**TABLE 3.—Continued**

| Study | Subjects | Pulmonary function measured | Outcome | Comments |
|---|---|---|---|---|
| Dodge (1982) | 558 children, aged 8–10, Arizona, United States | $FEV_1$ by age change $FEV_1/H^2$/year | No effect of parental smoking | Potential participation rate bias; cross-sectional data not controlled for child height; annual $FEV_1/H^2$ at ages 8, 9, and 11 consistently greater in nonsmoking households than two-parent smoker households; statistical test not significant |
| Tashkin et al. (1984) | 1,080 nonsmoking, nonasthmatic children, Los Angeles, United States | $\dot{V}_{max}$, $\dot{V}_{max75}$, $\dot{V}_{max25}$, $FEF_{25-75}$ | Decreased $\dot{V}_{max}$, $\dot{V}_{max25}$ for boys, and $FEF_{25-75}$, $\dot{V}_{max75}$ for girls with smoking mother at least | No effect of paternal smoking |
| Chen and Li (1986) | 571 children, aged 8–16, China | $FEV_1$ and MMEF | Significantly decreased $FEV_1$ and MMEF in children exposed to paternal cigarette smoke | Adjusted for child's own smoking, gas stoves, and parental symptoms |
| Hasselblad et al. (1981). | 16,689 children, aged 5–17, seven geographic regions, United States | $FEV_1$ as percent predicted | Significant effect of maternal but not paternal smoking | Large number of children excluded for invalid pulmonary function data or missing parental smoking data |
| Speizer et al. (1980) | 8,120 children, aged 6–10, six U.S. cities | FVC and $FEV_1$ as percent predicted | No effect for $FEV_1$ or FVC | Recent analysis demonstrated an effect for FVC and $FEV_1$ |
| Lebowitz (1984) | 117 families, Tucson, Arizona, United States | FVC and $FEV_1$ | No effect of parental smoking | Also assessed, TSP and ozone rates had little effect |
| Ekwo et al. (1983) | 1,355 children, aged 6–12, Iowa City, Iowa, United States | $FEV_1$, FVC | No effect of parental smoking | Data for this outcome not specifically analysed; increased bronchial responsiveness among smoke-exposed children |
| Spinaci et al. (1985) | 2,385 schoolchildren, Turin, Italy | $FEV_1$ | Statistically significant effect of maternal smoking | No passive smoking effect difference between boys and girls |

## TABLE 4.—Pulmonary function in children exposed to involuntary smoking; longitudinal studies

| Study | Subjects | Pulmonary function measured | Outcome | Comments |
|---|---|---|---|---|
| Tager et al. (1983) | 1,156 children, aged 5–10 at initial survey, East Boston, Massachusetts, United States | $FEV_1$, $FEF_{25-75}$ | Significantly decreased $FEV_1$ and $FEF_{25-75}$ growth rate for children of smoking mothers | 7-year followup; no effect of paternal smoking; magnitude roughly 4 to 5 percent |
| Ware et al. (1984) | 10,000 children, aged 6–11, six U.S. cities | FVC, $FEV_1$ | FVC positively associated with smoking; $FEV_1$ negatively associated with smoke exposure | $FEV_1$ dose–response with amount smoked by mother; magnitude of effect estimate 6 percent |
| Berkey et al. (1986) | 7,834 children, aged 6–10, six U.S. cities | FVC, $FEV_1$ | Slightly higher FVC level, slightly lower $FEV_1$ level in smoke-exposed; growth of both decreased by smoke exposure | Consistent with 3 percent deficit in $FEV_1$ growth |
| Burchfiel et al. (1986) | 3,482 children, aged 0–10, Tecumseh, Michigan, United States | FVC, $FEV_1$, $\dot{V}_{max50}$ | $FEV_1$ level and growth decreased by maternal smoking | Dose–response in male children with number of parental smokers |

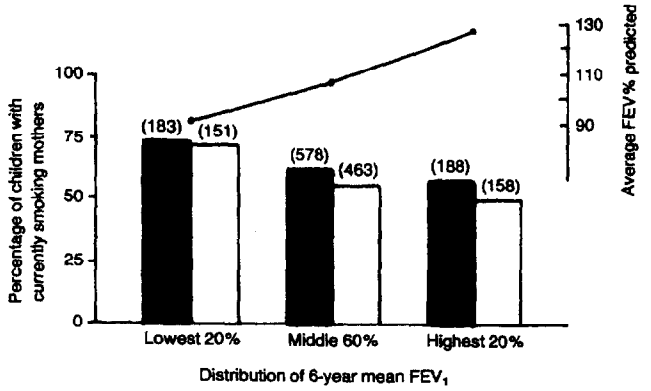


**FIGURE 2.—Percentage of children with mothers who were current cigarette smokers at initial examination (black columns) and sixth examination (white columns), according to distribution of mean age, height, and sex-corrected $FEV_1$ over the first six examinations**

NOTE: Lowest 20%, middle 60%, and highest 20% refer to children with values in the bottom one-fifth, middle three-fifths, and upper one-fifth, respectively, of the mean $FEV_1$ distribution; numbers in parentheses indicate number of children in each group; the three circles represent the average percent predicted values of $FEV_1$ for the three groups; results for male and female children were combined, because difference between sexes was not significant.

SOURCE: Tager et al. (1983).

study could not establish the ages at which children were most vulnerable to exposure to tobacco smoke.

Ware and colleagues (1984) followed 10,106 white children for two successive annual examinations as part of the Harvard Air Pollution Health Study in six U.S. cities. The forced vital capacity was significantly higher for children of mothers who were either current smokers or ex-smokers. However, children whose mothers were current smokers had a 0.6 percent lower mean $FEV_1$ at the first examination and 0.9 percent lower mean $FEV_1$ at the second examination. Maternal smoking had a greater effect than paternal smoking, although the effects of both were significant. The changes in level of $FEV_1$ observed were small. For exposure to a mother who smoked one pack of cigarettes per day, the $FEV_1$ was estimated to be decreased by less than 1 percent, or 10 to 20 mL for a child with an $FEV_1$ between 1.5 and 2.5 liters. Projecting the effect cumulatively to age 20 yields an approximately 3 percent deficit. This effect is comparable to that observed by Tager and colleagues (1983). These small average effects may underestimate the effects on populations of susceptible children.

A more extensive analysis of longitudinal data from the Harvard cohort was performed using a mathematical model to describe lung growth (Berkey et al. 1986). This analysis included 7,834 children between 6 and 10 years of age who were evaluated from two to five times over a 5-year period. The model estimated that a smoke-exposed child at age 8 would have an $FEV_1$ 0.81 percent lower than a non-smoke-exposed child, and growth of $FEV_1$ would be 0.17 percent lower per year. Both effects were statistically significant. For an 8-year-old child with an $FEV_1$ of 1.62 liters, these results translate into a deficit of 13 mL in $FEV_1$ and of 3 mL in annual increase in $FEV_1$. The magnitude of the maternal smoking effect is consistent with a deficit in $FEV_1$ of 2.8 percent in naturally attained growth, if the effect is sustained throughout childhood.

Burchfiel and colleagues (1986) have conducted a longitudinal study of 3,482 children observed over a 15-year period in Tecumseh, Michigan. The mean increase in $FEV_1$ for nonsmoking boys between the ages of 10 and 19 years was 82.3, 76.2, and 74.5 mL per year for subjects with zero, one, and two smoking parents, respectively. Boys with one parent who smoked experienced 92.6 percent and boys with two parents who smoked experienced 90.5 percent of the growth in $FEV_1$ seen in male children with nonsmoking parents. Effects of parental smoking were not found in girls.

The available data demonstrate that maternal smoking reduces lung function in young children. However, the absolute magnitude of the difference in lung function is small on average. A small reduction of function, on the order of 1 to 5 percent of predicted value, would not be expected to have functional consequences. However, some children may be affected to a greater extent, and even small differences might be important for children who become active cigarette smokers as adults.

A minority of adult cigarette smokers develop chronic obstructive lung disease, and factors influencing lung growth and development during childhood might predispose to disease in adulthood (Samet et al. 1983; Speizer and Tager 1979). In Figure 3 is depicted a model of growth and decline in pulmonary function from childhood through adulthood, as measured by the $FEV_1$. Pulmonary function peaks in early adult life and declines steadily thereafter in both smokers (curve B) and nonsmokers (curve A). In people who develop chronic lung disease (curve C), a more rapid decline has occurred. Childhood factors could predispose to the development of disease by reducing the functional level at which decline begins or by increasing susceptibility to cigarette smoke and increasing the rate of decline. Thus, in this model, small decrements in the maximally attained level of pulmonary function may be important in identifying the susceptible smoker. However, the prerequisite longitudinal studies needed to test this hypothesis have not yet been conducted.

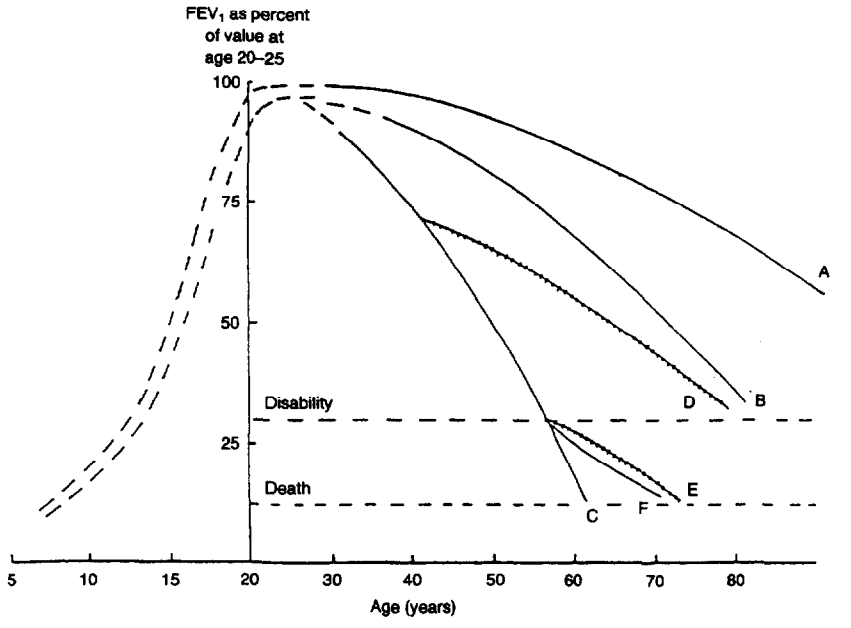


**FIGURE 3.—Theoretical curves representing varying rates of change in $FEV_1$ by age**

NOTE: Curve A, normal decline in $FEV_1$ (forced expiratory volume in 1 second); curve B, accelerated decline in $FEV_1$ with cigarette smoking; curve D, the effect of smoking cessation, also seen in disabled individuals (curve E); disability-related decline often continues as a variable rate (curves C and F).

SOURCE: Speizer and Tager (1979).

*Bronchoconstriction*

Nonspecific bronchial responsiveness has been considered a potential risk factor for the development of chronic obstructive lung disease in both adults and children (US DHHS 1984). This physiologic trait may be influenced by environmental exposures such as involuntary smoking by children and active smoking by adults, and by respiratory infections at all ages.

Asthma is a chronic disease characterized by bronchial hyperresponsiveness. Epidemiologic studies of children have shown no consistent relationship between the report of a doctor's diagnosis of asthma and exposure to involuntary smoking. Although one study showed an association between involuntary smoking and asthma (Gortmaker et al. 1982), others have not (Schenker et al. 1983; Horwood et al. 1985). This variability may reflect differing ages of the children studied, differing exposures, or uncontrolled bias. In several recent studies (Murray and Morrison 1986; O'Connor et al.

1986; Weiss et al. 1985; Martinez et al. 1985; Ekwo et al. 1983), nonspecific bronchial responsiveness was examined in relationship to involuntary smoking. The results of these studies suggest that exposure to maternal cigarette smoking is associated with increased nonspecific airways responsiveness. Some reports suggest that the increased responsiveness is present only in children known to be asthmatic (Murray and Morrison 1986; O'Connor et al. 1986), whereas others suggest that the increased responsiveness is seen in all children (Ekwo et al. 1983; Martinez et al. 1985). The pathophysiological mechanisms underlying the increased responsiveness and the long-term consequences of the increased responsiveness remain unknown. This section reviews the studies on asthma and on bronchial hyperresponsiveness.

Gortmaker and coworkers (1982) studied the relationship between parental smoking and the prevalence of asthma in children up to 17 years of age. Random community-based populations in Michigan (3,072 children) and Massachusetts (894 children) were surveyed. Parents reported on their own smoking habits and on the asthma histories of their children. Biased reporting by parents who smoked was assessed by examining the relationship between parental smoking and other conditions, and considered not to be present. Asthma prevalence declines with age, and asthmatic children are unlikely to tolerate active smoking; therefore, misclassification of actively smoking asthmatic children as nonsmokers seems unlikely. In comparison with children of nonsmokers, children whose parents smoked were more likely to have asthma (relative risks of 1.5 and 1.8 for Michigan and Massachusetts children, respectively) and severe asthma (relative risks of 2.0 and 2.4, respectively). The investigators estimated that between 18 and 23 percent of all childhood asthma and 28 and 34 percent of severe childhood asthma is attributable to exposure to maternal cigarette smoke.

Schenker and coworkers (1983) studied 4,071 children between 5 and 15 years of age in western Pennsylvania. These investigators found no relationship of parental smoking to the occurrence of asthma, after adjustment for potential confounding factors.

Horwood and coworkers (1985) conducted a cohort study of 1,056 children in New Zealand who were followed from birth to age 6 years. A family history of allergy and male sex were the only significant predictors of incident cases of asthma. Neither parental smoking nor respiratory illnesses were predictive of the occurrence of asthma in this investigation.

A recently reported cross-sectional study by Murray and Morrison (1986) suggests a mechanism by which maternal cigarette smoking might influence the severity of childhood asthma. These investigators studied 94 children, aged 7 to 17 years, with a history of asthma. The children of mothers who smoked had 47 percent more symp-

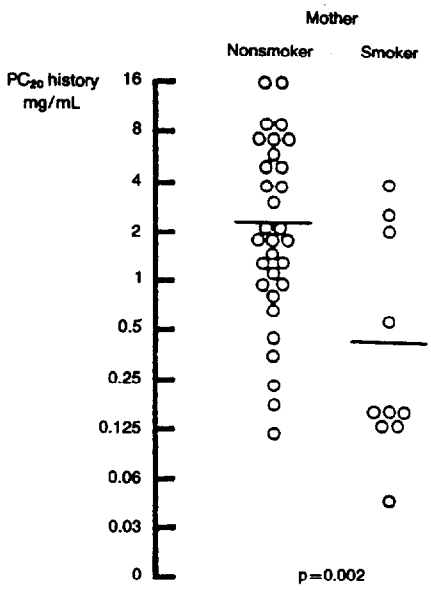


**FIGURE 4.—$PC_{20}$ in two groups of children with a history of wheezing**

NOTE: Mothers of 32 were nonsmokers; mothers of 10 were smokers.
SOURCE: Murray and Morrison (1986).

toms, a 13 percent lower $FEV_1$, and a 23 percent lower $FEF_{25-75}$ than the children of nonsmoking mothers. Forty-one children, who had been able to discontinue medication and had no recent respiratory illness, underwent a histamine challenge test. There was a fourfold greater responsiveness to histamine among the asthmatic children of mothers who smoked (Figure 4) compared with asthmatic children of nonsmoking mothers. Dose–response relationships were present for all outcome variables in this study: symptoms, pulmonary function, and airways responsiveness. The differences between children of smoking mothers and children of nonsmoking mothers were greatest in the older children. The father's smoking behavior did not influence the child's asthma severity. The sample of asthmatic children with mothers who smoked was small (N=10), and only 41 of 96 children had histamine challenge tests. Given the heterogeneity of asthma, the variable nature of bronchial hyperreactivity in asthma, and the potential for biased selection, these results must be interpreted with caution.

O'Connor and coworkers (1986) studied 286 children and young adults, 6 to 21 years of age, drawn from a community-based sample,

and confirmed the findings of Murray and Morrison (1986). Bronchial responsiveness was measured with eucapneic hyperpnea to subfreezing air. Among the 265 subjects without asthma there was no significant relationship between maternal cigarette smoking and nonspecific bronchial responsiveness. However, in the 21 subjects with active asthma, maternal smoking was significantly associated with increased levels of bronchial responsiveness.

In a study of 1,355 children 6 to 12 years of age, significant increases in FEV and $FEF_{25-75}$ were observed following isoproterenol administration in children whose parents smoked (Ekwo et al. 1983). Increases after isoproterenol were not observed in children of nonsmoking parents.

Weiss and coworkers (1985) evaluated 194 subjects between the ages of 12 and 16 drawn from the same population as those reported by O'Connor and coworkers (1986), with eucapneic hyperpnea to subfreezing air as a test for bronchial responsiveness and allergy skin tests as a test for atopy. Subjects defined as atopic (any skin test wheal greater than or equal to 5 mm) had twice the frequency of lower respiratory illnesses in early childhood and were twice as likely to have a mother who smoked. However, there was no relationship between maternal smoking and increased bronchial responsiveness.

Martinez and associates (1985) studied 170 9-year-old children in Italy. Nonspecific bronchial responsiveness to methacholine and allergy prick test positivity in these subjects was significantly associated with maternal cigarette smoking.

These data suggest that maternal cigarette smoking may influence the severity of asthma; a mechanism for this effect may be through alteration of nonspecific bronchial responsiveness. Further investigation is needed to determine whether exposure to environmental cigarette smoke can induce asthma in children and whether ETS exposure increases the frequency or severity of attacks of bronchoconstriction in asthmatics. The effect of involuntary smoking on increased bronchial responsiveness in asthmatics and in nonasthmatics has only recently been addressed. These initial data are provocative, but the magnitude of the effect, the target population at risk, the underlying mechanisms, and the long-term consequences have not been described. Furthermore, the complex interrelationships among respiratory illness, atopy, parental smoking, and airways responsiveness have not been clarified and require further study.

*Ear, Nose, and Throat*

Five studies (Said et al. 1978; Iverson et al. 1985; Kraemer et al. 1983; Black 1985; Pukander et al. 1985) show an excess of chronic

middle ear effusions and diseases in children exposed to parental smoke.

Said and colleagues (1978) questioned 3,920 children between 10 and 20 years of age about prior tonsillectomy or adenoidectomy, considered an index of frequent upper respiratory or ear infections. The investigators reported that, in general, this surgery was performed before the children were 5 years old. The prevalence of prior surgery increased with the number of currently smoking parents in the home.

Iverson and coworkers (1985) prospectively studied 337 children enrolled in all day-care institutions in a municipality over a 3-month period to evaluate the importance of involuntary smoking for middle ear effusion in children. Middle ear effusion was assessed with tympanometry, and the overall prevalence was found to be approximately 23 percent. Although various indoor environmental factors were assessed in this investigation, only parental smoking was significantly associated with middle ear effusion. The effect of parental smoking persisted with control for the number of siblings. The overall age-adjusted odds ratio was 1.6 (95 percent confidence interval 1.0–2.6). In 5- to 7-year-old children, 10 to 36 percent of all chronic middle ear effusions could thus be attributed to smoking on the basis of these results.

Kraemer and coworkers (1983) performed a case–control study of 76 children to examine the relationship of environmental tobacco smoke exposure to the occurrence of persistent middle ear effusions. Frequent ear infections, nasal congestion, environmental tobacco smoke exposure, and atopy were all more frequent in children with ear effusions. The effect of involuntary smoking was observed only if nasal congestion was present, and was greatest in children who were atopic.

Black (1985) performed a case–control study of glue ear with 150 cases and 300 controls. Parental smoking was associated with a relative risk of 1.64 (95 percent C.I. 1.03–2.61) for glue ear. In Finland, Pukander and coworkers (1985) conducted a case–control study of 264 2- to 3-year-old children with acute otitis media and 207 control children and found an association between parental smoking and this acute illness.

These studies are consistent in their demonstration of excess chronic middle ear effusions, a sign of chronic ear disease, in children exposed to parental cigarette smoke. Potential confounding factors for middle ear effusions should be examined carefully in future studies. The long-term implications of the excess middle ear problems deserve further study.

## Adults

### *Acute Respiratory Illness*

There are no studies of acute respiratory illness experience in adults exposed to environmental cigarette smoke.

### *Cough, Phlegm, and Wheezing*

Few studies have addressed the relationship of chronic respiratory symptoms in nonsmoking adults with environmental tobacco smoke exposure. Schilling and colleagues (1977) found that symptoms in adult men and women were related to personal smoking habits and that the occurrence of cough, phlegm, or wheeze in nonsmokers was not related to the smoking habits of their spouses. Schenker and colleagues (1982) confirmed these results in a telephone survey of 5,000 adult women in western Pennsylvania.

### *Pulmonary Function*

White and Froeb (1980) reported on 2,100 asymptomatic adults drawn from a population enrolled in a physical fitness program (Table 5). They reported statistically significant decreases in $FEV_1$ and maximum midexpiratory flow rate (MMEF) as a percent of predicted in nonsmokers exposed to tobacco smoke in the work environment for at least 20 years compared with nonsmoking workers not exposed. The magnitude of effect was comparable to that of actively smoking 1 to 10 cigarettes per day. However, the absolute magnitude of the difference in mean levels of function between the smoke-exposed group and the unexposed group was small: 160 mL (5.5 percent) for $FEV_1$ and 465 mL per second (13.5 percent) for MMEF. Carbon monoxide levels were measured in selected workplaces and ranged from 3.1 to 25.8 ppm. The study population was self-selected, and the exposure classification was crude and did not account for people who changed jobs. It is unclear how the ex-smokers in the population were handled in the analysis. Kentner and coworkers (1984) performed a cross-sectional investigation on 1,351 workers and found no influence of involuntary smoking on pulmonary function. In this study, involuntary smoking at home and at work was considered.

Comstock and colleagues (1981) examined 1,724 subjects drawn from two separate studies in Washington County, Maryland. Male and female nonsmokers married to smokers did not have a significantly increased risk of having an $FEV_1$ less than 80 percent of predicted or an $FEV_1/FVC$ ratio less than 70 percent. Schilling and colleagues (1977) also did not find an effect of involuntary smoking in adults. Effects were not examined within strata defined by age in either of these studies.

## TABLE 5.—Pulmonary function in adults exposed to involuntary smoking

| Study | Subjects | Pulmonary function measured | Outcome | Comments |
|---|---|---|---|---|
| White and Froeb (1980) | 2,100 adults, San Diego, California, United States | FVC, $FEV_1$, and MMF as percent predicted | Significant effect of office exposure to involuntary smoke | Potential selection bias; only current cigarette smoke exposure assessed; treatment of ex-smokers unclear |
| Comstock et al. (1981) | 1,724 adults, Washington County, Maryland, United States | $FEV_1$ as percent predicted | No effect of wives' smoking on husband's pulmonary function | Includes adults aged 20+<br>Cross-sectional study |
| Kauffmann et al. (1983) | 7,818 adults, selected subgroups, seven cities, France | $FEV_1$, FVC, and MMEF | All measures significant effect in wives of smoking husbands; only MMEF significant in husbands of smoking wives | Not height adjusted; dose-response to amount of husbands' smoking for MMEF in wives; no effect below age 40<br>Cross-sectional study |
| Brunekreef et al. (1985) | 173 adults, subgroups of larger study, the Netherlands | Peak flow, inspiratory vital capacity (IVC), $FEV_1$, and MMEF | Significant effect in wives of smoking husbands for peak flow $FEV_1$ cross-sectionally; no effect longitudinally | Small sample size |
| Kentner et al. (1984) | 1,851 adult office workers, Germany | FVC, $FEV_1$ | No effect of work exposure on pulmonary function | Cross-sectional study |

Kauffmann and colleagues (1983) suggested that the effects of exposure from a spouse who smoked may be manifest only after many years of exposure. These investigators assessed the effects of marriage to a smoker in 7,818 adults drawn from several cities in France. Among 1,985 nonsmoking women aged 25 to 59, 58 percent of whom had husbands who smoked, the level of MMEF was significantly reduced in women married to smokers compared with women married to nonsmokers; this effect did not become apparent until age 40. The reduction was small, on average.

Recently, studying another population, Kauffmann and colleagues (1986) suggested that the $FEV_1/FVC$ ratio may be a more sensitive test for detecting differences between exposed and nonexposed subjects, particularly in those with symptoms of wheezing; however, this suggestion has not been evaluated in other populations.

Brunekreef and coworkers (1985), from the Netherlands, reported on 173 nonsmoking women who were participants in a larger longitudinal study of pulmonary function. The women were classified by whether they were or were not exposed to tobacco smoke at study onset or at followup. Cross-sectionally, significant differences in pulmonary function were observed between smoke-exposed and nonexposed women. However, the rate of decline of lung function during the followup period was not affected by tobacco smoke exposure in the home. This study had a small number of subjects and inadequate statistical power to detect effects of exposure on rate of decline that were not extremely large.

Jones and colleagues (1983) selected women with either high or low FEVs from a population-based longitudinal study in Tecumseh, Michigan. Exposure to cigarette smoke at home from husbands who smoked was not significantly different in the two groups of women.

Nonsmoking men who participated in the Multiple Risk Factor Intervention Trial had significantly lower levels of pulmonary function if their wives smoked in comparison with similar men whose wives did not smoke (Svendsen et al. 1985).

The physiologic and clinical significance of the small changes in pulmonary function found in some studies of adults remains to be determined. The small magnitude of effect implies that a previously healthy individual would not develop chronic lung disease solely on the basis of involuntary tobacco smoke exposure in adult life. Whether particular characteristics increase susceptibility, such as childhood exposures or illnesses, atopy, reduced pulmonary function from whatever cause, and increased airways responsiveness, remains unknown. These small changes may also be markers of an irritant response, possibly transient, to the irritants known to be present in environmental tobacco smoke.

*Bronchoconstriction*

## Normal Subjects

Only limited data have been published on the acute effects of inhalation of environmental tobacco smoke on pulmonary function in normal subjects (Table 6) and none on bronchial responsiveness. The available data have been obtained in exposure chambers under carefully monitored and controlled circumstances (Pimm et al. 1978; Shephard et al. 1979; Dahms et al. 1981).

Pimm and colleagues (1978) exposed nonsmoking adults to smoke in an exposure chamber. Relatively constant levels of carbon monoxide (approximately 24 ppm) were achieved in the chamber during involuntary smoking. Peak blood carboxyhemoglobin levels were always less than 1 percent in these subjects before smoke exposure, but were significantly greater after the study exposure. Lung volumes, flow volume curves, and heart rates were measured for all subjects. Measurements were made at rest and following exercise under control and smoke-exposure conditions. Flow at 25 percent of the vital capacity was reduced at rest in men and with exercise in women. Although statistically significant, the magnitude of the change was small: a 7 percent decrease in flow in men and 14 percent in women.

Shephard and coworkers (1979) utilized a similar cross-over design in a chamber of exactly the same size as that used by Pimm and associates. Their results were similar, with a small (3 to 4 percent) decrease in FVC, $FEV_1$, $\dot{V}_{max50}$, and $\dot{V}_{max25}$. They concluded that these changes were of the magnitude anticipated from exposure to the smoke of less than one-half of a cigarette in 2 hours (the exposure anticipated for an involuntary smoker).

Dahms and colleagues (1981) used a slightly larger chamber and an exposure with an estimated peak carbon monoxide level of approximately 20 parts per million. They found no change in FVC, $FEV_1$, or $FEF_{25-75}$ in normal subjects after 1 hour of exposure.

The active smoker manifests acute responses to the inhalation of cigarette smoke; thus, high-dose involuntary exposure to tobacco smoke may plausibly induce similar responses in nonsmokers. The magnitude of these changes is quite small, even at moderate to high exposure levels, and it is unlikely that this change in airflow, per se, results in symptoms.

## Asthmatics

Dahms and colleagues (1981) exposed 10 patients with bronchial asthma and 10 normal subjects to cigarette smoke in an environmental chamber. Pulmonary function was measured at 15-minute intervals for 1 hour after smoke exposure. Blood carboxyhemoglobin levels were measured before and after the 1-hour exposure. The

## TABLE 6.—Acute effects on pulmonary function of passive exposure to cigarette smoke; normal subjects

| Study | Type of exposure | Magnitude of exposure | Effects | Comments |
|---|---|---|---|---|
| Pimm et al. (1978) | Chamber 14.6 m, furniture sparse, smoking machine in room | Peak [CO] ~ 24 ppm; particulates >4 mg/m$^3$ | Men: 5% increase FVC, 11% increase RV, 4% decrease $\dot{V}_{max25}$ during exercise<br>Women: 7% decrease $\dot{V}_{max25}$ after exercise; no effects on VC, TLC, FVC, $FEV_1$, $\dot{V}_{max50}$ | Nonsmokers; average age, men 22.7, women 21.9; sham exposure as control |
| Shephard et al. (1979) | As above | Low exposure: peak [CO] ~ 20 ppm, particulates ~ mg/m$^3$; high exposure: [CO] ~ 31 ppm | Low exposure: 3% decrease $FEV_1$, 4% decrease $\dot{V}_{max50}$, 5% decrease $\dot{V}_{max25}$ with exercise; no increased effect with high exposure | Nonsmokers: average age, men 23, women 25; sham exposure as control; subject estimated inhalation ~ 1/2 cigarette/2 hours |
| Dahms et al. (1981) | Chamber 30 m, climate controlled | Room levels not measured; estimated at peak [CO] ~ 20 ppm | 0.9% increase in FVC, 5.2% increase in $FEV_1$, 2.2% increase in FEF at 1 hour | 10 nonsmokers; age range 24–53 years; not blinded; no sham exposure |

carboxyhemoglobin levels in subjects with asthma increased from 0.82 to 1.20 percent. In normal subjects the increase was from 0.62 to 1.05 percent. The increases in carboxyhemoglobin in the two study groups were not significantly different. Asthmatic subjects had a decrease in forced vital capacity (FVC), $FEV_1$, and MMEF to a level significantly different from their preexposure values. The decreases in asthmatic subjects were present at 15 minutes, but worsened over the course of the hour to approximately 75 percent of the preexposure values. Normal subjects had no change in pulmonary function with this level of exposure. In this study, subjects were not blinded as to the exposure and were selected because of complaints about smoke sensitivity.

Shephard and colleagues (1979), in a very similar experiment, subjected 14 asthmatics to a 2-hour cigarette smoke exposure in a closed room (14.6 $m^3$). The carbon monoxide levels (24 ppm) were similar to those predicted in the study of Dahms and coworkers (1981). Blood carboxyhemoglobin levels were not measured. Subjects were randomized and blinded to sham (no smoke) and smoke exposure and tested on two separate occasions. Data were expressed as the percentage change from the sham exposure. Significant changes in FVC and $FEV_1$ were not observed between the sham and the smoke exposure periods, although 5 of 12 subjects did report wheezing or tightness in the chest on the day of smoke exposure.

Wiedemann and associates (1986) examined nonspecific bronchial responsiveness to methacholine in 9 asthmatic subjects and 14 controls and the effect of acute involuntary smoking on nonspecific bronchial responsiveness. At the time of the study, all asthmatics were stable with normal or near normal pulmonary function. The subjects underwent baseline pulmonary function and methacholine challenge testing. On a separate day they were exposed to cigarette smoke for 1 hour at 40 to 50 ppm of carbon monoxide and underwent pulmonary function and methacholine challenge testing. Pulmonary function was not influenced by exposure. Nonspecific bronchial responsiveness decreased significantly, rather than increasing, as would be anticipated following an irritant exposure.

Acute exposure in a chamber may not adequately represent exposure in the general environment. Biases in observation and the in selection of subjects and the subjects' own expectations may account for the widely divergent results. Studies of large numbers of individuals with measurement of the relevant physiologic and exposure parameters will be necessary to adequately address the effects of environmental tobacco smoke exposure on asthmatics.

### *Ear, Nose, and Throat*

There are no studies of chronic ear, nose, and throat symptoms in adults with involuntary smoking exposure.

## Lung Cancer

This section reviews the epidemiological evidence on involuntary smoking and lung cancer in nonsmokers, which has been derived from retrospective and prospective epidemiological studies. First, common methodological issues that apply to all these studies are considered. Second, for each type of study design, individual studies are reviewed for their methodological approach (Tables 7 and 8), findings associated with tobacco smoke exposure (Table 9, Figure 5), and strengths and limitations. Third, the lung cancer risk associated with involuntary smoking is examined as a low-dose exposure to cigarette smoke by combining the dose–response relationships for active smoking with the exposure data for involuntary smoking to predict the expected lung cancer risk due to involuntary smoking. This expected risk is then compared with the actual risks observed in studies of involuntary smoking. Finally, the existing epidemiological evidence is summarized and the plausibility of the association between lung cancer and involuntary smoking is evaluated on the basis of our current knowledge.

### Observed Risk

*General Methodological Issues*

For both retrospective and prospective studies, the common methodologic concerns are disease misclassification and misclassification of the subject's personal smoking status or exposure to ETS. Disease misclassification, for example, refers to the incorrect classification of the lung as the primary site of a cancer that originated elsewhere. Disease misclassification is of greatest concern in studies in which the diagnosis of lung cancer was not histologically confirmed. Such misclassification tends to be random and to bias relative risk estimates toward unity (Copeland et al. 1977). Patients with lung cancer, or any disease associated with cigarette smoke exposure, may report exposure to ETS more frequently than controls because of bias in recall.

Misclassification of the subject's personal smoking status may occur in both retrospective and prospective studies; this misclassification refers to incorrectly classifying a subject as a nonsmoker when the subject is actually an ex-smoker or a current smoker, or to incorrectly classifying the subject as a smoker when the subject is a nonsmoker. Biochemical markers such as cotinine and nicotine, which can be used to detect unadmitted active smokers, are sensitive only to a recent exposure to tobacco smoke; thus, they are not particularly useful for identifying ex-smokers who deny their past smoking histories. Misclassification of smokers or ex-smokers as nonsmokers may produce the appearance of an involuntary smoking effect when, in fact, the true relationship is with active smoking.

## TABLE 7.—Description of prospective studies

| Factor | Studies | | |
|---|---|---|---|
| | Hirayama | Garfinkel | Gillis |
| Source of subjects | Census population, 29 health districts, Japan | Volunteers, 25 States, United States | Health survey participants, two urban areas, Scotland |
| Nonsmoker population size (sex) | 91,450 (F) | 176,739 (F) | 827 (M)<br>1,917 (F) |
| Age range | ≥40 | 35–84 | 45–64 |
| Years of enrollment | 1966 | 1959–1960 | 1972–1976 |
| Last year of followup | 1981, 1983 | 1972 | 1982 |
| Method of followup | Record linkage between risk factor records and death certificates | Monitored by ACS volunteers, death certificates from local/State health departments | Record linkage with Registrar General files |
| Verification of diagnosis | None | Verified method of diagnosis and histology for first 6 years' followup | Local cancer registry |
| Method and type of information obtained | Interview (?): smoking and drinking habits, dietary history, occupation, other health-related variables | Self-administered questionnaire: education, residence, occupational exposure, smoking and medical history | In-person interview: smoking habits, symptoms of respiratory and cardiovascular diseases |
| Index of passive smoking | Husband's smoking at entry: nonsmoker, ex-smoker, current smoker (cig/day) | Husband's smoking at entry: nonsmoker, current smoker, and cig/day; ex-smokers excluded | Spouse's smoking at entry: current or never smoker; ex-smokers excluded (quit ≥5 years before entry) |
| Number of lung cancer deaths in nonsmokers | 200 (F) | 153 (F) | 6 (M), 8 (F) |

SOURCE: Hirayama (1981a, 1983, 1984a, b), Garfinkel (1981), Gillis et al. (1984).

Misclassification of involuntary smoking exposure refers to the incorrect categorization of exposed subjects as nonexposed and of nonexposed subjects as exposed. Most studies of lung cancer to date have used the number of cigarettes smoked by spouses as a measure of exposure to involuntary smoking, and thus have disregarded duration of exposure, exposure from other sources, and factors that influence exposure, such as proximity to the smokers or size and ventilation of the room where the exposure occurred. Moreover, all

## TABLE 8.—Description of case–control studies

| Study | Country | Case | Control | Respondent and type of interview | Confirmed histology | | Index of passive smoke: habits of spouses and others |
|---|---|---|---|---|---|---|---|
| | | Source and type | Source and type | | Pathological/ cytological | Adenocarcinoma | |
| Trichopoulos et al. (1981, 1983) | Greece | Chest and cancer hospitals; 77 NS (F) | Orthopedic hospital; 225 NS; not matched | Self; not blinded | 65% | Presumed none | Current and former spouses (amount, yr); no other |
| Correa et al. (1983) | New Orleans, United States | Hospitals; 30 NS (8 M, 22 F) | Same hospitals, non-tobacco-related diseases; 313 NS (180 M, 133 F); matched for age, sex, race, hospital | Self, and proxy (case, 23%; control, 11%); blinded | 97% | 54% among women | Current spouse (type, amount, yr); parents |
| Chan and Fung (1982) | Hong Kong | Four hospitals; 84 NS (F) | Orthopedic, same hospitals; 139 NS; not matched | Self; not blinded | 82% | 45% | Not spouse specifically; one question: at home and at work |
| Koo et al. (1983, 1984) | Hong Kong | Eight hospitals; 88 NS (F) | Population; 137 NS; matched for age, race, sex, socioeconomic status, residence district | Self; not blinded | 97% | 59% | Current and former spouses (amount, yrs, hrs); parents, other cohabitants, coworkers (amount, yrs, hrs) |
| Kabat and Wynder (1984) | United States | Most from one NY hospital; 134 NS; passive smoking data on only 78 NS (25 M, 53 F) | Same hospital (?); non-tobacco-related disease; 78 NS (25 M, 53 F); matched for age, sex, race, hospital, date of interview, nonsmoking status | Self; not blinded | 100% | 54% M 74% F of 134 NS | Current spouse (present or past smoking habits); current exposure at home and work |

**TABLE 8.—Continued**

| Study | Country | Case: Source and type | Control: Source and type | Respondent and type of interview | Confirmed histology: Pathological/ cytological | Confirmed histology: Adenocarcinoma | Index of passive smoke: habits of spouses and others |
|---|---|---|---|---|---|---|---|
| Wu et al. (1985) | Los Angeles, United States | Population-based registry; 29 NS (F) | Population; 62 NS; matched for age, race, sex, neighborhood | Self; not blinded | 100% | 100% | Current and former spouses (amount, yrs); parents, cohabitants (amount, yrs), coworkers (hr/day, yrs) |
| Garfinkel et al. (1985) | New Jersey, Ohio, United States | Four hospitals; 134 NS (F) | Same hospitals, colorectal cancer patients; 402 NS; matched for age, hospital, nonsmoking status | Self (case, 12%; control, ?) and proxy; blinded | 100% | 65% | Current spouse or cohabitant (total and at home: amount, yrs); other exposure, average hrs/day (at home, work, other) 5 and 25 yrs before diagnosis; childhood exposure |

## TABLE 8.—Continued

| Study | Country | Case: Source and type | Control: Source and type | Respondent and type of interview | Confirmed histology: Pathological/ cytological | Confirmed histology: Adenocarcinoma | Index of passive smoke: habits of spouses and others |
|---|---|---|---|---|---|---|---|
| Lee et al. (1986) | United Kingdom | Hospital-based; 47 NS (15 M, 32 F) | Same hospitals; 96 NS (30 M, 66 F); matched for age, sex, marital status, hospital | Self, hospital inpatient interview; Spouse, followup interview; not specified | ? | ? | Current spouse (smoking habit during admission yr and maximum during marriage); other exposure at home, at work, during travel and leisure |
| Akiba et al. (1986) | Japan | Hiroshima and Nagasaki bomb survivors; 103 NS (19 M, 84 F) | Same cohort, noncancer or chronic respiratory disease; 380 NS (110 M, 270 F); matched for age, sex, city of residence, vital status, yr of death | Self (case, 10%; control, 12%) and proxy; not blinded | 57% | ? | Current spouse (amount, age start, age stop, yrs cohabited); parents |
| Pershagen et al. (in press) | Sweden | National census of Sweden and Swedish Twin Registry; 67 NS (F) | Two controls from each source; 347 NS; matched for year of birth, vital status at followup end for twin registry control | Self, and proxy (case, almost all; control, ≥65%); not applicable, mailed questionnaire | 99% | 57% | Spouse lived with longest (amount, yrs); parents |

## TABLE 9.—Results from selected prospective and case-control studies; lung cancer risk associated with spouses' smoking

| Study | Spouses' smoking | | | | |
|---|---|---|---|---|---|
| | Nonsmoker | Ex-smoker | 1–14/day | 15–19/day | 20+/day |
| Hirayama (1984a) | 1.0 | 1.4 (0.9, 2.2)[1] | 1.4 (1.0, 2.0) | 1.6 (1.0, 2.4) | 1.9 (1.3, 2.71) |
| | Nonsmoker | <20/day | | 20+/day | |
| Garfinkel (1981) | 1.0 | 1.3 (0.9, 1.9) | | 1.1 (0.8, 1.6) | |
| | | Not exposed | | Exposed | |
| Gillis et al. (1984) | Men | 1.0 | | 4.3 | |
| | Women | 1.0 | | 1.0 | |
| | Nonsmoker | Ex-smoker | 1–20/day | 21+/day | |
| Trichopoulos et al. (1983) | 1.0 | 1.9 (0.9, 4.1) | 1.9 (1.0, 3.7) | 2.5 (1.7, 3.8) | |
| | Nonsmoker | 1–40 pack-yr | | >41 pack-yr | |
| Correa et al. (1983) | 1.0 | 1.5 (0.6, 3.8) | | 3.1 (1.1, 8.5) | |
| | No | Yes | | | |
| Chan and Fung (1982) | 1.0 | 0.8 (0.5, 3.1) | | | |
| | Nonsmoker | ≤35,000 hrs[2] | | >35,000 hrs | |
| Koo et al. (1984) | | 1.3 (0.8, 2.4) | | 1.0 (0.2, 2.7) | |
| | No | Yes | | | |
| Kabat and Wynder (1984) | 1.0 | 0.9 (0.3, 2.1) | | | |
| | Nonsmoker | 1–20 yrs | | 21+ yrs | |
| Wu et al. (1985) | 1.0 | 1.4 (0.4, 4.9) | | 1.2 (0.4, 3.7) | |
| | Nonsmoker | Cigar/pipe | <10/day | 10–19/day | ≥20/day |
| Garfinkel et al. (1985) | 1.0 | 1.2 (0.8, 1.7) | 1.2 (0.8, 1.6) | 1.1 (0.8, 1.5) | 2.1 (1.1, 4.0) |
| | No | Yes | | | |
| Lee et al. (1986) | 1.0 | 1.1 (0.5, 2.4) | | | |
| | Nonsmoker | 1–19/day | 20–29/day | 30+/day | |
| Akiba et al. (1986) | 1.0 | 1.3 (0.7, 2.3) | 1.5 (0.8, 2.8) | 2.1 (0.7, 2.5) | |
| | Nonsmoker | Low[3] | | High[4] | |
| Pershagen et al. (in press) | 1.0 | 1.0 (0.6, 1.8) | | 3.2 (1.0, 9.5) | |

[1] Numbers in parentheses are the 95 percent confidence limits.

[2] Total exposure from spouses, cohabitants, coworkers.

[3] Husband smoked ≤15 cigarettes/day or 1 pack (50 g) of pipe tobacco/week or any amount during <30 years of marriage.

[4] Husband smoking >15 cigarettes/day or 1 pack of pipe tobacco/week during ≥30 years of marriage.

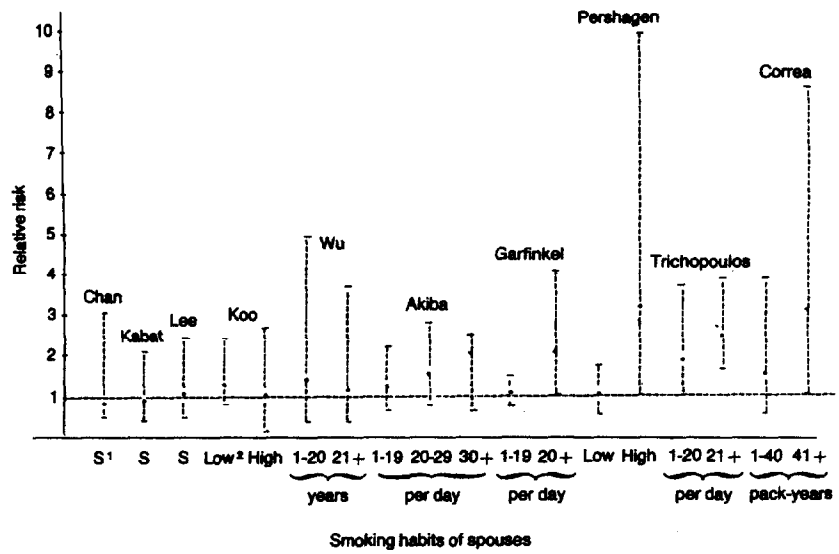


**FIGURE 5.—Relative risks and 95 percent confidence intervals in case-control studies of passive smoking and lung cancer**

[1] S=smoker.

[2] Low and high exposure levels are described in Table 9.

SOURCE: Chan and Fung (1982); Kabat and Wynder (1984); Lee et al. (1986); Koo et al. (1984); Wu et al. (1985); Akiba et al. (1986); Garfinkel et al. (1985); Pershagen et al. (in press); Trichopoulos et al. (1983); Correa et al. (1983).

of the published studies have based involuntary smoking exposure measures on questionnaires without validation of these data with biochemical markers or environmentally measured concentrations of tobacco smoke constituents. Misclassification of involuntary smoking exposure is likely to be random and to bias the effect measures toward the null (Copeland et al. 1977).

Misclassification of exposure to environmental tobacco smoke is inherent in epidemiological studies of involuntary smoking. Tobacco smoking has not been restricted in most indoor environments until recently, and exposure has been almost inevitable in the home, the workplace, or other locations. Studies with the biological markers nicotine and cotinine confirm that tobacco smoke exposure is widespread; detectable levels of these markers are found even in people without reported recent exposure. Thus, the exposure variables employed in epidemiological studies do not separate nonexposed subjects from exposed subjects; instead, they discriminate more exposed groups from less exposed groups. As a result, the

epidemiological approach is conservative in estimating the effects of involuntary smoking. A truly nonexposed but otherwise equivalent comparison population has not been identified. The extent of the resulting bias cannot be readily estimated and probably varies with the exposure under consideration, which may be one reason for the variability in risk estimates obtained by different studies.

Information bias is an added concern in case–control studies, since neither interviewer nor respondent bias can be ruled out. It is not feasible to blind interviewers to the case or control status of respondents because of the usually obvious manifestations of lung cancer and because of the setting in which some of the interviews are conducted. Moreover, blinding of interviewers and respondents to the study hypothesis is difficult because the majority of questions are concerned with exposure to tobacco smoke. The direction of the information bias may be dependent on the type of respondent. Self-respondents may be more apt to interpret their disease as related to exposure to tobacco smoke and thus overreport the exposure. However, the direction of the information bias is less clear when interviews are conducted with surrogate respondents. The ability of a surrogate to provide accurate information may depend on the relationship of the surrogate respondent to the subject, whether the surrogate lived with the subject during the time frame of the questions asked, the degree of detail requested, and the amount of time elapsed since the event in question (Gordis 1982; Pickle et al. 1983; Lerchen and Samet 1986). Surrogate respondents may minimize the reporting of their own smoking because of guilt, or may overreport about involuntary smoking exposure in an attempt to explain their relative's illness. Thus, depending on the direction of the information bias, it may dilute or strengthen the effect being measured (Sackett 1979). In general, however, the information on smoking status and on amount smoked provided by surrogates has been found to be fairly comparable to that provided by the individuals themselves (Blot and McLaughlin 1985).

Finally, participants and nonparticipants in case–control studies may be inherently different with respect to their exposure to involuntary smoking because their awareness of the hypothesis under study may motivate the decision to participate. However, participants in case–control studies are generally not informed of the hypothesis under study.

### *Spousal Exposure: Prospective Studies*

#### The Japanese Cohort Study

Hirayama (1981a, 1983, 1984a) has presented data from a large cohort study that included 91,540 nonsmoking married women who were residents of 29 health districts in Japan. Subjects were 40 years

of age or older at enrollment in 1965; information was collected on smoking and drinking habits, diet (e.g., green-yellow vegetables, meat), occupation, and other health-related variables.

The initial report on involuntary smoking was based on 14 years of followup (1966–1979). The husbands' smoking histories were available for 174 of 240 lung cancer cases identified among the nonsmoking married women (Hirayama 1981a); this number increased to 200 with 2 additional years of followup (Hirayama 1983, 1984a). Results pertaining to the association of spouses' lung cancer risk with the husbands' smoking were essentially identical in the first and second reports.

On the basis of the smoking habits of the husbands at entry, the 200 nonsmoking women were classified as married to a nonsmoker, an ex-smoker, or a current smoker. The lung cancer mortality ratios standardized by husband's age were 1.00, 1.36, 1.42, 1.58, and 1.91 for women whose husbands were nonsmokers, ex-smokers, and daily smokers of 1 to 14, 15 to 19, and 20 or more cigarettes, respectively (one-sided p for trend, 0.002). Similarly significant dose–response trends were observed when the mortality ratios were standardized by age of the wives, by occupation of the husbands (agricultural, industrial, other), by age and occupation of the husbands, and by the time period of observation (1966–1977 versus 1978–1981). The risk of lung cancer among nonsmoking wives of smokers was reduced to 0.7 (two-sided $p=0.05$) if they ate green-yellow vegetables daily compared with 1.0 if they ate such vegetables less often than daily (Hirayama 1984b). No other characteristic of the wives (e.g., drinking habits, parity, occupation, nonvegetable dietary items) or of the husbands (e.g., drinking habits) was significantly predictive of lung cancer risk.

Nonsmoking men whose wives were smokers also showed an elevated lung cancer risk. On the basis of 67 lung cancers in nonsmoking married men, the lung cancer mortality ratios were 1.00, 2.14, and 2.31 if their wives had never smoked or had smoked 1 to 19 cigarettes or 20 or more cigarettes per day, respectively (one-sided p for trend, 0.023) (Hirayama 1984b).

This study has been critically discussed in correspondence since its initial publication. Because a detailed breakdown of the at-risk population was not presented in the initial report, the lung cancer mortality rate was thought by some to be higher in the unmarried nonsmoking women than in the nonsmoking women married to smokers (Rutsch 1981; Grundmann et al. 1981). This impression was clarified by the researcher (Hirayama 1981b,c,d) and shown to be the result of incorrect interpretation of data in the original paper. Other potential problems cited were sampling bias in the study cohort, misclassification in the diagnosis of lung cancer, misclassification of the nonsmoking status of wives, misclassification of involuntary

smoking exposure, failure to control for potential confounders, and inadequate statistical treatment of data. Each of these points of criticism is discussed below.

MacDonald (1981a,b) questioned the representativeness of the 29 health districts selected in the study cohort and suggested that industrial pollution, such as asbestos exposure from shipbuilding industries specific to the selected health districts, may have biased the results. However, the levels of exposure to this factor would have to coincide with the husbands' smoking level to explain the effect observed. Such an association seems unlikely. If the cohort were not representative, the generalizibility but not the validity of the findings would be challenged (Criqui 1979).

The accuracy of the diagnosis of primary lung cancer on the basis of death certificates and the adequacy of the data without information on the histology of the tumor were questioned (Grundmann et al. 1981; MacDonald 1981a). From a sample of 23 cases, Hirayama (1981b) reported that the distribution by histology of lung cancer in nonsmoking women whose husbands smoked was similar to that in women who smoked. Failure to discriminate in some cases between primary and metatastic lesions to the lung may be a potential problem with disease diagnosis. Although Hirayama was unable to assess the accuracy of the diagnosis listed on the death certificate, there is no reason to believe that error in recording the causes of death of wives was influenced by the smoking habits of their husbands, and any misclassification is likely to be random. Inclusion of nonlung cancer cases would tend to bias the risk ratio toward unity or no effect (Barron 1977; Greenland 1980).

The relatively high risks observed for nonsmokers whose husbands smoked led to speculation that Japanese women may report themselves as nonsmokers when they actually smoke (Lehnert 1984). However, some assurance of the reliability of the smoking data provided by the Japanese women comes from an investigation in Hiroshima and Nagasaki (Akiba et al. 1986) that found strong concordance between smoking status reported by the women themselves and that reported by their next of kin.

Classifying nonsmoking women solely on the basis of the smoking habits of their current husbands probably does not quantify their exposure with precision because it accounts for only one of the many possible sources of tobacco smoke exposure. Moreover, using the number of cigarettes smoked per day by the husbands as a measure of exposure dose assumes that the husbands' increasing daily cigarette consumption is directly related to an increasing ETS exposure of the wives (Kornegay and Kastenbaum 1981; Lee 1982b).

The analyses were further criticized for not accounting for potential confounding factors such as socioeconomic status (SES) and exposure to indoor air pollutants (e.g., from heating and cooking