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An Epidemiological Study of Lung Cancer in Xuan Wei County, China: Current Progress. Case-Control Study on Lung Cancer and Cooking Fuel

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In Xuan Wei County, Yunnan Province, lung cancer mortality rates are among China's highest in males and females. Previous studies have shown a strong association of lung cancer mortality with air pollution from "smoky" coal combustion. In the present quantitative risk assessment of indoor air pollution study, the result strongly shows an obvious on-site exposure-response relationship between benzo[*a*]pyrene concentration in indoor air and lung cancer mortality and strongly supports the hypothesis that indoor air pollution is the main risk factor in inducing lung cancer in Xuan Wei County. In the present case-control study, the result shows that in females, the presence of lung cancer is statistically significantly associated with chronic bronchitis and family history of lung cancer. The results also suggest an association of lung cancer with duration of cooking food, but not with passive smoking. In males, the presence of lung cancer is associated with smoking, bronchitis, family history of lung cancer, and personal history of cooking food.

Introduction

During 1979 to 1983, investigators from the Chinese Academy of Preventive Medicine, Yunnan Province, Qujin and Xuan Wei County Antiepidemic Station, jointly conducted etiological studies of lung cancer, including a descriptive epidemiological study of lung cancer (smoking rate and lung cancer, domestic fuels and lung cancer), environmental monitoring of the pollutants of indoor air, bioassays (Ames, sister chromatid exchange), and animal tests. The results showed that there was a weak association of smoking and lung cancer, but a strong association of domestic fuel types and lung cancer (*1,2*). Occupation was not considered a risk factor of lung cancer in Xuan Wei because much higher lung cancer mortality was observed in farmers than in mine workers and officers.

In 1983, under the China-U.S. Protocol for Scientific and Technical Cooperation in the Field of Environmental Protection, researchers from the Chinese Academy of Preventive Medicine and the U.S. Environmental Protection Agency jointly conducted multidisciplinary studies in more detail. The results showed that there was strong association of indoor air pollution from burning smoky coal and high lung cancer mortality. The strong carcinogenic substances that were found in the pollutant emitted from combustion of smoky coal included polycyclic aromatic hydrocarbon (PAH) carcinogens such as BaP (benzo[*a*]pyrene), BA (benz[*a*]anthracene), SMC (5-methylchrysene), IDP (indeno[1,2,3-*c,d*]pyrene), BFT (benzofluoranthene), and DBP (dibenzo[*a,e*]pyrene) (*3*).

In order to make sure of the relationship between the indoor air pollution from smoky coal burning and lung cancer, scientists from China have conducted studies of dose-response relationships between BaP concentration in indoor air and lung cancer mortality in 11 Xuan Wei communes since 1986. At the same time, a case-control study was conducted to find other risk factors of lung cancer besides smoky coal, such as smoking, cooking, years and amount of smoky coal used, history of bronchitis, and family history of lung cancer. This paper presents results of the study that have just been finished in Xuan Wei. A large-scale case-control study and a etiological study of lung cancer in females (nonsmokers) are being now conducted in Xuan Wei County, China.

Background

Xuan Wei County, with a population of about 1 million, is located in the northeast of Yunnan Province, China, and its lung cancer mortality rates are among China's highest (*4*). Over 90% of the population is residentially stable. The local residents have used the three major types of fuel, smoky coal, smokeless coal, and wood, for heating and cooking. Smoky coal is glossy black,

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has a lower sulfur content, and smokes heavily on firing. Smokeless coal is dull black, has high sulfur and ash content, and produces little smoke. The fuel has traditionally been burned in a shallow, unventilated pit in the floor of the dwelling. Women are responsible for most household chores, which include starting the fire and cooking. A survey of 64 Xuan Wei residents showed that women on the average spent about 7 hr near the household fire, and men spent more time (9.6 hr) working outdoors than women. More than 40% of males but less than 0.2% of females smoke tobacco. Factory-made cigarettes and locally grown tobacco are used. Cigarettes are frequently smoked through water pipes.

Results

Study I. BaP Concentration in Indoor Air and Lung Cancer Mortality

Exposure Assessment. ON-SITE SELECTION. In 1986, 11 communes were selected as our study setting according to former investigation. In each commune, representative households were selected on the following conditions: fuel types used by each commune's resident, living in Xuan Wei at least 15 years, traditional house structure, and unventilated shallow pit. Twenty-seven representative households were selected from 11 communes.

SAMPLING TIME AND SAMPLE SIZES. According to starting fire and cooking time, the sampling times in each day were about 6:00 to 8:00 (starting fire and breakfast), 11:30 to 1:30, 4:30 to 6:30 (supper), and 9:30 to 3:30 (next morning), respectively. In each household, the samples were collected 3 consecutive days. About 640 air samples were collected.

SAMPLER. A KC-8301 inhalable particle sampler and glass fiber filter was used in sampling.

MEASUREMENT OF INDOOR AIR POLLUTANT. BaP was selected as the index of exposure. After extracting the glass fiber filter by vacuum sublimation under a nitrogen environment, the extracts were separated by paper chromatography, and BaP concentration in the extract was determined by using fluorescence spectrophotometry.

Response Assessment. According to the data of cancer retrospective investigation from 1973 to 1979 through China, age-adjusted lung cancer mortality of each of 11 communes was selected as the response index.

Data Analysis. All the data were processed and analyzed by using SAS and SYSTAT software. In counting BaP concentration, two weighted steps were used: 24-hr time weight and fuel-type weight. The formula for 24-hr time weight was as follows:

$$\text{BaP (smoky coal)} = (c1*1.5+c2*8+c3*1.5+c4*13)/24$$
$$\text{BaP (wood)} = (c1*2+c2*8+c3*2+c4*12)/24$$
$$\text{BaP (smokeless coal)} = (c1*2+c2*7+c3*2+c4*13)/24$$

where BaP means the average concentration per day; c1, c2, c3, and c4 are practical, measured concentrations at separate times each day; the coefficient represented the time that fuel burning persisted.

The formula of fuel-type weight was

$$\text{BaP concentration} = c1*N1+c2*N2+c3*N3$$

Table 1. Percentage of households burning fuel before 1958, BaP concentration in indoor air, and 1973–1979 age-adjusted lung cancer mortality in 11 Xuan Wei communes.

Commune	Smoky coal, %	Wood, %	Smokeless coal, %	BaP, $\mu g/100\ m^3$	Mortality, 1/100,000
Chengguan	100.0	0.0	0.0	108.56	174.21
Laibin	89.7	8.7	1.6	67.97	128.31
Rongcheng	81.9	18.1	0.0	248.50	104.09
Longtan	78.0	22.0	0.0	55.98	22.96
Longchang	76.1	17.9	6.0	107.99	39.46
Banqiao	34.0	16.4	49.6	39.95	19.03
Baoshan	87.1	12.9	0.0	46.37	9.18
Haidai	49.7	22.5	27.8	53.94	13.48
Puli	35.2	52.0	12.8	28.62	7.49
Luoshui	2.7	39.0	58.3	43.76	9.55
Reshui	0.0	66.6	33.4	35.60	2.08

where c1, c2, and c3 mean the time-weighted BaP concentration of different fuel types; N1, N2, and N3 mean the percentage of fuels used by each commune residents.

Relationship between BaP Concentration and Lung Cancer Mortality. The observation in Table 1 appears to show a close relationship of percentage of households burning smoky coal and BaP concentration with subsequent lung cancer mortality in contrast to the percentage of households burning wood and smokeless coal.

These data suggest that the more smoky coal smoke and BaP concentration an individual breathes, the more likely he or she is to develop lung cancer. The result of statistical analysis shows a high correlation between BaP concentration in indoor air and lung cancer mortality ($r = 0.778, p < 0.01$). This result suggests that BaP pollution in indoor air from smoky coal burning plays an important role in developing lung cancer in Xuan Wei, China.

Study II. Lung Cancer and Tobacco Smoking

Data gathered to date in Xuan Wei discloses a stronger association of lung cancer with domestic coal use than any other risk factors so far assessed, including tobacco smoking. The results presented in Table 2 show a very high percentage of smoking in males and not much difference of smoking percentage among communes. Women seldom smoke. Smoking may be contributing to lung cancer in males in Xuan Wei, but it is difficult to explain the marked differences of lung cancer mortality among Xuan Wei communes and the high lung cancer mortality in females. These data suggest that smoking may not be a main risk factor of lung cancer in Xuan Wei.

A case-control study has been done in Xuan Wei. In this study, the target population was confined to farmers in order to increase the validity of the findings. During 1985 to 1986, 110 cases (56 males and 54 females) newly diagnosed at Xuan Wei hospital and clinic were identified. Of these, 19 (17%) had been diagnosed on the basis of cytologic/pathologic findings and the remainder on the basis of clinical history and X-ray findings.

Controls were selected to matched lung cancer patients with respect to age (± 2 years), sex, and village of residence. Because fuel-use habits and dwelling types are similar within individual Xuan Wei villages, this design was expected to provide effective matching with respect to indoor fuel type and dwelling type. Such matching was sought because it would increase the

Table 2. Percentage of tobacco smoking and 1973–1979 adjusted lung cancer mortality in 11 Xuan Wei communes.

Commune	Tobacco smoking, %			BaP,	Mortality, 1/100,000		
	Male	Female	Combined	$\mu g/100\ m^3$	Male	Female	Combined
Chengguan	38.27	0.01	16.36	108.56	173.44	175.29	174.21
Laibin	45.11	0.08	22.85	67.97	119.42	137.82	128.31
Rongcheng	37.62	0.01	16.08	248.50	101.01	107.55	104.09
Longchang	32.64	0.03	16.67	107.99	48.86	30.31	39.46
Longtan	37.02	0.03	18.83	55.98	31.11	14.52	22.96
Haidai	33.50	0.02	16.98	53.94	16.95	10.15	13.48
Puli	42.44	0.23	21.42	28.62	5.94	9.23	7.49
Banqiao	35.94	0.06	17.62	39.95	22.04	16.25	19.03
Luoshui	45.79	0.01	22.50	43.76	9.93	9.20	9.55
Xize	42.69	0.03	21.63	—	—	—	3.81
Reshui	40.42	0.10	20.42	35.60	3.11	1.03	2.08

effectiveness with which factors other than fuel type could be assessed. Patients were generally matched with as many eligible controls as could be located. After exclusion of 26 controls due to erroneous questionnaire responses, 426 controls were included in data analysis, for an average of 3.87 controls per case.

A standardized questionnaire of the closed-question type was developed. Study factors included tobacco use history, family and personal medical history, domestic fuel use history, indoor fuel use history, history of cooking food, dwelling type, ethnic group (nationality), and socioeconomic and educational levels. After strict interviewer training and field testing, this questionnaire was administered to all lung cancer patients and controls were interviewed directly.

An index of tobacco smoking was calculated by multiplying the duration of smoking (in years) by the amount of tobacco smoked (in kilograms per month), and dividing by the age (in years) at which the subject started smoking. A subject was considered to have a positive family history of chronic bronchitis if he or she had been diagnosed by a doctor to have this condition or reported cough for at least 3 months per year for more than 2 years.

To assess the effects of individual independent variables, unmatched, unadjusted odds ratios (OR) were calculated (*5*). Confidence intervals around these OR were calculated by Miettinen's method (*6*). Dose-response trends were tested by extension of the Mantel-Haenszel procedure (*7*).

To develop adjusted estimates of ORs associated with selected factors and interactions, conditional logistic regression models were also constructed for males and females. In these models, all variables were dichotomous, assuming values of 0 or 1. The selected risk factors and interactions were treated as independent variables, and the presence or absence of lung cancer was treated as the dependent variable. These anallyses were performed by using the PECAN program (*8,9*).

Table 3 presents the analysis result of unadjusted odds ratios and confidence intervals (CI) for lung cancer and smoking in males. No relationship between lung cancer and ever having smoked tobacco is observed. There is a suggestion of monotonic dose-response trend of lung cancer with the age at which smoking began, duration of smoking, and monthly amount of smoking. However, none of these trends is statistically significant at alpha = 0.05. In contrast, a statistically significant dose-response trend of lung cancer with smoking index is observed. The results suggest that smoking plays a role in lung cancer in males, but the odds ratios is much lower than expected in view of the fact that in studies of smoking and cancer, the smoking-associated odds ratios often exceed 15 (*10*).

Table 3. Unadjusted odds ratios (OR) and 95% confidence intervals (CI) for lung cancer in males according to smoking and cooking, Xuan Wei, China.

Factor	No. of cases	No. of controls	OR	95% CI
Ever smoked				
No	4	19	1.00	
Yes	52	205	1.20	0.39–3.69
Age started to smoke, years				
Never	4	19	1.00	
≥ 20	20	80	1.19	0.36–3.88
< 20	32	125	1.22	0.39–3.82
Trend (*p*-value)			($p > 0.05$)	
Years of smoking				
0	4	19	1.00	
< 35	30	146	0.98	0.31–3.07
≥ 35	22	59	1.77	0.55–5.73
Trend (*p*-value)			($p > 0.05$)	
Amount of smoking, kg/per month				
Never	4	19	1.00	
< 1.2	45	190	1.12	0.36–3.47
≥ 1.2	7	15	2.22	0.55–8.86
Trend (*p*-value)			($p > 0.05$)	
Smoking index[a]				
< 0.1	4	34	1.00	
0.1–2.2	44	179	2.09	0.72–6.07
> 2.2	8	11	6.18	1.69–22.57
Trend (*p*-value)			($p < 0.01$)	
Often cooks food				
No	44	200	1.00	
Yes	12	24	2.27	0.98–5.24

[a]Smoking index = years of smoking × amount of smoking/age started to smoke.

As shown in Table 4, a statistically significant relationship of lung cancer with age at which the woman began to cook food is observed, though none of the individual odds ratios is significant. No association of lung cancer with passive smoking is observed.

In both sexes, lung cancer is significantly associated with family history of lung cancer and personal history of chronic bronchitis (Table 5).

The results of conditional logistic regression analysis are consistent with that of the above analysis, and no interaction is observed (Tables 6 and 7).

Discussion

In studying the relationship between air pollution and carcinomas, it is important to understand the time sequence of the

Table 4. Unadjusted odds ratios (OR) and 95% confidence intervals (CI) for lung cancer in females according to cooking and passive smoking, Xuan Wei, China.

Factor	No. of cases	No. of controls	OR	95% CI
Age started to cook				
> 15	13	73	1.00	
10–15	35	117	1.68	0.84–3.37
< 10	6	12	2.81	0.92–8.54
Trend (p-value)			($p = 0.05$)	
Years of cooking				
< 30	7	53	1.00	
30–44	28	85	2.49	1.04–5.99
≥ 45	19	64	2.25	0.85–5.66
Trend (p-value)			($p > 0.05$)	
Passive smoking				
No	9	26	1.00	
Yes	45	176	0.74	0.32–1.68

Table 5. Unadjusted odds ratios (OR) for lung cancer in males and females according to familial history of lung cancer, history of chronic bronchitis, and years using unventilated fire pit, Xuan Wei, China.

	Male			Female			Total		
Factor	Case	Control	OR	Case	Control	OR	Case	Control	OR
Family history of lung cancer									
No	43	202		46	192		89	394	
Yes	13	22	2.78*	8	10	3.34*	21	32	2.90*
History of chronic bronchitis									
No	39	209		38	184		77	393	
Yes	17	15	6.07*	16	18	4.30*	33	33	5.10*
Years using unventilated fire pit									
< 45	22	107		21	84		43	191	
≥ 45	34	117	1.41	33	118	1.12	67	235	1.27

*$p < 0.01$.

Table 6. Conditional logistic regression odds ratios for lung cancer in males, Xuan Wei, China, 1985–1986.

Factor	Model 1	Model 2	Model 3	Model 4
Often cooks food	3.99†	2.75*	3.31*	3.37*
Smoking index[a]				
< 0.1	1.00		1.00	1.00
0.1–2.2	3.14		4.53	4.91
> 2.2	8.29*		11.32*	12.55
Family history of lung cancer	2.91†	2.92†	2.70†	2.73†
History of chronic bronchitis		7.12†	7.94†	9.66†
Interaction between smoking and chronic bronchitis[b]				0.63

[a]Smoking index = years of smoking × amount of smoking/age started to smoke.

[b]Interaction equals one when the smoking index is 1.0 or more and the subject has a history of chronic bronchitis. Otherwise interaction equals zero.

*$p < 0.05$.

†$p > 0.01$.

causes and results because there is long, latent duration from first exposure to cancer onset. In the present study, does the air pollution measured represent the past exposure? From the history records of Xuan Wei County (*11*), the living condition and style (including fuel types used among communes, burning in unventilated shallow pits, and house structure) has changed little for over 100 years, and most residents are farmers (90%). From death data of 1973–1979, the lung cancer mortality has been stable for 7 years, perhaps due to stable carcinogens existing in the environment. It is reported that inhalable particles are very harmful

Table 7. Conditional logistic regression odds ratios for lung cancer in females, Xuan Wei, China, 1985–1986.

Factor	Model 1	Model 2	Model 3	Model 4
Family history of lung cancer	3.30†	3.74†	3.62†	3.32†
History of chronic bronchitis	7.66†	6.43†	6.73†	7.78†
Age started to cook, years				
> 15		1.00		
10–15		1.68		
< 10		2.33		
Years of cooking				
< 30			1.00	
30–44			7.23*	
> 44			8.43	
Passive smoking				1.12

*$p < 0.05$.

†$p > 0.01$.

to human health (*12*), and in Xuan Wei County, 98.4% of BaP existed as particles smaller than 7μm (*13*), so it is reasonable to select BaP as an exposure index. In assessing BaP concentration, two-step weight methods were used (time and fuel-type), and we think this is practical.

On balance, the exposure and response assessment in our study is representative and practical. A more detailed study of the dose-response relationship between lung cancer and air pollution and a case-control study are now in progress in Xuan Wei.

Conclusion

PAH (BaP as index) pollution in indoor air induced by smoky coal burning in unventilated, shallow pits plays an important role in lung cancer. Smoking is not a main risk factor of lung cancer in Xuan Wei County, China.

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