Public Health Classics

This section looks back to some ground-breaking contributions to public health, reproducing them in their original form and adding a commentary on their significance from a modern-day perspective. To complement this month's theme of the *Bulletin*, Elisa Ong and Stanton A. Glantz review the 1981 paper by Takeshi Hirayama on the risk of lung cancer from passive smoking. The original paper is reproduced with permission from the *British Medical Journal*.

Hirayama's work has stood the test of time

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In January 1981, Takeshi Hirayama published his epidemiological study demonstrating that second-hand smoke increased the risk of lung cancer in non-smoking Japanese women married to men who smoked compared with non-smoking women married to non-smoking men (*1*). Hirayama is generally credited with publishing the first evidence linking passive smoking and lung cancer, though there were two other studies published at about the same time, by Trichopoulos et. al (*2*) from Greece and Garfinkel (*3*) from the USA. While both studies showed an elevation in the point estimate of lung cancer risk associated with passive smoking, Garfinkel's study did not reach statistical significance.

Moving well beyond its usual efforts to create controversy about scientific studies that reach bothersome conclusions, the tobacco industry responded with a multimillion-dollar advertising campaign designed specifically to discredit Hirayama's paper (*4*). The industry commissioned epidemiologist Nathan Mantel to write a critique and used it, together with a cleverly worded description of the Garfinkel study, to suggest that it disputed the passive smoking–lung cancer connection, in advertisements that reached an estimated 80% of the American population (*5*). This campaign was particularly cynical since it was run despite the fact that the industry's own scientists, after reviewing Hirayama's work, concluded "Hirayama is a good scientist and his non-smoking wives publication was correct" and "that Hirayama was correct, that TI [Tobacco Institute] knew it, and that TI published its statement about Hirayama knowing that the work was correct" (*6, 7*).

The *British Medical Journal* took note of these public attacks and re-opened correspondence about Hirayama's paper to provide him with an opportunity to respond in a scientific forum. The editors took the exceptional step of publishing Mantel's criticisms, which had been addressed to the Tobacco Institute and not the *British Medical Journal*, nine months after Hirayama's paper was originally published (*9, 10*). Hirayama and others demolished the criticisms (*9, 10*).

The campaign against Hirayama's findings was not limited to the United States. The tobacco industry ran similar advertisements worldwide. In Australia, the Australian Federation of Consumer Organizations took the Australian Tobacco Institute to court for misleading advertising over these claims, and won on the grounds that the advertisement was false and misleading (*11*).

The controversy generated by the tobacco industry attracted the attention of other epidemiologists who sought to see who was right. As a result, by 1986, 13 studies had been done on passive smoking and lung cancer, and the evidence was strong and consistent enough for the US Surgeon General to issue the first report dealing entirely with the effects of passive smoking (*12*), which concluded that "involuntary smoking causes disease, including lung cancer, in healthy nonsmokers". A few weeks later, the US National Academy of Sciences issued a similar report reaching the same conclusion (*13*). Concerning anything other than tobacco, the issue would have been considered closed at that point.

As time passed, several independent scientific bodies around the world reviewed the evidence that passive smoking causes lung cancer (and a wide variety of other diseases) and reached similar conclusions (Table 1). These reports helped stimulate the passage of clean indoor air ordinances, which not only protect non-smokers from second-hand smoke but also create an environment that makes it easier for smokers to stop (*14, 15*).

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Ref. No. **00-0752**

Since publication of Hirayama's original paper, 37 studies of passive smoking and lung cancer have been published (*16*). Yet, needless to say, the tobacco industry continues to fight against the conclusion that second-hand smoke causes lung cancer. Recently the International Agency for Research on Cancer (IARC) published a study (*17*) similar to Hirayama's and supported the large body of evidence that second-hand smoke is a carcinogen (*18*). Years before the IARC report was published, however, the tobacco industry organized a sophisticated campaign against the study in an effort to prevent worldwide smoking restrictions, with the same kinds of misrepresentations it used against Hirayama (*19*).

Almost two decades have passed since publication of Hirayama's work and, despite the tobacco industry's best efforts, his conclusion that passive smoking causes lung cancer has stood the test of time. ■

Table 1. **Risk of lung cancer in passive smokers: results of study by Hirayama (*1*) confirmed by major international consensus reports**

Report	Year	Country	Relative risk	Confidence interval[a]
Hirayama (*1, 9, 10*)	1981	Japan		
1–19 cigarettes a day			1.61	1.09–2.39
20 cigarettes a day or more			2.08	1.39–3.11
US Environmental Protection Agency (*20*)	1992	USA	1.19	1.01–1.39
National Research Council (*13*)	1986	USA	1.34	1.18–1.53
Surgeon General (*12*)	1986	USA	1.53	na
California Environmental Protection Agency (*21*)	1997	USA	1.20	na
National Health and Medical Research Council (*22*)	1997	Australia	1.32	1.10–1.69
Scientific Committee on Tobacco and Health (*23*)	1998	UK	1.20–1.30	na

[a] Confidence intervals are two-tailed 95%, except US EPA which is one-tailed 95% (two-tailed 90%).

na = not available.

Acknowledgement

This work was supported by NCI Grant CA-61021.

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PAPERS AND SHORT REPORTS

Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan

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Abstract

In a study in 29 health centre districts in Japan 91 540 non-smoking wives aged 40 and above were followed up for 14 years (1966-79), and standardised mortality rates for lung cancer were assessed according to the smoking habits of their husbands. Wives of heavy smokers were found to have a higher risk of developing lung cancer and a dose-response relation was observed. The relation between the husband's smoking and the wife's risk of developing lung cancer showed a similar pattern when analysed by age and occupation of the husband. The risk was particularly great in agricultural families when the husbands were aged 40-59 at enrolment. The husbands' smoking habit did not affect their wives' risk of dying from other disease such as stomach cancer, cervical cancer, and ischaemic heart disease. The risk of developing emphysema and asthma seemed to be higher in non-smoking wives of heavy smokers but the effect was not statistically significant.

The husband's drinking habit seemed to have no effect on any causes of death in their wives, including lung cancer.

These results indicate the possible importance of passive or indirect smoking as one of the causal factors of lung cancer. They also appear to explain the long-standing riddle of why many women develop lung cancer although they themselves are non-smokers. These results also cast doubt on the practice of assessing the relative risk of developing lung cancer in smokers by comparing them with non-smokers.

Introduction

The possible consequences to the health of non-smokers of long-term exposure to cigarette smoke (passive smoking) should be studied thoroughly because the side-stream and second-hand smoke of cigarettes contain various toxic substances, including carcinogens.[1 2] The need for such a study increased by the report of small-airways dysfunction in non-smokers chronically exposed to tobacco smoke.[3]

The effect of passive smoking on lung cancer was studied by following 91 540 non-smoking housewives aged 40 and above and measuring their risk of developing lung cancer according to the smoking habits of their husbands.

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Methods

To study the consequences to health of such factors as cigarette smoking, alcohol drinking, occupation, and marital status, a prospective population study has been in progress in 29 health centre districts in six prefectures in Japan since the autumn of 1965. In total 265 118 adults (122 261 men and 142 857 women) aged 40 years and over, 91-99% of the census population, were interviewed and followed by establishing a record linkage system between the risk-factor records, a residence list obtained by special yearly census, and death certificates.

Since the effect of direct smoking of cigarettes in this study has already been reported,[4-7] my study focused on the effect of husband's smoking on the risk of lung cancer in their non-smoking wives. Such observation was possible since detailed questions about lifestyle, including smoking habits, were asked of husbands and wives independently at the start of this study. No subjective bias was therefore conceivable.

A total of 346 deaths from lung cancer in women were recorded during 14 years of follow-up (1966-79). Of these women 245 were married, and 174 of these were also non-smokers. These cases occurred among 91 540 non-smoking married women whose husbands' smoking habits were studied. The risk of lung cancer was carefully measured, taking into consideration possible confounding variables.

Results

Wives of heavy smokers were found to have a higher risk of developing lung cancer than wives of non-smokers and a statistically significant dose-response relationship was observed (Mantel-extension χ test result being 3·299; two-tailed $p = 0{\cdot}00097$). Age-occupation standardised annual mortality rates for lung cancer were 8·7/100 000 (32 out of 21 895) when husbands were non-smokers or occasional smokers,

14·0 (86 out of 44 184) when husbands were ex-smokers or daily smokers of 1-19 cigarettes, and 18·1 (56 out of 25 146) when husbands were daily smokers of 20 or more cigarettes. These figures gave risk ratios of 1·00, 1·61, and 2·08 respectively. A similar trend was observed in age and occupation groups of husbands (table I).

TABLE I—*Standardised mortality for lung cancer in women by age, occupation, and smoking habit of the husband (patient herself a non-smoker)*

Husband's smoking habit:	Non-smoker	Ex-smoker or 1-19/day	⩾20/day
Husband's age: 40-59 years			
Population of wives	14 020	30 676	20 584
No of deaths from lung cancer	11	40	36
Occupation-standardised mortality/100 000	5·64	9·34	13·14
Husbands age: ⩾60 years			
Population of wives	7875	13 508	4877
No of deaths from lung cancer	21	46	20
Occupation-standardised mortality/100 000	15·79	24·44	29·60
Standardised risk ratio for all ages	1·00	1·61	2·08
Husband working in agriculture			
Population of wives	10 406	20 044	9391
No of deaths from lung cancer	17	52	24
Age-standardised mortality/100 000	9·54	17·02	18·40
Husband working elsewhere			
Population of wives	11 489	24 140	16 070
No of deaths from lung cancer	15	34	32
Age-standardised mortality/100 000	9·13	10·46	17·78
Standardised risk ratio for all occupations	1·00	1·43	1·90

The relation between the husband's smoking habit and the wife's risk of developing lung cancer was particularly significant in agricultural families when the husband was aged 40-59 at enrolment (Mantel-extension chi being 2·597 or two-tailed p=0·0094); lung cancer risk ratios were 1·00, 3·17, and 4·57 when husbands were non-smokers or occasional smokers, ex-smokers or smokers of 1-19 cigarettes daily, and smokers of 20 or more cigarettes daily respectively (table II).

TABLE II—*Mortality for lung cancer in women by occupation and by smoking habit of husband among men aged 40-59 (patient herself a non-smoker)*

Husband's smoking habit:	Non-smoker	Ex-smoker or 1-19/day	⩾20/day
Agricultural workers:			
Population of wives	5 999	12 753	7150
No of deaths from lung cancer	3	20	16
Mortality/100 000	3·48	11·03	15·92
Other workers			
Population of wives	8 021	17 923	13 434
No of deaths from lung cancer	8	20	20
Mortality/100 000	7·15	8·09	11·05
Standardised risk ratio for all occupations	1·00	1·67	2·36

The husbands' smoking habits seemed to have no effect on their wives' risk of developing other major cancers, such as cancers of the stomach (n=716) and of the cervix (n=250) or ischaemic heart disease (n=406). The risk of developing emphysema and asthma seemed to be higher among the non-smoking wives of smokers, but the effect was not statistically significant (table III).

Other characteristics of the husbands, such as their alcohol drinking habits did not affect mortality from lung cancer in their wives. The relative risk ratios of death from lung cancer were 1·00, 1·13, and 1·18 (p=0·396) respectively when husbands were non-drinkers, occasional or rare drinkers, and daily drinkers. Similar results were found with other causes of death (table IV).

Finally, the effect of passive smoking was compared with the effect of direct smoking. The effect of passive smoking was around one-half to one-third that of direct smoking. The relative risk of developing lung cancer by passive smoking was about 1·8 compared with about 3·8 in direct smokers (fig 1).

TABLE III—*Age-occupation standardised risk ratio for selected causes of death in women by smoking habit of the husband (patient herself a non-smoker)*

Cause of death	Husband's smoking habit			p value
	Non-smoker	Ex-smoker, or 1-19/day	⩾20/day	
Lung cancer (n=174)	1·00	1·61	2·08	0·001
Emphysema, asthma (n=66)	1·00	1·29	1·49	0·474
Cancer of cervix (n=250)	1·00	1·15	1·14	0·249
Stomach cancer (n=716)	1·00	1·02	0·99	0·720
Ischaemic heart disease (n=406)	1·00	0·97	1·03	0·393

TABLE IV—*Age-standardised risk ratio for selected causes of death in women by alcohol-drinking habit of the husband*

Cause of death	Husband's drinking habit			p value
	Non-drinker	Occasional or rare drinker	Daily drinker	
Lung cancer (n=174)	1·00	1·13	1·18	0·396
Emphysema, asthma (n=66)	1·00	0·92	1·39	0·292
Cancer of cervix (n=250)	1·00	0·84	0·89	0·514
Stomach cancer (n=716)	1·00	0·88	0·95	0·285
Ischaemic heart disease (n=406)	1·00	1·09	0·93	0·567

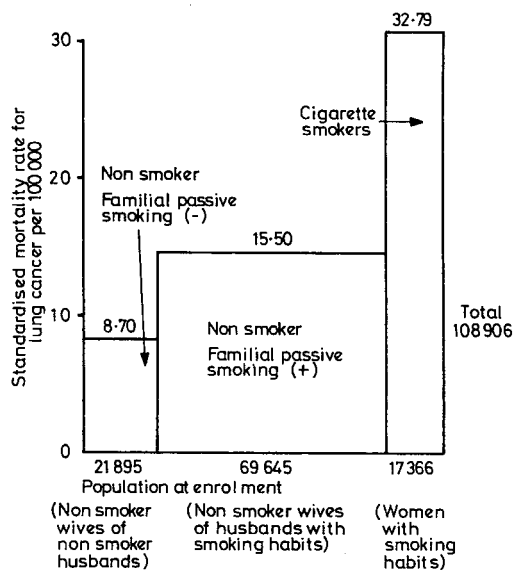

FIG 1—Lung cancer mortality in women according to the presence or absence of direct and familial indirect smoking.

Discussion

The possible effect of passive smoking was studied by following many non-smoking wives whose husbands had various smoking habits, and measuring their risk of developing lung cancer. Continued exposure to their husbands' smoking increased mortality from lung cancer in non-smokers up to twofold. The extent of the increase in the risk of developing cancer reached as high as 4·6 for non-smoking wives of agricultural workers aged 40-59 who smoked 20 or more cigarettes a day.

The fact that there was a statistically significant relation (two-tailed p=0·00097) between the amount the husbands smoked and the mortality of their non-smoking wives from lung cancer suggests that these findings were not the result of chance. To determine whether such an effect was limited to lung cancer, similar studies were conducted with other causes of death. Although there seemed to be a relation between husbands' smoking habits and deaths from emphysema and asthma in their wives, the effect of passive smoking was strongest with

lung cancer. Passive smoking did not seem to increase the risk of developing stomach cancer, cervical cancer, or ischaemic heart disease. We found that smoking was the only habit of the husbands to affect wives' mortality. The absence of an effect of husbands' drinking habits on mortality in their wives was shown as an example.

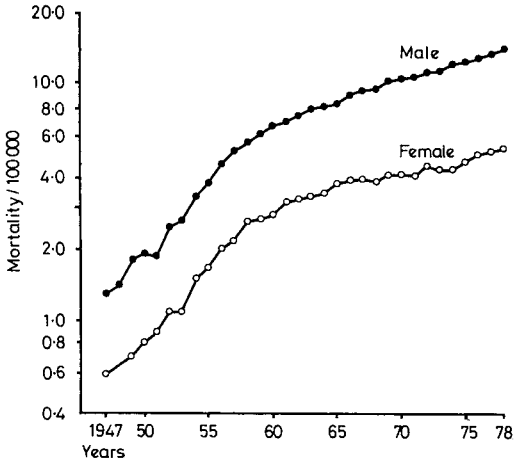

FIG 2—Age-adjusted mortality for lung cancer in Japan (1947-78).

The most important confounding variables would have been urban factors. Similar observations were therefore made for agricultural families and for non-agricultural families, and a similar dose-response relation was observed in both groups. The effect of passive smoking was most striking in younger couples in agricultural families, relative risk reaching 4·6, probably because of the lesser extent of the exposure to passive smoking outside the family in the case of rural residents. That the rate for non-smoking wives with husbands who were heavy smokers in urban families was lower than that in rural families is puzzling but probably reflects a longer period of mutual contact of couples in rural families. In urban families some couples meet only for a short period in the day.

Finally, the effects of passive smoking were compared with the effects direct smoking. The results clearly indicated that the effect of passive smoking is about one-half to one-third that of direct smoking in terms of mortality ratio or relative risk. In terms of attributable risk, however, the effect of passive smoking on lung cancer in women must be much more important than that of direct smoking (fig 1), especially in countries such as Japan where 73% of men but only 15% of women smoke. Therefore, although the relative risk of indirect smoking was smaller than that of direct smoking, the absolute excess deaths from lung cancer due to passive smoking must be important because of the large size of the exposed group.

The age-adjusted mortality rates for lung cancer have been sharply increasing both for men and for women in Japan (fig 2). As only a fraction of Japanese women with lung cancer smoke cigarettes, the reasons why their mortality from lung cancer parallels that in men have been unclear. The present study appears to explain at least a part of this long-standing riddle.

This observation also questions the validity of the conventional method of assessing the relative risk of developing lung cancer in smokers by comparing them with non-smokers. This study shows that non-smokers are not a homogenous group and should be subdivided according to the extent of previous exposure to indirect or passive smoking.

This work was supported by Grants-in-Aid for Cancer Research from the Ministry of Health and Welfare.

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(*Accepted 13 November 1980*)