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Review

Effects of Air Pollution and Smoking on Chronic Obstructive Pulmonary Disease and Bronchial Asthma

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Sasaki, H., Sekizawa, K., Yanai, M., Arai, H., Yamaya, M. and Ohrui, T. *Effects of Air Pollution and Smoking on Chronic Obstructive Pulmonary Disease and Bronchial Asthma.* Tohoku J. Exp. Med., 1998, **186** (3), 151-167 —— Although both tobacco smoking and air pollution are believed to be environmental factors affecting the prevalence of chronic obstructive pulmonary disease (COPD) and bronchial asthma, the mechanisms by which they induce/aggravate these diseases are still not known in detail. While smoking has been demonstrated to cause and aggravate COPD and bronchial asthma, the influence of air pollution, suspected to have hazardous environmental effects since the historical episodes of severe air pollution such as the London Smog, on the prevalence of airway diseases remains unclear. This is due, in part, to changes over time in the nature of the air pollutants concerned. There have been no consistent findings on the effects on airway diseases of air pollutants at levels currently observed in developed countries. It is believed that cessation of smoking is the most important factor in preventing the development of COPD. ———— COPD; bronchial asthma; smoking; air pollutants; London Smog

Smoking, a well-known risk factor for a wide range of diseases and conditions including cancer, hypertension, arteriosclerosis, and cerebral apoplexy, is an important cause of chronic obstructive pulmonary disease (COPD) (Bascom et al. 1996a, b). Tobacco smoke contains about 4000 chemicals that have been identified, and about 200 of these chemicals are considered toxic. Examples include hydrogen cyanide (HCN), ammonia, formaldehyde and acrolein, which may inhibit ciliary movement in the airway, and stimulants such as glycol, aldehyde and ketones may cause coughing, airway narrowing, inhibition of ciliary movement, and hypersecretion of airway mucosa at levels of 60 ppm for acrolein, 120 ppm for formaldehyde, and 300-1500 ppm for HCN. People have come to recognize the hazards of smoking, but, the number of female smokers has tended

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to increase over time, even over the hazards of maternal smoking for infants and fetuses.

Episodes of severe air pollution have occurred in many parts of the world including the pollution disasters in the Meuse Valley in Belgium, in Donora in the United States, and the London Smog in England. In Japan, episodes of severe air pollution causing Yokkaichi asthma have occurred, and air pollution has been acknowledged as an environmental factor in the development of COPD. Since the occurrence of these episodes, developed countries have promoted pollution control activities, and air pollution by dust and sulfur oxides associated with the combustion of petroleum and coal have all but ended. However, new concerns must be faced: Outdoor air pollution associated with the increased use of motor vehicles, and indoor air pollution resulting from the use of heaters and cooking ranges.

COPD and bronchial asthma differ in etiology and pathology, and environmental factors affecting these diseases are usually discussed separately. However, some patients have intermediate types of respiratory diseases that make distinguishing between COPD and asthma difficult. This article discusses external environmental factors that may affect COPD and asthma, focusing on air pollution and smoking.

Changes in Definition of COPD and Bronchial Asthma

In 1995, the Expert Committee of the American Thoracic Society defined COPD as "a pathological state characterized by the presence of airflow obstruction caused by chronic bronchitis or emphysema," and mentioned that patients with chronic bronchitis or emphysema who do not exhibit findings of obstructive airway disorders should not be diagnosed with COPD. Based on these criteria, some types of chronic bronchitis, i.e., all types of uncomplicated chronic bronchitis and chronic purulent bronchitis without obstructive airway disorder, are excluded from the category of COPD (Celli et al. 1995). In fact, it has been reported that patients suffering cough and excessive sputum production but free of obstructive airway disorder account for at least half of the patients with chronic bronchitis (Satake 1975).

In the past, chronic bronchitis was thought to follow a course from simple bronchitis to mucopurulent bronchitis, to obstructive type bronchitis, and all types of chronic bronchitis including uncomplicated and mucopurulent types were generically referred to as COPD. However, this type of progression of chronic bronchitis was denied by Fletcher et al. (1976). Fletcher et al. (1976) followed male workers for 8 years and reported that while patients with chronic bronchitis and obstructive airway disorder had a poor prognosis characterized by progressive respiratory failure and death, patients who had chronic bronchitis but were free of obstructive airway disorder exhibited only the natural rate of decline in ventilatory function associated with aging. Their condition did not result in

death from poor ventilation, even if they developed recurrent airway infections. Patients with obstructive airway disorder exhibit more rapid deterioration of ventilatory function associated with aging than those without obstructive airway disorder; the curve shows that some patients over 65 years of age develop COPD and disability due to difficulty of breathing. The ventilatory function tests obtained from individuals with obstructive airway disorder usually exhibit a Gaussian distribution. Although there might not be a definite threshold separating from those without obstructive airway disorder, it is generally believed that the subgroup does not change over time (Fletcher and Peto 1977).

Celli et al. (1995) also mentioned that in the past, bronchial asthma, a disease most typically characterized by airway hyperresponsiveness, was categorized as COPD. However, bronchial asthma is now thought to be characterized by airway inflammation in which complicated cellular/chemical mediator mechanisms play roles. It is therefore appropriate and useful to consider COPD and bronchial asthma as separate disease entities. However, Celli et al. (1995) also mentioned that "airflow obstruction noted in many patients with COPD may include some important reversible factors, and some patients with bronchial asthma may develop irreversible airflow obstruction that is difficult to distinguish from COPD." It is also true that there are some patients for whom neither COPD nor bronchial asthma can be clearly diagnosed.

Effects of Tobacco Smoking

It has been clearly shown that tobacco smoking significantly affects the development/aggravation of COPD, and the causal relationship between smoking and the development/aggravation of COPD appears to have been clearly demonstrated as well. However, it is still unclear which components of tobacco smoke and which mechanisms play roles in the development of COPD. Further studies of these components and mechanisms should be investigated. One of the most convincing hypotheses is the so-called "imbalance hypothesis," in which oxygen radicals in tobacco smoke damages the protease/antiprotease balance.

Effects of active smoking

It has been demonstrated that tobacco smoking is a cause of COPD (Hanraha et al. 1996). The rate of progression of obstructive airway disorder is increased by tobacco smoking, depending on the number of cigarettes smoked (Xu et al. 1992). A large number of animal experiments have demonstrated a dose-effect relationship between smoking and hyperplasia of bronchial glands (Mawdesley-Thomas and Peto 1973). Fletcher and Peto (1977) reported that about 15% of smokers are susceptible to smoking-related irreversible obstructive changes which may negatively impact activities of daily living, and some of these susceptible smokers may suffer disability by 65 years of age. Even if these susceptible smokers quit smoking at a younger age, airway obstruction is irreversible: Ex-smokers exhibit

progression of airway obstruction at a rate similar to that in healthy never-smokers. They also mentioned that ventilatory function in the remaining 85% of smokers exhibits a Gaussian distribution, from a level similar to that in healthy individuals who have never smoked to severe airway obstruction usually noted in the 15% "susceptible" smokers noted above. It has also been reported that tobacco smoking accounts for 80–90% of the risk of development of COPD (Celli et al. 1995); only 5% of male patients with chronic bronchitis are non-smokers (Oswald et al. 1953); the rate of mortality from COPD in non-smokers is less than 10% of that of lifetime smokers (Doll et al. 1994); and that the number of deaths from COPD increases depending on the number of cigarettes smoked, but even modest smoking, of 1–14 cigarettes/day, increases the rate of mortality from COPD by at least 8 times compared with that of non-smokers (Doll et al. 1994).

It has been demonstrated that tobacco smoking can cause emphysema (Saetta et al. 1985). This is supported by necropsy findings: While only a small percentage of non-smokers aged 60 years or older exhibited mild emphysema at necropsy, most smokers aged 60 years or older exhibited emphysema-like lesions, and a quarter of such patients exhibited severe emphysematous changes (Ryder et al. 1971). In a necropsy study of smokers, emphysematous lesions were noted in almost all smokers who died of respiratory failure, and even among smokers who died for other reasons, emphysematous lesions were noted in 65% of cases (Snider 1989). Many studies have demonstrated that animals exposed to tobacco smoke often exhibit emphysematous changes (Hermandes et al. 1966; Auerbach et al. 1967; Park et al. 1977; Huber et al. 1981).

Inconsistent findings have been obtained concerning the presence or absence of a relationship between smoking and bronchial asthma: Some studies have found an increase in serum IgE associated with smoking (Arshad et al. 1992), while others have found no difference in serum IgE levels between non-smokers and smokers (Thien et al. 1993). However, it appears that smoking may play a role in the onset of bronchial asthma (Martinez et al. 1988).

Effects of passive smoking

Passive smoking may be related to some extent to the development of respiratory disease. Passive smoking causes a relatively mild obstructive airway disorder (from 1 to 5% reduction in pulmonary function level) in children (Weiss et al. 1983). The prevalence of asthma in children 5 to 9 years of age was 1.8% for those whose parents were nonsmokers (0 cigarettes/day), 6.8% for those with one smoking parent, and 11.8% when both parents smoked (Weiss et al. 1980). The prevalence of chronic cough in children aged 11 or under was 35% for those whose parents were non-smokers, 42% for those with one parent who smoked, and 48% when both parents smoked, suggesting an increase in prevalence of chronic cough associated with parenteral smoking (Charlton 1984). Asthma is frequently observed in children when a parent, particularly the mother, smokes (Newman-

Taylor 1995). However, many studies have found no relationship between passive smoking and the onset of pediatric asthma. The prevalence of pulmonary infection was high in infants under 1 year of age whose parent(s) smoked (Harlap and Davies 1974). The prevalence of respiratory disease was about 3 times higher for children aged 16 years or under whose parent(s) smoked than for non-smokers' children of the same age group (Cameron et al. 1969). Passive smokers had bronchial asthma, chronic bronchitis and difficulty breathing more frequently than do non-smokers (Leuenberger et al. 1994). Individuals exposed to tobacco smoke had respiratory symptoms significantly more frequently than did non-smokers (Simecek 1980). Studies consistently described a significantly higher prevalence of respiratory symptoms for passive smokers than for non-smokers (Martinez et al. 1988). Indoor air pollutants such as NO_2 did not induce respiratory symptoms in children, while passive smoking did increase wheezing in children (Dijkstra et al. 1990). However, it has yet to be determined whether passive smoking causes COPD.

Effcts of Air Pollution

The London Smog was an episode of air pollution mainly caused by the combustion of coal for domestic heating. During a several-day period beginning December 5, 1952, airborne particles and sulfur dioxide remained in a sub-inversion layer that developed over the entire country of England. The levels of pollutants peaked on December 7 and 8 at 4.46 mg/m^3 for airborne particles and 1.339 ppm for sulfur oxide (During this period many individuals, particularly elderly ones, manifested severe illness characterized by respiratory distress, cyanosis, slight fever and/or bubbling rales, and excess mortality was especially pronounced in elderly individuals aged 70–80 years or older.) (Holland and Reid 1965).

In Japan, air pollution mainly by sulfur oxides began to occur in major industrialized areas in the early 1960's. Particularly in the region surrounding the Yokkaichi petrochemical complex, gale pollution, a type of air pollution distinctly different from the calm smog of the London Smog, by sulfur dioxides was severe. The episode known as Yokkaichi air pollution was especially severe in the Shiohama area, where respiratory disease developed in many residents. It has recently been pointed out that the direct cause of air pollution in this case was the direct exposure of individuals to sulfuric acid mist emitted at high levels from certain plants (Toyama 1979). The Yokkaichi episode attracted public attention, and air pollution began to be considered a serious social problem. This severe air pollution lasted until the early 1970's (Fig. 1).

In these circumstances, air pollution came to be considered an environmental cause of COPD and asthma. However, the principal environmental problem in developed countries is currently air pollution due primarily to NO_2 emitted from motor vehicles. Diesel exhaust particles (DEP) are another pollutant of current

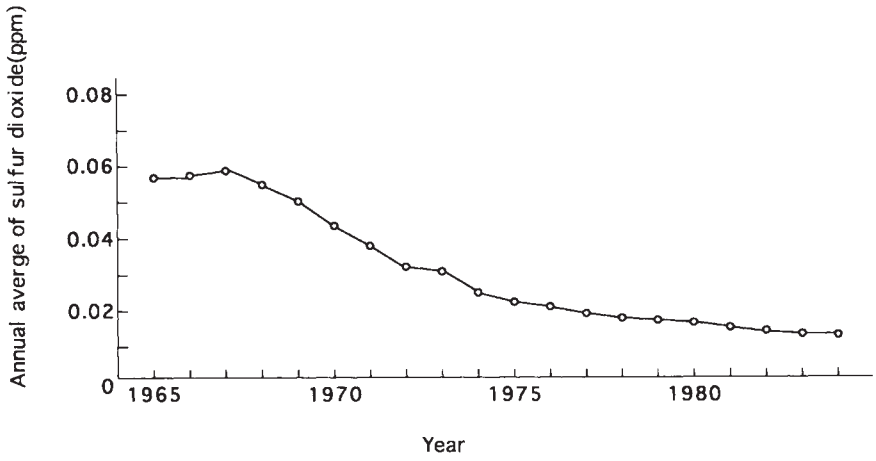

Fig. 1. Changes over time in simple mean of average sulfur oxide levels obtained from 15 fixed stations. Quoted from the Report of the Expert Committee on an Assessment of the Relationship between Air Pollution and Health Hazards by the Environmental Health Section, Central Council for Environmental Pollution Control of the Ministry of Health and Welfare Japan (April 1986).

concern.

Outdoor air pollution

School children are the principal subjects in reports describing the occurrence of asthmatic attacks or aggravation of airway hyperresponsivenss associated with outdoor air pollutants such as SO_2, NO_2 and O_3. Orehek et al. (1976) noted that one-hour exposure to NO_2 at 0.01 ppm, a level and a duration which may be encountered in modern daily living conditions, increased airway hyperresponsiveness in patients with bronchial asthma. However, some studies have found no changes in airway hyperresponsiveness in patients with bronchial asthma who were exposed to NO_2 at levels higher than 0.01 ppm for 1 hour (Avol et al. 1981; Linn et al. 1986; Bylin et al. 1995). Even recently, school children living in industrialized areas exhibited an increase in airway hyperresponsiveness compared with those living in non-industrialized areas (Soyseth et al. 1995). It has also been reported that even healthy volunteers exhibited an increase in airway hyperresponsiveness following inhalation of O_3. A study found that continuous inhalation of O_3 for 3 days or longer may instead lead to adaptation to O_3 exposure (Dimeo et al. 1981). A study conducted in Philadelphia in the United States reported that total mortality including deaths from COPD, bronchial asthma and heart diseases was proportional to levels of SO_2 and total density of suspended particles (Schwarts and Dockey 1992). Patients with bronchial asthma who inhaled an allergen together with SO_2 0.02 ppm and NO_2 0.4 ppm for 6 hours exhibited increased reactivity to the allergen (Devalia et al. 1994a). These findings indicate that air pollution may aggravate symptoms in patients who already have asthma or other respiratory diseases. However, many studies

found no changes in the severity or frequency of asthmatic symptoms during air pollution, and a report on air pollution prepared by the American Thoracic Society failed to yield consistent findings in an evaluation of effects of air pollutants on the rate of occurrence of asthmatic attacks (Bascom et al. 1996a, b).

Can the above-mentioned air pollutants induce the onset of asthma? Some studies have suggested that asthmatic attacks are caused mainly by allergic reactions in younger patients, but, as patients age, attacks tend to be caused by infection. Burrows et al. (1989), however, suggested that even in elderly patients who generally have low IgE levels as a result of the natural aging process, asthmatic attacks are caused by allergic reactions. This is based on the finding in a comparison of asthmatic and non-asthmatic elderly individuals that the relationship between IgE levels and timing of asthmatic attacks in elderly individuals is similar to that between IgE levels and asthmatic attacks in younger asthmatics. Inhalation of diesel-exhaust particulates (DEP) increased the number of IgE secretory cells in nasal lavage fluid (Diaz-Sanchez et al. 1994). However, since an increased IgE level itself does not provoke bronchial asthma, the findings of the studies noted above do not support the hypothesis that air pollution provokes bronchial asthma. Mice given intraperitoneal injections of ovalbumin mixed with DEP exhibited significantly greater IgE antibody production than mice treated with ovalbumin alone (Murakami et al. 1987). This finding suggests that a relationship may exist between the increase in number of diesel vehicles and increased prevalence of pollinosis. Enhanced IgE production has also been demonstrated in mice exposed to transnasal ovalbumin (Takafuji et al. 1987). It has been reported that air pollutant gases may aggravate the severity of allergic airway diseases (Devalia et al. 1994b).

Of the 5 areas in the United States which have experienced major air pollution from the beginning of the 1970s, 4 areas have exhibited an increase in the prevalence of chronic bronchitis, with the amount of increase depending on the level of sulfur oxides (Champan et al. 1973). In a study of younger children, the prevalence of respiratory infection was highest in the geographical area with the highest SO_2 concentration (0.06 ppm) (Douglas and Waller 1966). In another study, the prevalence of symptoms of chronic bronchitis was related to the severity of air pollution; however, no such relationship was observed for bronchial asthma (Bjorsson et al. 1994). In an evaluation of findings obtained in Yokkaichi during the 21-year period between 1963 and 1983, increases in SO_2 levels were found to be related to increased mortality from chronic bronchitis and bronchial asthma, and a decrease in SO_2 levels was associated with a prompt decrease in mortality from bronchial asthma, and, with a time lag of 4–5 years, a decrease in mortality from chronic bronchitis (Imai et al. 1986). Similarly, seasonal alleviation of air pollution has been found to be associated with an improvement of obstructive airway disorders in patients with COPD (Pope et al. 1993). However, it appears that these results were obtained without making a clear distinction

between the effects of air pollution and those of tobacco smoking.

In the United States, smokers have COPD symptoms more frequently than do non-smokers. However, one study reported that the prevalence of symptoms of COPD was high in a geographical region with no air pollution (Detels et al. 1979), while another study found a correlation between the level of dust fall and mortality from bronchitis (Toyama 1979).

In contrast to smoking, air pollutants only minimally induce COPD or bronchial asthma in experimental animals. Studies of the effects of SO_2 on bronchitis models reported that SO_2 had no effects on the airways of animals exposed at levels which humans might encounter in daily life (Alarie et al. 1972; Amdur 1974), but that exposure to SO_2 at 10 ppm for 72 hours had severe effects including swelling of the airway and exfoliation of airway epithelium in mice (Giddens and Fairchild 1972). SO_3 has been used for the preparation of animal models of bronchitis (Reid 1963; Chakrin and Saunders 1974), but the level of SO_3 required to induce pathological changes in airway epithelium has been reported to be much higher than the levels commonly measured during episodes of air pollution.

There have been no reports suggesting that air pollution can cause emphysema in humans. An animal study reported that exposure to NO_2 at 20 ppm for 30 days caused emphysema-like changes (Evans et al. 1976). Exposure to NO_2 at levels lower than 20 ppm have been reported to induce slight and localized alveolar disruption only when exposure is accompanied by administration of a protease (Lafuma et al. 1987) or viral infection (Fenters et al. 1973). Low level NO_2 alone does not appear to induce emphysema (Port et al. 1977; Ehrlich and Fenters 1973). It appears that the differences in water solubility between SO_2 and NO_2 affect the distances these molecules can reach in the lung. While SO_2 tends to deposit in the central conducting airways, NO_2 can reach peripheral airways. Thus, depending on the site of their deposition, gases which are transformed to strong acids following deposition in tissues may cause different diseases: Chronic bronchitis by SO_2, and emphysema by NO_2 (Bascom et al. 1996a and b).

Indoor air pollution

In addition to outdoor air pollution, indoor air pollution caused by the use of household appliances has been considered a possible cause of respiratory symptoms. Cooking with a gas stove will result in emission of 0.2–0.4 ppm of NO_2 in the kitchen. The NO_2 level resulting from this emission may peak as high as 1.0 ppm (Harlos 1988). However, an indoor NO_2 concentration of about 0.04 ppm did not affect the prevalence of cough and asthmatic symptoms in infants under 18 months of age (Samet et al. 1993). Indoor air pollution aggravates the symptoms of adult asthmatic patients (Ostro et al. 1994). One-hour inhalation of NO_2 at 0.4 ppm resulted in a significant decrease in forced expiratory volume in one second (FEV1) in patients with bronchial asthma, suggesting that indoor NO_2

may aggravate asthmatic symptoms in individuals with asthma as an underlying disease (Tunnicliffe et al. 1994). Risk factors for asthma in 3- and 4-year-old children were smoking by the mother, use of a humidifier in the child's room, a history of pneumonia, the absence of breast feeding, a family history of asthma, and high indoor NO_2 concentration (Rivard 1993). By contrast, one study reported the absence of a relationship between indoor concentrations of various pollutants and the onset of bronchial asthma (Strachen 1988). Increases in the rates of respiratory illnesses and symptoms found in children were more strongly associated with maternal smoking than paternal smoking, but were not significantly associated with exposure to gas cooking in the child's home (Ware et al. 1984). Another study reported that 2 smokers in a room emit respirable particles at an annual average of 70 $\mu g/m^3$ (Spengler et al. 1981).

As mentioned above, modest increases in indoor air pollution may induce respiratory symptoms in children and asthmatic individuals, although the occurrence of this type of air pollution is limited to the few hours during which a cooking stove is used.

Assessment of Effects of Air Pollution with Adjustment for Effects of Tobacco Smoking

Other than those of epidemiological studies, there are few findings available with which the combined effects of smoking and air pollution can be evaluated.

In order to identify air pollution, an assessment of dose-effect relationships in humans using the results of epidemiological studies requires a suitable study design. This includes appropriate methods of analysis to avoid the effects of between-group bias in confounding factors (such as gender, age, environmental history, life style, constitutional factors and past history), to determine the effects of individual inhaled dose and the prevalence of newly developed symptoms, and to assess the relationship between the inhaled dose and the prevalence of respiratory symptoms. These requirements are in fact extremely difficult to meet.

Keeping these limitations of epidemiological studies in mind, we will discuss the findings of epidemiological studies conducted in England and Japan, a comparison of which will be useful for evaluating the relative effects of tobacco smoking and air pollution.

Epidemiological findings in England

The reports by Holland and Reid (1965) and Lambert and Reid (1970), in both of which smoking and air pollution are evaluated separately, are quoted here.

Holland and Reid (1965) evaluated the presence/absence of persistent cough and excessive sputum production in 293 residents of London and 477 residents of a suburb with low air pollution from 1960 to 1961. The air pollution level at that time in London was 136 mg/m^2 for dust fall (determined as mean amount of deposition through 1960 and 1961 measured using a deposit gauge) and 1.65 mg/

100 cm^2/day for sulfur oxide measured by the PbO_2 method. They found that non-smokers in London had a prevalence of respiratory symptoms similar to that of non-smokers in the suburb, while in both London and the suburb even those who smoked only lightly had twice the prevalence of these symptoms of non-smokers in the corresponding area. In addition, prevalence increased with the amount of tobacco consumption. Smoking plus air pollution further increased the prevalence of cough and excessive sputum production, compared with that for individuals smoking the same amount in the area without pollution.

In 1970, Lambert and Reid (1970) published the results of a study of the prevalence of chronic bronchitis as related to smoking of 9975 residents in low- and high-air pollution areas. In the low-pollution area, smoking increased the prevalence of chronic bronchitis by 4–5 fold compared with that for non-smokers. In a comparison of the prevalences of chronic bronchitis in non-smokers, no effects of air pollution were observed in residents aged under 50 years, but gradually became more apparent in residents over 50 years of age and increasing with age. However, the effects of air pollution were not as strong as those of smoking: The prevalence of chronic bronchitis for residents in the high pollution area aged 65–69 years remained at most twice that for residents of the low pollution area. The combination of smoking and exposure to air pollution resulted in a much larger increase in the prevalence of chronic bronchitis. In the study by Lambert and Reid (1970) no description of the measurement of concentrations of air pollutants was included, but since their study was conducted 13 years after the London Smog in 1950, air pollution in the area investigated may have been much less severe. Nevertheless, the findings of their study suggested that smoking was associated with a prevalence of cough and excessive sputum production several times that associated with exposure to air pollution.

The areas investigated in the above studies, London and a city with a high level of air pollution, might have had more severe air pollution in the 1950s than during the test periods; the levels of air pollutants in the 1950s might have been associated with higher prevalences of cough and excessive sputum production than those observed in the above two studies. However, it is probably true that the effect of smoking on the prevalence of respiratory symptoms was stronger than that of the air pollution present at the time these studies were performed. If the severe air pollution occurring during the London Smog in the 1950s caused severe irreversible bronchitis such as that accompanied by obstructive airway disorder, the prevalence of respiratory symptoms associated with air pollution should have remained high in 1960 through 1965, when air pollution began to decrease. However, the prevalence of respiratory symptoms in 1960–1965 was, in fact, not as high as that just after the London Smog. It might be assumed that air pollution in England had improved, as in Japan, continuously during the late 1960s and thereafter, and that smoking affected the prevalence of respiratory symptoms more strongly than did the air pollution present at that time.

Although transient aggravation of bronchial asthma associated with episodes of air pollution during the period in which these 2 studies were conducted was reported in a study of school children, no studies suggesting a consistent relationship between severity of air pollution and the onset of symptoms of COPD have been published.

Findings in Japan

Fig. 2 shows the results of a survey of the prevalence of chronic bronchitis (diagnosed using Fletcher's criteria) by gender, age, socioeconomic factors and tobacco consumption conducted by the Kinki District Air Pollution Surveillance Group (1969). Both men and women exhibited an age-associated increase in the prevalence of chronic bronchitis. When stratified by age, all subgroups consistently exhibited a tendency toward an increase in the prevalence of chronic bronchitis with increasing tobacco consumption; the prevalence was lowest for the group of non-smokers and highest for the group of heaviest smokers, between which a cigarette consumption-dependent increase in prevalence was noted for different amounts of smoking. As Fig. 3 shows, the age-adjusted prevalence of chronic bronchitis increased in all subgroups stratified by smoking habit as the level of air pollution increased (level of sulfur oxides measured using the PbO_2 method), and when subgroups were stratified by level of sulfur oxides, the prevalence of chronic bronchitis was lowest in non-smokers and increased as subjects smoked more. These findings clearly demonstrate the effects of smoking on the prevalence of chronic bronchitis.

In the study on the health effects of a combination of different pollutants

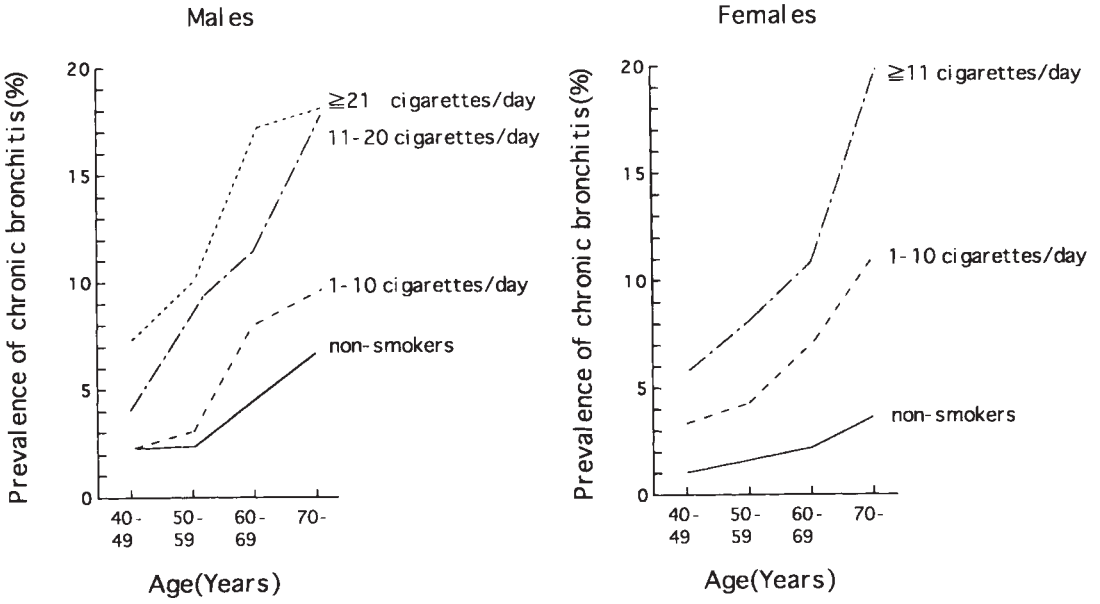

Fig. 2. Prevalence of chronic bronchitis by age and tobacco consumption. Quoted from the Report on Effects of Smoking and Other Air Pollutants by the Kinki District Air Pollution Surveillance Group, Japan 1969.

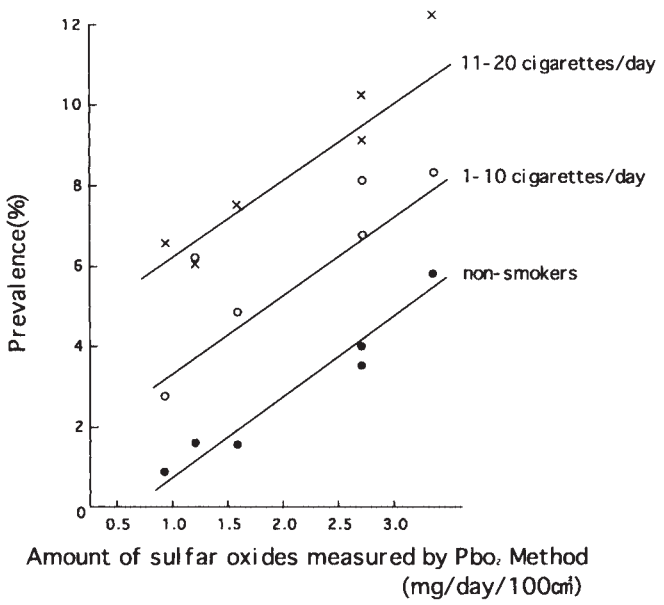

Fig. 3. Relationship between air pollutant level and age-adjusted prevalence of respiratory symptoms by tobacco consumption. Quoted from the Environment Agency of the Ministry of Health and Welfare of Japan study on the health effects of a combination of differeent Pollutants in 6 Areas in Japan, 1974.

conducted by the Ministry of Health and Welfare and the Environment Agency of Japan in 1970-1974 (1974), the prevalence of cough and excessive sputum production was evaluated, and respiratory function testing using a spirometer was performed. The prevalences of cough, excessive sputum production and persistent cough with sputum were 2 to 3 times higher for smokers than for non-smokers. Although this study did not find a relationship between the level of air pollution and deterioration of pulmonary function, smokers exhibited decreases in forced expiratory vital capacity (2.3 ± 0.51 vs. 2.1 ± 0.41, mean $\pm$ S.D.), pulmonary capacity percentage ($94 \pm 16\%$ vs. $90 \pm 15\%$, mean $\pm$ S.D.), forced expiratory volume in one second (FEV_1) (1.9 ± 0.41 vs. 1.7 ± 0.41, mean $\pm$ S.D.), and percentage forced expiratory volume in one second percent (FEV_1) ($77 \pm 14\%$ vs. $72 \pm 15\%$, mean $\pm$ S.D.), compared with non-smokers. These findings also clearly demonstrate an effect of smoking on lung function.

A study group led by the Amagasaki Medical Association conducted on the survey of health effects of environmental factors in Amagasaki, Japan, a city in the Hanshin industrial zone, by mailing a standardized questionnaire to residents. This survey also found that respiratory symptoms were correlated more significantly with smoking than with air pollution level (Seo 1996).

Conclusion

Air pollution and smoking have long been described in textbooks as environmental factors that may cause COPD and bronchial asthma. In this review, we have demonstrated again the important health effects of tobacco smoking, and

that tobacco effects are very much stronger than those of other factors on respiratory health.

The severe episodes of air pollution that occurred in the past now no longer occur, but other air pollutants have emerged as matters of concern. The health-related effects of outdoor air pollution associated with increased use of motor vehicles and of indoor air pollution need to be studied.

Smoking cessation programs should be administered as the most important health promoting intervention for smokers with pulmonary disease.

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