association between some other factor and the disease, then this latter factor must be more strongly related to the disease (that is possessing a higher relative risk) than is the former factor (21). None of the other risk factors (genetic or viral) not investigated in this study has been shown to exhibit such a strong association with NPC.

Aside from lack of alternative explanations, Breslow and Day (21) stated the strength and specificity of the association, a dose-response effect, temporal relation of risk to exposure, consistency with other studies, and biological plausibility as criteria for assessing causality.

The strength of the association between Cantonese-style salted fish intake and NPC found in this study is among the largest ever reported between an exogenous factor and a human cancer. A dose-response effect is observed in both childhood and adulthood consumption. The stronger association with childhood consumption is compatible with the observed age pattern of NPC among southern Chinese. No other factors examined in this study showed an association with NPC that is of the same magnitude as that with intake of Cantonese-style salted fish. As a matter of fact, all other significant associations could be explained by the consumption of Cantonese-style salted fish.

Three earlier case-control studies of NPC in Chinese have investigated the possible role of Cantonese-style salted fish intake in the etiology of NPC. Henderson and Louie (10) studied...
only current consumption; their relative risk estimates are very similar to ours for the comparable time period. Armstrong et al. (11) examined childhood and adolescent consumption in Malaysian Chinese; again their results are comparable to our findings. Geser et al. (14) studied weaning habits of babies in NPC versus control households in Hong Kong Chinese and observed that NPC households were 2.6 times more likely to feed Cantonese-style salted fish to babies after weaning. Such an indirect measure of the actual consumption pattern of the case or control after weaning could explain the much lower magnitude of their reported relative risk.

The hypothesis that Cantonese-style salted fish intake causes NPC in Chinese is consistent with many aspects of the observed pattern of this disease in Chinese. Cantonese-style salted fish is a favorite food among southern Chinese especially those in Guangdong Province, but the food is rarely eaten by northern Chinese whose incidence rates of NPC are around 1 per 100,000 (2). NPC in southern Chinese displays an inverse relationship of the cheapest foods available to supplement rice in south China. NPC is the most common cancer in southern Chinese ages 15–34 years (20) suggesting that exposure to the etiologic agent(s) occurs early in life. Consumption of Cantonese-style salted fish early in life would also explain the high rates observed among migrants residing in low-risk areas such as North America (3, 7).

Volatile nitrosamines, including dimethyl nitrosamine and diethylnitrosamine, were detected in samples of Cantonese-style salted fish (16, 17). N-Nitroso compounds are potent animal carcinogens; specifically, diethylnitrosamine has been shown to induce carcinomas of the nasal cavity in rats (19, 22), gerbils (23, 24), hamsters (25–27), and bushbabies (28). More significantly, rats fed Cantonese-style salted fish have developed carcinomas of the nasal cavity (19). Thus, there is strong evidence to suggest the presence of preformed nasopharyngeal carcinogens or their precursors in Cantonese-style salted fish.

In southern Chinese, NPC is twice as common among males than females. Interestingly, we did not find any difference in frequency of consumption of salted fish between the two sexes and the association with salted fish holds equally strong for both sexes. We did not investigate portion size, which may account for the male preponderance, or there may be constitutional differences between the two sexes in their susceptibility to NPC. We estimate, based on population attributable risk computed from the data on frequency of consumption at age 10 years, that over 90% of NPC occurring in young Hong Kong Chinese can be attributed to consumption of Cantonese-style salted fish during childhood.

There are other factors that have been shown to be associated with an increased risk of NPC. Exposure to wood fires for cooking has been implicated in the development of NPC in Indonesia (29) and Malaysia (30). Our data suggest that it is not a significant risk factor for NPC in Hong Kong Chinese. Exposure to inhalants in an occupational setting has been shown to be related to NPC (3, 10, 11). Our study was unsuited for the evaluation of the association between NPC and occupational exposure; these young cases had worked only 10–15 years. Even though our young cases were more likely to be exposed to smoke, dust, or fumes on their jobs, these relatively weak associations did not persist after adjustment was made for Cantonese-style salted fish intake. Numerous studies have demonstrated an association between specific immune response to Epstein-Barr virus and NPC independent of race and geography (31), suggesting an etiologic role for the virus. However, it is unlikely that the virus is capable of inducing the disease by itself. The dissimilarity in geographical and racial distribution between Epstein-Barr virus infection and NPC incidence indicates that some critical cofactor(s) must be present. Epstein-Barr virus is a ubiquitous virus; there is serological evidence in Asia and Africa to suggest that practically everyone in those regions is infected very early in life (31). On the other hand, NPC has one of the most marked geographical and racial distribution of all cancers.

ACKNOWLEDGMENTS

We thank Malcolm C. Pike and Ronald K. Ross for their editorial suggestions, Neeltje M. Mack for her technical assistance, Ong-Sheng Wang for editing the data, and Beth Woodin and Cecilia Cedillo for preparation of this manuscript.

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