

# Chapter 9

## Respiratory Effects in Adults from Exposure to Secondhand Smoke

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## Introduction

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There have been far fewer studies of involuntary smoking and adverse respiratory effects on adults compared with the number of studies on children. In fact, the evidence for children has causally linked secondhand smoke exposure to a number of adverse respiratory effects (Chapter 6, *Respiratory Effects in Children from Exposure to Secondhand Smoke*). The more limited research on adults may partly reflect the methodologic challenges in designing studies of nonmalignant respiratory diseases in adults, who are exposed in multiple and often complex environments: the home, the workplace, transportation environments, and additional public and other places. The potential for misclassifying smoking status, with former or current smokers categorized as involuntary smokers, has been a concern in studies that rely on self-reports of former smoking. Measuring past secondhand smoke exposure presents a challenge in studies of chronic effects and diseases that may become clinically apparent only after 20 or more years of exposure. Bias in the reporting of symptoms attributed to involuntary smoking is increasingly possible as public awareness of involuntary smoking and its health consequences increases. It may also be difficult to measure exposures to potential confounding or modifying agents (e.g., infectious agents and dusty occupations) that may need to be considered in studies of involuntary smoking.

Despite these challenges, the literature has been growing since the 1986 reports released by the Surgeon General (U.S. Department of Health and Human Services [USDHHS] 1986) and the National Research Council (NRC 1986). Subsequently, the literature has been summarized by federal and state agencies including the U.S. Environmental Protection Agency (USEPA 1992) and the California Environmental Protection Agency (Cal/EPA) (National Cancer Institute [NCI] 1999), and by several authors in peer-reviewed publications (Trédaniel et al. 1994; Coultas 1998; Weiss et al. 1999). Major reviews of the health effects of involuntary smoking in adults published between 1986

and 1999 examined respiratory health outcomes such as odor and irritation, respiratory symptoms, pulmonary function, and respiratory diseases (e.g., asthma and chronic obstructive pulmonary disease [COPD]) (Table 9.1). This table includes agency reviews as well as systematic reviews carried out by individual authors (Trédaniel et al. 1994; Coultas 1998). The evidence documented a strong link between secondhand smoke exposure and odor annoyance and irritation of mucous membranes of the eyes and nose. Weaker evidence suggested that involuntary smoking is associated with respiratory symptoms and small decrements in lung function among adults. Although experimental studies suggested that some persons with asthma may be susceptible to the effects of secondhand smoke exposure, only scant epidemiologic data consisting of a small number of studies on involuntary smoking and COPD were available on this issue at the time. This chapter reexamines the literature from these earlier reviews (Table 9.1), updates the literature with more recent publications, and evaluates the evidence supporting causal inferences. This discussion does not specifically review sinonasal disease because the evidence remains limited (Samet 2004).

The research strategy for this chapter consisted of searching the Medline database to identify references between 1990 and 2001 using any of five terms for secondhand smoke: environmental tobacco smoke (ETS), tobacco smoke pollution, sidestream smoke, second hand smoke, or secondhand smoke. These terms were then linked to a series of terms: (1) respiratory symptoms (i.e., respiratory symptom, cough, coughing, wheeze, or dyspnea [difficulty breathing]); (2) lung function; (3) lung diseases (i.e., lung diseases, obstructive, asthma, emphysema, and bronchitis); (4) etiology (i.e., cause or risk factor) and morbidity; (5) irritation or irritating of eye or nose or throat; and (6) tobacco smoke sensitivity or odor. In addition, bibliographies from recent studies were reviewed for additional references (Trédaniel et al. 1994; Coultas 1998; NCI 1999; Weiss et al. 1999).

**Table 9.1 Major conclusions from reports on adverse respiratory effects of secondhand smoke exposure in adults**

**Odor and Irritation**

*U.S. Department of Health and Human Services (USDHHS) 1986*

"The main effects of the irritants present in ETS [environmental tobacco smoke] occur in the conjunctiva of the eyes and the mucous membranes of the nose, throat, and lower respiratory tract. These irritant effects are a frequent cause of complaints about poor air quality due to environmental tobacco smoke." (p. 252)

*National Research Council (NRC) 1986*

"ETS arouses odor responses. The objectionable odor generated by ETS greatly exceeds that generated by simple occupancy under comparable conditions of occupancy, density, temperature, and relative humidity, and is more persistent." (p. 178)

"Whereas odor will govern the reactions of visitors to a smoking space, irritation will largely govern the reactions of occupants. Over time, eye irritation grows to become the most important negative response of the occupant. Dissatisfaction observed in chamber studies is commensurate with that found in field studies." (p. 178)

*Trédaniel et al. 1994*

"The acute irritating effect of ETS on respiratory mucous membranes is well-established." (p. 180)

*California Environmental Protection Agency (Cal/EPA) 1997 (National Cancer Institute [NCI] 1999)*

"Eye and nasal irritation are the most commonly reported symptoms among adult nonsmokers exposed to ETS; in addition, odor annoyance from indoor exposure to ETS has been shown in several studies." (p. 253)

**Respiratory Symptoms**

*USDHHS 1986*

"The implications of chronic respiratory symptoms for respiratory health as an adult are unknown and deserve further study." (p. 107)

*NRC 1986*

"The extent to which normal and asthmatic adults are affected by short-term exposures to ETS needs to be studied further." (p. 217)

*USEPA 1992*

". . .new evidence also has emerged suggesting that exposure to ETS may increase the frequency of respiratory symptoms in adults. These latter effects are estimated to be 30% to 60% higher in ETS-exposed nonsmokers compared to unexposed nonsmokers." (pp. 7-68-7-69)

*Trédaniel et al. 1994*

". . .no definite conclusion can be drawn from the studies that have investigated chronic respiratory symptoms in relation to ETS exposure." (p. 181)

*Cal/EPA 1997 (NCI 1999)*

". . .regular ETS exposure in adults has been reported to increase the risk of occurrence of a variety of lower respiratory symptoms." (p. 255)

**Pulmonary Function**

*USDHHS 1986*

"Healthy adults exposed to environmental tobacco smoke may have small changes on pulmonary function testing, but are unlikely to experience clinically significant deficits in pulmonary function as a result of exposure to environmental tobacco smoke alone." (p. 107)

**Table 9.1 Continued**

*NRC 1986*

“Future cross-sectional studies of ETS exposure and lung function in adults need to be designed to control for other factors that may affect lung function.” (p. 217)

“Little information is available from long-term longitudinal studies of the effect of exposure to ETS by nonsmokers on lung function in either children or adults.” (p. 217)

*USEPA 1992*

“Recent studies have confirmed the conclusion by the Surgeon General’s report (U.S. DHHS, 1986) that adult nonsmokers exposed to ETS may have small reductions in lung function (approximately 2.5% lower mean FEV<sub>1</sub> [forced expiratory volume in 1 second]). . . .” (p. 7-68)

*Trédaniel et al. 1994*

“It remains controversial whether acute passive smoking is associated with important pulmonary physiological hazards. . . . Most of the available studies are cross-sectional, and the relationship to long-term changes in lung function is not established.” (p. 181)

*Cal/EPA 1997 (NCI 1999)*

“The effect of chronic ETS exposure upon pulmonary function in otherwise healthy adults is likely to be small, and is unlikely by itself to result in clinically significant chronic disease.” (p. 255)

**Respiratory Diseases**

*NRC 1986*

“It is unlikely that exposure to ETS can cause much emphysema.” (p. 212)

*Trédaniel et al. 1994*

“Conflicting evidence exists on the association in asthmatic patients between ETS exposure and appearance of symptoms and functional abnormalities (including change in bronchial responsiveness).” (p. 181)

“Four out of five studies offer support to the hypothesis of an association between ETS exposure and risk of COPD [chronic obstructive pulmonary disease].” (p. 181)

*Coultas 1998*

“While growing evidence suggests that passive smoking is a risk factor for adult onset asthma and COPD, the magnitude of the associations is small. However, additional evidence on the relationship between passive smoking and asthma and COPD is needed to fulfill the criteria for causality, particularly the criteria of temporality and dose-response.” (p. 386)

“Although the available literature is limited, it does show that exposure to ETS is associated. . .with worsening of respiratory symptoms and lung function in adult asthmatics.” (p. 383)

“. . . little is known about the effects of ETS exposure on respiratory symptoms or lung function among patients with COPD.” (p. 385)

*Cal/EPA 1997 (NCI 1999)*

“There is suggestive evidence that ETS exposure may exacerbate adult asthma.” (p. 194)

“. . . chamber studies. . . suggest that there is likely to be a subpopulation of asthmatics who are especially susceptible to ETS exposure.” (p. 203)

## Biologic Basis

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Chapter 2 (Toxicology of Secondhand Smoke) reviews mechanisms by which secondhand smoke exposure may generally cause respiratory disease in populations. This section focuses more specifically on adults. Active cigarette smoking causes inflammatory injury throughout the respiratory tract, leading to chronic airway and alveolar injury and chronic respiratory symptoms and diseases (Floreani and Rennard 1999; Saetta et al. 2001; USDHHS 2004). Although the evidence on active smoking provides a strong basis of support for the plausibility of adverse respiratory effects from involuntary smoking, differences in the dose from involuntary versus active smoking limit direct inferences from active to involuntary smoking. Experimental studies in animals (Escolar et al. 1995; Joad et al. 1995; Seymour et al. 1997) and humans (Anderson et al. 1991; Yates et al. 1996, 2001; NCI 1999) provide relevant evidence of and insights into underlying mechanisms for the effects of involuntary smoking on the respiratory tract.

The biologic outcomes examined in animal models of involuntary smoking have included antibody responses (Seymour et al. 1997), alterations of airway defense receptors (Joad et al. 1995), and pathologic changes of emphysema (Escolar et al. 1995). Using a mouse allergy model, Seymour and colleagues (1997) exposed the animals to secondhand smoke for 43 days (6 hours per day, 5 days per week, mean total suspended particulates at 1.04 milligrams per cubic meter [ $\text{mg}/\text{m}^3$ ], mean carbon monoxide [CO] at 6.1 parts per million [ppm]). Secondhand smoke exposure resulted in elevated levels of antibodies to allergens delivered by aerosol challenge, suggesting that such exposures enhance allergic inflammatory responses. Joad and colleagues (1995) exposed 29 developing guinea pigs aged 8 through 43 days to sidestream smoke (CO =  $5.6 \pm 0.7$  ppm) for six hours per day, five days a week. Although lung morphology was unchanged, responsiveness of airway C-fiber receptors (a component of lung defense mechanisms) was reduced, which may facilitate further exposure and injury over time. Escolar and colleagues (1995) exposed 60 rats to secondhand smoke (mean CO at 35 ppm) for 90 minutes per day for three months. Morphometry showed changes in the alveoli consistent with emphysema, including the loss of elasticity in the lung tissue.

Human experimental studies have involved short-term exposures of volunteers to known

concentrations of sidestream smoke measured by CO and/or particulate levels in exposure chambers. The effects examined included eye and nasal irritation, nasal mucociliary clearance, respiratory symptoms, pulmonary function changes, and systemic inflammation. Although controlled human exposure studies have the advantages of accurate measurements and controlled levels of exposure, such studies have inherent limitations. Because the duration of exposure must be brief, only short-term effects can be measured. Exposure to sidestream smoke under controlled conditions may not accurately reflect exposure-response relationships associated with multiple exposures found in real-world conditions such as the workplace. These studies are necessarily restricted to a small number of volunteers, thus limiting the generalizability of the findings and the statistical power to detect effects. Moreover, variations in the duration of the exposures limit the comparability of the results.

Controlled human exposures to sidestream smoke have been used to characterize effects on the nose such as odor detection, nasal symptoms, and physiologic changes (USDHHS 1986; Bascom et al. 1991, 1995, 1996; Cummings et al. 1991; Willes et al. 1992, 1998; Nowak et al. 1997a). In general, these exposures have been at the upper end of the range of measured secondhand smoke concentrations in various environments (Chapter 3, Assessment of Exposure to Secondhand Smoke, and Chapter 4, Prevalence of Exposure to Secondhand Smoke). Bascom and colleagues (1991, 1995, 1996) and Willes and colleagues (1992, 1998) conducted a series of chamber studies to characterize nasal responses to sidestream smoke. In an early investigation, Bascom and colleagues (1991) found that posterior nasal resistance (a measurement of nasal sensitivity in the bottom of the passageway) increased after 15 minutes of exposure to sidestream smoke (45 ppm of CO) among 10 healthy persons without asthma who reported nasal sensitivity to secondhand smoke (congestion, rhinorrhea, or sneezing), but not among 11 participants who did not report nasal sensitivity. However, assay of nasal secretions for histamine, kinin, esterase, or albumin provided no evidence for allergic inflammation or increased vascular permeability, indicating a nonallergic mechanism for the physiologic response. Nowak and colleagues (1997a) reported similar findings after examining nasal fluid for markers of inflammation 30 minutes

before and 30 minutes after exposing 10 persons with mild asthma to secondhand smoke at 22.4 ppm of CO. Bascom and colleagues (1996) examined exposure-response relationships among 13 persons with reported secondhand smoke sensitivity and 16 persons who were not sensitive; the experiment involved two hours of sidestream smoke exposure at 1 ppm, 5 ppm, and 15 ppm of CO. Nasal resistance increased significantly in both groups after exposure to the highest level of sidestream smoke (15 ppm of CO). Bascom and colleagues (1995) also assessed the effect of sidestream smoke exposure on nasal mucociliary clearance in 12 volunteers. The rate of clearance increased in some participants but slowed in three others; all three had a history of rhinitis associated with secondhand smoke exposure.

Human volunteers, including healthy nonsmokers and persons with asthma, have been exposed to secondhand smoke under controlled conditions to examine symptoms, pulmonary function changes, inflammatory markers, and lung injury (Trédaniel et al. 1994; Yates et al. 1996, 2001; Nowak et al. 1997a,b; NCI 1999; Weiss et al. 1999). The 1997 Cal/EPA report reviewed results from 10 studies of persons with asthma and concluded that "although the design constraints of the chamber studies limit the interpretation of the results, they do suggest that there is likely to be a subpopulation of asthmatics who are especially susceptible to ETS exposure. The physiological responses observed in these investigations appear to be reproducible in both 'reactors' and 'nonreactors.' It is unlikely that the physiological and symptomatic responses reported are due exclusively to either stress or suggestion" (NCI 1999, p. 203). Nowak and colleagues (1997b) provided additional evidence for this conclusion by exposing 17 persons with mild asthma to secondhand smoke (20 ppm of CO) or ambient air ("sham") for three hours. The investigators measured spirometry and bronchial responsiveness one hour, five hours, and nine hours after the exposure. The overall average decline in forced expiratory volume in one second (FEV<sub>1</sub>) levels was 9.1 percent after the secondhand smoke exposure and 5.9 percent after the sham exposure. However, the mean FEV<sub>1</sub> decline largely reflected declines in three persons, and secondhand smoke-induced symptoms were not associated with the FEV<sub>1</sub> decline. In a separate study of 10 persons with mild asthma who were exposed to secondhand smoke at 22.4 ppm of CO for three hours, the FEV<sub>1</sub> level and the levels of markers of inflammation obtained by bronchoalveolar lavage were unchanged by the exposure (Nowak et al. 1997a).

Studies have associated nonspecific bronchial hyperresponsiveness with an accelerated decline in lung function, which may thus be a marker for susceptibility to the development of COPD (Kanner et al. 1994; Paoletti et al. 1995; Rijcken et al. 1995; Tracey et al. 1995). Menon and colleagues (1992) exposed 31 smoke-sensitive persons with asthma and 39 smoke-sensitive persons without asthma to secondhand smoke at relatively high levels (suspended particles >1,000 micrograms/m<sup>3</sup>) for four hours in a test chamber. Compared with pre-exposure bronchial reactivity among those without asthma, bronchial reactivity to methacholine increased in 18 percent of the participants 6 hours after exposure, in 10 percent of the participants 24 hours after exposure, and in 8 percent of the participants three weeks after exposure. These results suggest that secondhand smoke exposure may increase bronchial hyperreactivity even in asymptomatic persons who do not have asthma. In contrast to these results, a study of 17 secondhand smoke-exposed persons with mild asthma did not find an increase in airway responsiveness when measured by the methacholine challenge (Nowak et al. 1997b). Jindal and colleagues (1999) measured bronchial hyperresponsiveness in a sample of 50 women aged 20 through 40 years with asthma who were from a chest clinic in India. Exposure to secondhand smoke was assessed with a questionnaire that included questions on smoking by the husband, smoking by other family members, and smoking by coworkers. Women exposed to secondhand smoke had significantly greater bronchial hyperreactivity than did unexposed women; the mean provocative dose of histamine used to produce a 20 percent drop in FEV<sub>1</sub> was 50 percent lower in the exposed group compared with the unexposed group.

In active smokers, the uptake of inhaled technetium<sup>99m</sup> (labeled diethylenetriamine pentaacetate [<sup>99m</sup>Tc-DTPA]) was increased, suggesting an increase in alveolar permeability (Jones et al. 1980). Yates and colleagues (1996) applied this technique to 20 healthy nonsmokers and assessed whether exposure to secondhand smoke for one hour in a chamber affected alveolar permeability. The exposure was followed by an increase in the time for <sup>99m</sup>Tc-DTPA clearance, from 69.1 to 77.4 minutes. In contrast to active smoking, these results imply a decrease in alveolar permeability following exposure. The findings do, however, provide evidence of a physiologic response to even a very brief exposure to secondhand smoke.

Nowak and colleagues (1997a) also provided indirect evidence for a decrease in epithelial

permeability associated with secondhand smoke exposure in a study of 10 persons with mild asthma. Albumin levels from nasal and bronchoalveolar lavage were lower after three hours in a chamber at 22.4 ppm CO compared with a sham exposure. An increase in permeability would be expected to increase albumin leakage into the alveoli.

Nitric oxide (NO) regulates a number of airway and vascular functions and can be measured in exhaled air. Compared with nonsmokers, active smokers had lower exhaled NO levels, and intermediate decrements were found in exhaled NO levels from nonsmokers exposed to secondhand smoke (Yates et al. 2001). Fifteen healthy nonsmoking volunteers were exposed to secondhand smoke at 23 ppm CO in a chamber for one hour, and exhaled NO was measured before and every 15 minutes during the exposure (Yates et al. 2001). Secondhand smoke exposure was associated with a significant decline in exhaled NO (134 parts per billion [ppb] before and 99 ppb 60 minutes after the exposure).

Only limited information is available on the systemic effects of secondhand smoke exposure (Anderson et al. 1991; Oryszczyn et al. 2000). Anderson and colleagues (1991) exposed 16 healthy nonsmokers (mean age 29 years) to cigarette smoke from 6 smokers in a poorly ventilated room for three hours with hourly respirable particulate levels averaging 2.3 to 2.6 mg/m<sup>3</sup>. This exposure was associated with significant increases in peripheral blood leukocyte counts, chemotaxis, and the release of reactive oxidants; these findings are consistent with the mechanisms of respiratory tract injury in active smokers (Saetta et al. 2001; USDHHS 2004). Oryszczyn and colleagues (2000) examined the relationship between self-reported secondhand smoke exposure (i.e., currently living with one or more smokers) and the total serum immunoglobulin E (IgE) level, which is higher in persons with asthma than in those without asthma. The study included 122 persons with asthma, 430 of their first-degree relatives, and 190 controls. Among lifetime nonsmokers with and without asthma, involuntary smoking was associated with higher IgE levels. The

highest levels were among those with asthma who had been exposed to secondhand smoke. However, significant differences in IgE levels were observed only in women after adjusting for asthma.

In summary, compared with research on active smoking, the literature on respiratory tract injury from involuntary smoking is limited. There are only a few animal investigations, and they examined different outcomes (e.g., antibody response to allergens, responsiveness of C-fiber receptors, and morphologic signs of emphysema). Most human studies have examined inflammatory and physiologic effects of short-term secondhand smoke exposure in chambers. The few studies that investigated markers of local inflammation in the nose and lower respiratory tract did not find any evidence of an increased inflammatory response to brief secondhand smoke exposures. Exhaled NO, which has a number of physiologic functions including inflammatory regulation, decreased in persons exposed to secondhand smoke, an effect also found in active smokers. Two studies suggest that there may be an enhanced systemic inflammatory and antibody response to secondhand smoke exposure. Similarly, one human study and one animal study provide complementary evidence that secondhand smoke exposure may enhance antibody responses to allergens. Two other investigations provide evidence that short-term secondhand smoke exposure may actually result in a protective physiologic response based on a decrease in epithelial permeability in the nose and alveoli. Another study paired variable effects with nasal mucociliary clearance.

The physiologic responses to secondhand smoke exposure were examined by measuring lung function in healthy persons and in patients with asthma. These studies documented inconsistent results, but the small number of participants and the types of exposures may not accurately reflect secondhand smoke exposure in the "real" world. Despite these limitations, available evidence suggests that some people, regardless of whether they are healthy or have asthma, experience a short-term decline in lung function from secondhand smoke exposures.

## Odor and Irritation

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Secondhand smoke contains compounds such as pyridine that produce unpleasant odors (NCI 1999), and other agents such as particles, nicotine, acrolein, and formaldehyde, which may cause mucosal irritation (Lee et al. 1993). The topics of odor, odor annoyance, and mucosal irritation from secondhand smoke were reviewed in the 1986 Surgeon General's report (USDHHS 1986), in the 1986 NRC report (1986), and by Samet and colleagues (1991). Controlled chamber studies (USDHHS 1986; NCI 1999) and epidemiologic studies (USDHHS 1986) have assessed the association of these symptoms with secondhand smoke exposure. The 1986 Surgeon General's report reviewed results of 13 experimental studies and 5 field studies. The conclusions from that review have remained consistent with subsequent reviews of the topic (Table 9.1).

In addition to the level of secondhand smoke exposure, other factors that may determine an odor response to secondhand smoke include the age of the exposed person as it relates to olfactory acuity and visual contact with the smoker (Moschandreas and Relwani 1992), and individual traits such as annoyance thresholds and coping styles (Winneke and Neuf 1996). Limited data suggest that olfactory acuity decreases with age, and seeing a smoker increases the perceived odor intensity and annoyance of secondhand smoke (Moschandreas and Relwani 1992). Although these factors are relevant to designing and interpreting studies of odor responses to secondhand smoke, available studies provide little information on these factors.

Both experimental (Bascom et al. 1991, 1996; Willes et al. 1992, 1998; Nowak et al. 1997a) and observational studies (Cummings et al. 1991; Norback and Edling 1991; Ng and Tan 1994) have assessed nasal symptoms (e.g., congestion, excessive secretions, or sneezing) as measures of upper respiratory tract irritation. In a survey of 77 healthy, nonsmoking adults 18 through 45 years of age, Bascom and colleagues (1991) found that 34 percent reported one or more nasal symptoms following secondhand smoke exposure. Allergen sensitivity, measured by skin-prick testing in 21 persons, was more frequent among secondhand smoke-sensitive persons (70 percent) compared with persons not sensitive to secondhand smoke (27 percent). Bascom and colleagues (1991) then exposed 10 sensitive and 11 persons not sensitive to secondhand smoke (45 ppm of CO for

15 minutes) in a chamber; significant increases in nasal secretions and nose-throat irritation were reported by both groups. Only the secondhand smoke-sensitive persons reported significant increases in nasal congestion, headache, and cough. In a subsequent investigation, Bascom and colleagues (1996) examined exposure-response relationships between secondhand smoke exposure and nasal symptoms among 13 persons with a history of secondhand smoke sensitivity and 16 persons without secondhand smoke sensitivity. Compared with no exposure, the lowest level of secondhand smoke exposure at 1 ppm of CO was associated with a significant increase in selected symptoms (eye irritation, nose irritation, and odor perception) reported by both groups. After the exposure, three of the nine symptoms (headache, eye irritation, and odor perception) increased significantly among persons sensitive to secondhand smoke compared with those who were not sensitive. Nasal congestion, increased nasal secretions, and cough increased significantly in both groups at 15 ppm of CO. Nowak and colleagues (1997a) exposed 10 persons with mild asthma to secondhand smoke ( $22.4 \pm 1.2$  ppm of CO) in a chamber and measured nose and mouth symptoms (dry nose, running nose, blocked nose, dry mouth, and mucus accumulation). Three hours of exposure produced increases in nose and mouth symptoms.

The 1986 Surgeon General's report reviewed five cross-sectional studies that described the prevalence of annoyance and symptoms of irritation associated with secondhand smoke exposure, but only one study included an unexposed comparison group (USDHHS 1986). The main indicators of annoyance and irritation were self-reported annoyances (e.g., disturbed by tobacco smoke, poor air quality, frustration, and hostility) and symptoms (e.g., eye, nose, and throat irritation; rhinorrhea; headache; fatigue; nausea; dizziness; and wheeze).

Since that report, a limited number of new observational studies have specifically examined odor annoyance and nasal irritation associated with secondhand smoke exposure (Cummings et al. 1991; Ng and Tan 1994). A larger number of investigations with conflicting results examined the role of secondhand smoke in building-related illnesses that included irritation of the skin and mucous membranes of the eyes, nose, and throat; headache; fatigue; and difficulty concentrating (Norback and Edling 1991;

Menzies and Bourbeau 1997). The inconsistent findings in these studies may be explained by several methodologic challenges (Menzies and Bourbeau 1997) that severely compromise the usefulness of examining the role of indoor secondhand smoke exposures at work, specifically in associations with odor annoyance and nasal irritation. These challenges include the multifactorial basis of building-related symptoms and illnesses, the potential for multiple pollutants to contribute to symptom risk, and limitations of the designs of many of the epidemiologic studies on this issue. Therefore, there is no further discussion of secondhand smoke and nonspecific building-related illnesses in this chapter.

Cummings and colleagues (1991) conducted a cross-sectional survey of 723 volunteers aged 18 through 84 years who attended a free cancer screening at a cancer center in New York. Overall, a high proportion of lifetime nonsmokers reported being bothered by tobacco smoke, with the highest rates among people who were atopic (81 percent) or who had a history of a respiratory illness (82 percent), compared with all others (74 percent). A similar pattern was found for reports of nose irritation (54 percent among those who were atopic, 48 percent among those who had a history of respiratory illnesses, and 30 percent among all others) and sneezing (23 percent among those who were atopic, 17 percent among those who had a history of respiratory illnesses, and 12 percent among all others) associated with secondhand smoke exposure.

To assess risk factors for allergic rhinitis in Singapore, Ng and Tan (1994) conducted a population-based cross-sectional study of 2,868 adults aged 20 through 74 years. Overall, 4.5 percent of the participants had allergic rhinitis defined by self-reports during the previous year of usual nasal blockage and discharge apart from colds or the flu, provoked by allergens, with or without conjunctivitis. Compared with having no household exposure to smokers, exposure to one or more light smokers was not associated with allergic rhinitis (odds ratio [OR] = 0.96 [95 percent confidence interval (CI), 0.6–1.53]), whereas exposure to one or more heavy smokers was weakly associated with allergic rhinitis (OR = 1.43 [95 percent CI, 0.94–2.18]).

## Evidence Synthesis

Prior reviews have led to the conclusion that secondhand smoke exposure causes odor

annoyance (Table 9.1). Coherent and consistent results from experimental and observational studies provide a strong basis for inferring a causal link between secondhand smoke exposure and odor annoyance and symptoms of nasal irritation. Moreover, experimental studies established both the temporal and dose-response relationships of odor annoyance and nasal irritation with secondhand smoke exposure. The intensity of odor annoyance and nasal irritation increased with increased levels of secondhand smoke exposure. In addition, persons with nasal allergies or a history of respiratory illnesses may be more susceptible to nasal irritation from secondhand smoke exposure compared with persons without these conditions. However, because few observational studies have included unexposed comparison groups, the strength of the association is more difficult to evaluate. Moreover, methodologic limitations, including exposure misclassification and nonspecificity of symptoms, may result in underestimates of the strength of the association.

## Conclusions

1. The evidence is sufficient to infer a causal relationship between secondhand smoke exposure and odor annoyance.
2. The evidence is sufficient to infer a causal relationship between secondhand smoke exposure and nasal irritation.
3. The evidence is suggestive but not sufficient to conclude that persons with nasal allergies or a history of respiratory illnesses are more susceptible to developing nasal irritation from secondhand smoke exposure.

## Implications

Although the symptoms of odor annoyance and nasal irritation may appear to be minor adverse health consequences, they have the potential to negatively affect daily functioning and quality of life. For example, studies have documented for a long time the potential of secondhand smoke to cause annoyance and irritation. This acute and adverse response is possibly only avoidable in smoke-free environments.

## Respiratory Symptoms

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The 1986 Surgeon General's report included only a few studies on secondhand smoke exposure and respiratory symptoms in adults (Table 9.1). Although a number of investigations since 1986 have studied this relationship, conclusions from major reviews of this topic (Table 9.1) have been inconsistent. The sources of information on respiratory symptoms include experimental studies of acute exposures and symptoms (Table 9.2) and observational studies of chronic symptoms (Table 9.3).

### Experimental Studies

Persons with and without asthma were exposed to secondhand smoke in exposure chambers in efforts to characterize physiologic responses (see "Biologic Basis" earlier in this chapter) and acute symptom responses to secondhand smoke (Table 9.2). Most of the studies are small and provide limited information as to how the participants were recruited. Some were recruited through hospital-based asthma and allergy clinics (Shephard et al. 1979; Danuser et al. 1993) and others through advertisements to students (Bascom et al. 1996).

Out of 10 studies (Table 9.2), 5 were restricted to persons with asthma and did not have a control group (Knight and Breslin 1985; Wiedemann et al. 1986; Stankus et al. 1988; Magnussen et al. 1992; Nowak et al. 1997a), 3 included persons with asthma and a control group without asthma (Shephard et al. 1979; Dahms et al. 1981; Danuser et al. 1993), and 2 were limited to persons without asthma (Bascom et al. 1991, 1996). The investigations using only persons with asthma and no control group provided only limited information on the occurrence of respiratory symptoms with secondhand smoke exposure. In one of these investigations (Magnussen et al. 1992), there was no difference in respiratory symptom responses between the sham and the secondhand smoke exposures. In the three studies that included persons with asthma and controls without asthma, results suggest that acute respiratory symptoms occur with a similar or slightly increased frequency with secondhand smoke exposure among persons with mild to moderate asthma compared with healthy controls. Moreover, the dose-response relationship that was found in persons with asthma (Danuser et al. 1993) and in healthy persons

without asthma (Bascom et al. 1996) strengthens the argument for a causal link between secondhand smoke exposure and acute respiratory symptoms. However, the generalizability of these results may be questioned because of the small numbers in the studies and the use of volunteers. Persons who volunteer may do so because of a perceived sensitivity to secondhand smoke, and may thus overreport symptoms compared with persons randomly selected from the general population.

### Observational Studies

Chronic respiratory symptoms of cough, phlegm, wheeze, and dyspnea (difficulty breathing) associated with secondhand smoke exposure have been investigated largely in cross-sectional studies; there have been only a few longitudinal investigations (Schwartz and Zeger 1990; Robbins et al. 1993; Jaakkola et al. 1996). Table 9.3 describes these studies and their results. The documented symptoms are heterogeneous in etiology and vary with gender, age, associated diseases (e.g., allergy or respiratory illness), and smoking status (e.g., never versus former) (Cumplings et al. 1991). For example, cough may result from irritation or inflammation of the upper and lower respiratory tract, but it may also be caused by gastroesophageal reflux disease. Similarly, dyspnea is often attributed to a respiratory disease, but it may also result from a cardiovascular disease. It is not feasible in observational studies to separate respiratory from nonrespiratory causes of these symptoms. However, variations in the distribution of the determinants of these symptoms among populations may contribute in part to the inconsistent findings. Moreover, numerous other environmental factors such as outdoor and indoor air pollution, allergens, and occupational exposures may vary among populations and may cause respiratory symptoms. Studies evaluating the relationship between secondhand smoke exposure and respiratory symptoms have not consistently included some of these other environmental factors (Table 9.3).

Although not all of the available observational studies have found significant associations of secondhand smoke exposure with cough (Table 9.3) (Schwartz and Zeger 1990; Jaakkola et al. 1996; Zhang et al. 1999), the point estimates of risk with exposure

**Table 9.2 Chamber studies of exposure to secondhand smoke and acute respiratory symptoms**

Study	Population	Exposure	Symptoms	Comments																													
Shephard et al. 1979	14 patients with mild to moderate asthma Aged 19–65 years  No controls without asthma	Average CO* = 24 ppm†, 2 hours	<table border="1"> <thead> <tr> <th rowspan="2"></th> <th colspan="2">Persons with asthma (%)</th> <th colspan="2">Normal controls (%)</th> </tr> <tr> <th>Rest</th> <th>Exercise</th> <th>Rest</th> <th>Exercise</th> </tr> </thead> <tbody> <tr> <td>Wheeze</td> <td>36</td> <td>10</td> <td>0</td> <td></td> </tr> <tr> <td>Chest tightness</td> <td>43</td> <td>5</td> <td>0</td> <td></td> </tr> <tr> <td>Cough</td> <td>36</td> <td>45</td> <td>58</td> <td></td> </tr> <tr> <td>Dyspnea</td> <td>21</td> <td>15</td> <td>17</td> <td></td> </tr> </tbody> </table>		Persons with asthma (%)		Normal controls (%)		Rest	Exercise	Rest	Exercise	Wheeze	36	10	0		Chest tightness	43	5	0		Cough	36	45	58		Dyspnea	21	15	17		Regular asthma medications were not withheld before the test in 13 out of 14 patients; 1 or more may have been smokers; normal controls were from another study
	Persons with asthma (%)		Normal controls (%)																														
	Rest	Exercise	Rest	Exercise																													
Wheeze	36	10	0																														
Chest tightness	43	5	0																														
Cough	36	45	58																														
Dyspnea	21	15	17																														
Dahms et al. 1981	10 persons with asthma (5 smoke-sensitive) Aged 18–26 years  10 healthy controls Aged 24–53 years	Estimated CO = 15–20 ppm (based on carboxy-hemoglobin levels), 1 hour	All had similar degrees of eye and nasal irritation	Exposure levels were not measured directly; no individual data were reported																													
Knight and Breslin 1985	6 patients with mild to moderate asthma	CO level was not determined, 1 hour	Wheeze was reported by 33% of participants; increase in chest tightness was reported by 50% of participants	Participants and methods were not well described																													
Wiedemann et al. 1986	9 asymptomatic persons with asthma Aged 19–30 years	CO = 40–50 ppm, 1 hour	Cough was reported by 33% of participants	None																													
Stankus et al. 1988	21 smoke-sensitive persons with asthma Aged 21–50 years	Average CO = 8.7 ppm, 2 hours; if no change occurred in lung function, exposure was then increased to average CO = 13.3 ppm, 2 hours	Cough, chest tightness, and dyspnea were reported by 7 participants who had a >20% decline in forced expiratory volume in 1 second	No information was provided on symptoms among those who did not have a decline in lung function																													
Bascom et al. 1991	21 healthy nonsmokers	45 ppm CO for 15 minutes	Cough and chest tightness were greater among sensitive participants	11 not sensitive and 10 sensitive participants by questionnaire																													
Magnussen et al. 1992	18 persons with mild to moderate asthma Aged 21–51 years	Average CO = 20.5 ppm, 1 hour	Cough and chest tightness symptom scores were not significantly different for the secondhand smoke exposure compared with the sham exposure	None																													

Table 9.2 Continued

Study	Population	Exposure	Symptoms	Comments
Danuser et al. 1993	10 persons with hyperreactive airways (5 asthma, 3 suggestive of asthma) Aged 24–51 years  10 healthy controls Aged 24–52 years	Average CO = 0, 2, 4, 8, 16, and 32 ppm; 2 minutes at each level	Over the entire exposure, 7 hyperreactive persons and 6 healthy controls reported cough, chest tightness, or dyspnea	Small likelihood of “suggestibility” because of the mode of secondhand smoke delivery; symptom severity was mild for both groups, even at the highest level of exposure; there was a dose-response relationship between symptom scores and CO levels
Bascom et al. 1996	29 healthy nonsmokers Aged 22–31 years	Average CO = 0, 1, 5, and 15 ppm; 2 hours at each level	Cough and chest tightness scores increased with increasing CO levels	None
Nowak et al. 1997a	10 persons with mild asthma Aged 22–29 years	Average CO = 22.4 ppm, 3 hours	Throat and chest symptom scores (breathing difficulty, chest tightness, dyspnea, and chest pain) significantly increased with exposure	Unable to determine an effect on chest symptoms alone because throat and chest symptoms were combined

\*CO = Carbon monoxide.

†ppm = Parts per million.

compared with no exposure have been greater than one (Schwartz and Zeger 1990; White et al. 1991; Pope and Xu 1993; Lam et al. 1995; Jaakkola et al. 1996; Zhang et al. 1999). The studies range in size and in the precision of their estimates; however, many did not consider other factors (e.g., other indoor and outdoor pollutants, allergy, asthma, and occupation) that may influence the occurrence of cough. Pope and Xu (1993) highlight the complexity of investigating the relationship between secondhand smoke exposure and respiratory symptoms. Among 973 Chinese women aged 20 through 40 years who had never smoked, there was a dose-response relationship between cough and the number of smokers at home (OR = 1.02 for 1 smoker and 1.87 for  $\geq 2$  smokers). In addition, the combination of heating with coal, a source of indoor smoke, and two or more smokers in the home was associated with a further increase in the occurrence of cough (OR = 3.07). This finding indicates the potential for a joint effect of secondhand smoke exposure with other environmental exposures. Similarly, the findings of Cummings and colleagues (1991) (Table 9.3) suggest that associated illnesses, such as allergy and respiratory illnesses, increase the

occurrence of cough with secondhand smoke exposure compared with persons without these conditions. Phlegm production is a symptom often associated with cough, and findings for this symptom are similar to those for cough (Table 9.3) (Schwartz and Zeger 1990; White et al. 1991; Pope and Xu 1993; Lam et al. 1995; Jaakkola et al. 1996; Zhang et al. 1999). The point estimates for the association between secondhand smoke exposure and phlegm production have ranged from 0.69 to 8.3 (Table 9.3).

Out of five studies that examined the association between secondhand smoke exposure and wheeze, two found significant associations (Leuenberger et al. 1994; Baker and Henderson 1999) and three did not (Pope and Xu 1993; Jaakkola et al. 1996; Zhang et al. 1999). The point estimates ranged from 0.62 to 1.94 (Table 9.3). Although Leuenberger and colleagues (1994) found a dose-response relationship between wheeze and the amount of the exposure, Pope and Xu (1993) did not. Moreover, Pope and Xu (1993) did not find an interaction for wheeze between the number of smokers at home and the use of coal heat as they did find for cough and phlegm.

**Table 9.3 Observational studies of exposure to secondhand smoke and chronic respiratory symptoms**

Study	Population	Period of study	Findings		Comments																																										
Schwartz and Zeger 1990	Approximately 100 nursing students Los Angeles	Follow-up for up to 3 years	<u>Exposure</u> Roommate smoked	<u>Phlegm OR* (95% CI)</u> 1.41 (1.08–1.85)	There was no association with an increased risk of cough																																										
Cummings et al. 1991	723 volunteers attending a free cancer screening, 56% women, 90% White Aged 18–84 years United States	1986	<u>Symptom</u> Bothered by tobacco smoke Watery eyes Nose irritation Cough episodes Sore throat Sneezing	<p>Lifetime nonsmokers</p> <table border="1"> <thead> <tr> <th><u>Atopic (%)</u></th> <th><u>Respiratory illness (%)</u></th> <th><u>All Others (%)</u></th> </tr> </thead> <tbody> <tr> <td>81</td> <td>82</td> <td>74</td> </tr> <tr> <td>57</td> <td>60</td> <td>43</td> </tr> <tr> <td>54</td> <td>48</td> <td>30</td> </tr> <tr> <td>36</td> <td>37</td> <td>21</td> </tr> <tr> <td>23</td> <td>19</td> <td>13</td> </tr> <tr> <td>23</td> <td>17</td> <td>12</td> </tr> </tbody> </table> <p>Former smokers</p> <table border="1"> <thead> <tr> <th><u>Atopic (%)</u></th> <th><u>Respiratory illness (%)</u></th> <th><u>All Others (%)</u></th> </tr> </thead> <tbody> <tr> <td>68</td> <td>77</td> <td>65</td> </tr> <tr> <td>48</td> <td>39</td> <td>35</td> </tr> <tr> <td>38</td> <td>40</td> <td>21</td> </tr> <tr> <td>32</td> <td>25</td> <td>17</td> </tr> <tr> <td>24</td> <td>14</td> <td>12</td> </tr> <tr> <td>14</td> <td>17</td> <td>10</td> </tr> </tbody> </table>	<u>Atopic (%)</u>	<u>Respiratory illness (%)</u>	<u>All Others (%)</u>	81	82	74	57	60	43	54	48	30	36	37	21	23	19	13	23	17	12	<u>Atopic (%)</u>	<u>Respiratory illness (%)</u>	<u>All Others (%)</u>	68	77	65	48	39	35	38	40	21	32	25	17	24	14	12	14	17	10	None
<u>Atopic (%)</u>	<u>Respiratory illness (%)</u>	<u>All Others (%)</u>																																													
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48	39	35																																													
38	40	21																																													
32	25	17																																													
24	14	12																																													
14	17	10																																													
Norback and Edling 1991	466 persons from the general population Aged 20–65 years Sweden	1989	<u>Symptom</u> Eye irritation or swollen eyelids  Nasal catarrh, blocked-up nose, dry/sore throat, irritative cough	<u>Adjusted OR (95% CI)</u> 1.3 (0.8–2.2)  1.1 (0.7–1.8)	Secondhand smoke exposure at work																																										
White et al. 1991	40 persons exposed to secondhand smoke at work and 40 nonsmokers evaluated as part of a fitness profile Aged 38–65 years United States	1979–1985	<u>Symptom</u> Cough Phlegm Breathlessness Colds	<u>Secondhand smoke exposure at work (OR)</u> 7.0 8.3 11.8 22.7	None																																										

Table 9.3 Continued

Study	Population	Period of study	Findings		Comments
Pope and Xu 1993	973 lifetime nonsmoking women Aged 20–40 years China	1992	No coal heat		Adjusted for age, job title, and mill employment
			<u>Symptom</u>	<u>1 smoker in home</u> <u>≥2 smokers in home</u>	
			Chest illness	0.98 (0.50–1.94)    NR <sup>†</sup>	
			Cough	1.02 (0.60–1.75)    1.87 (0.71–4.88)	
			Phlegm	1.43 (0.85–2.40)    2.07 (0.85–5.01)	
			Dyspnea	1.17 (0.61–2.25)    1.46 (0.39–5.52)	
			Wheeze	0.93 (0.50–1.75)    1.00 (0.27–3.71)	
			Coal heat		
			<u>Symptom</u>	<u>1 smoker in home</u> <u>≥2 smokers in home</u>	
			Chest illness	1.57 (0.74–1.39)    3.79 (1.28–11.2)	
Cough	1.03 (0.97–1.10)    3.07 (1.23–7.65)				
Phlegm	1.89 (1.07–3.35)    3.64 (1.56–8.52)				
Dyspnea	1.88 (0.93–3.81)    3.55 (1.2–10.5)				
Wheeze	1.20 (0.60–2.41)    1.07 (0.29–4.00)				
Robbins et al. 1993	3,914 participants Aged ≥25 years at completion of baseline questionnaire United States	Baseline: 1977 Follow-up: 1987	Obstructive airway disease symptoms		None
			<u>Age of participant at exposure</u>	<u>OR (95% CI)</u>	
			Childhood only	1.09 (0.69–1.79)	
			Adulthood only	1.28 (0.90–1.79)	
			Childhood and adulthood	1.72 (1.31–2.23)	
Leuenberger et al. 1994	4,197 lifetime nonsmokers Aged 18–60 years Switzerland	NR	<u>Symptom</u>	<u>OR (95% CI)</u>	There was a positive dose-response relationship
			Wheeze apart from colds	1.94 (1.39–2.70)	
			Dyspnea on exertion	1.45 (1.20–1.76)	
			Bronchitis	1.59 (1.17–2.15)	
Ng and Tan 1994	2,868 participants Aged 20–74 years Singapore	1989	Unadjusted OR (95% CI)		None
			<u>Secondhand smoke exposure</u>	<u>Allergic rhinitis</u>	
			≥1 light smoker	0.96 (0.60–1.53)	
			≥1 heavy smoker	1.43 (0.94–2.18)	
Lam et al. 1995	2,558 lifetime nonsmoking women Hong Kong	1989	<u>Symptom</u>	<u>Adjusted OR (95% CI)</u>	Exposure to husband's smoking; adjusted for area of residence, education, type of housing, others smoking at home, use of fuel, and use of incense/ mosquito coil
			Sore throat	1.20 (0.89–1.64)	
			Cough, morning	1.72 (1.06–2.79)	
			Cough, evening	1.61 (0.97–2.68)	
			Phlegm, morning	1.43 (1.04–1.98)	
			Phlegm, day or night	1.67 (1.11–2.50)	
			Phlegm for 3 months	1.27 (0.82–1.95)	
			Any symptom	1.26 (0.99–1.59)	

**Table 9.3 Continued**

Study	Population	Period of study	Findings	Comments
Jaakkola et al. 1996	117 lifetime nonsmokers Aged 15–40 years Montreal, Canada	Baseline: 1980–1981 Follow-up: 1988–1989	Per 10 cigarettes of secondhand smoke exposure/day  <u>Symptom</u> Wheeze Dyspnea Cough Phlegm Any symptom	None  <u>OR (95% CI)</u> 1.15 (0.64–2.06) 2.37 (1.25–4.51) 1.55 (0.61–3.90) 0.69 (0.21–2.26) 1.48 (0.88–2.49)
Baker and Henderson 1999	1,954 randomly selected women who gave birth England	1991–1992	Wheeze <u>Secondhand smoke exposure</u> Partner smoked	None  <u>OR (95% CI)</u> 1.73 (1.05–2.85)
Zhang et al. 1999	4,108 adults China	1988	Women exposed to secondhand smoke by ≥1 household member  <u>Symptom</u> Cough Phlegm Wheeze	None  <u>OR (95% CI)</u> 1.18 (0.95–1.46) 0.96 (0.75–1.24) 0.62 (0.44–0.87)
Trinder et al. 2000	2,996 randomly selected patients from two general practices Aged ≥16 years England	NR	Reported severe respiratory symptoms  <u>Smoking status</u> Involuntary smokers Former smokers Current smokers	10 respiratory symptoms were reported during the previous month  <u>OR (95% CI)</u> 1.4 (1.0–1.8) 1.5 (1.2–1.8) 2.9 (2.3–3.6)

\*OR = Odds ratio.  
 †CI = Confidence interval.  
 ‡NR = Data were not reported.

Although dyspnea is nonspecific with many causes, studies have consistently associated it with secondhand smoke exposure (White et al. 1991; Pope and Xu 1993; Leuenberger et al. 1994; Jaakkola et al. 1996). Leuenberger and colleagues (1994) also found a dose-response relationship between secondhand smoke exposure and dyspnea.

In addition to specific respiratory symptoms, several investigators have examined the association between secondhand smoke exposure and the presence of any respiratory symptom (Robbins et al. 1993; Lam et al. 1995; Jaakkola et al. 1996), the severity of respiratory symptoms (Trinder et al. 2000), chest illness (Pope and Xu 1993), or colds (White et al. 1991). Although not statistically significant, the magnitudes of the associations between secondhand smoke exposure and having any respiratory symptom have been

similar and the relative risk (RR) estimates are above one (Lam et al. 1995; Jaakkola et al. 1996). Among 2,996 randomly selected patients from general practices in England, Trinder and colleagues (2000) found an association between secondhand smoke exposure and reports of severe respiratory symptoms (OR = 1.4 [95 percent CI, 1.0–1.8]).

### Evidence Synthesis

Since the 1986 Surgeon General's report (USDHHS 1986), there have been numerous experimental and observational studies on the relationship between secondhand smoke exposure and acute and chronic respiratory symptoms, respectively. Overall, the experimental studies provide consistent evidence

for a link between secondhand smoke exposure and acute respiratory symptoms. Furthermore, these studies document that secondhand smoke exposure produced symptoms that meet the criterion of temporality and weigh against the possibility that secondhand smoke exposure leads to a heightened perception of already present symptoms. A limited number of investigations have also documented dose-response relationships. However, the experimental studies are limited by the small number of participants and by the use of volunteers.

Of the chronic respiratory symptoms, cough and dyspnea have been most consistently associated with secondhand smoke exposure in the observational studies. In contrast, this association has been less consistently observed for phlegm and wheeze. Partly because exposures and symptoms often are misclassified in observational studies, the magnitude of the association with chronic respiratory symptoms probably has been underestimated, with weak ORs generally less than 2.0. Little information is available on the temporal or dose-response relationships between chronic symptoms and secondhand smoke exposure.

## Conclusions

1. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and acute respiratory symptoms including cough, wheeze, chest tightness, and difficulty breathing among persons with asthma.

2. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and acute respiratory symptoms including cough, wheeze, chest tightness, and difficulty breathing among healthy persons.
3. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and chronic respiratory symptoms.

## Implications

These new conclusions strengthen prior statements with regard to respiratory symptoms and secondhand smoke exposure. Because respiratory symptoms are common and may adversely affect functional status, quality of life, and the use of health care resources, the relationship between respiratory symptoms and secondhand smoke exposure has substantial relevance to clinical care, to public health, and to the general comfort of nonsmokers. Eliminating or reducing secondhand smoke exposure will likely decrease the occurrence of acute respiratory symptoms. However, further research on the relationship between secondhand smoke exposure and chronic respiratory symptoms needs to overcome the methodologic limitations of the available observational studies. To overcome these limitations, future studies should be population-based, longitudinal, restricted to lifetime nonsmokers, and should have sufficient power to comprehensively address confounding factors.

## Lung Function

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Studies of volunteers exposed experimentally to secondhand smoke have examined short-term effects on lung function. Observational studies of real-world exposures have addressed the long-term effects. Acute effects of secondhand smoke exposure on lung function have been examined primarily in patients with mild asthma (see “Biologic Basis” earlier in this chapter). As stated previously, the Cal/EPA report reviewed results from 10 experimental studies of persons with asthma and concluded that despite constraints in interpreting the results of the chamber studies, “they do suggest that there is likely to

be a subpopulation of asthmatics who are especially susceptible to ETS exposure” (NCI 1999, p. 203). Nowak and colleagues (1997b) subsequently provided further support for this conclusion by finding greater average declines in FEV<sub>1</sub> levels compared with baseline FEV<sub>1</sub> levels after a secondhand smoke versus a sham exposure. Nowak and colleagues (1997a) found no changes in FEV<sub>1</sub> levels, but the small number of participants severely limited the statistical power. Bascom and colleagues (1991) recruited 77 healthy nonsmoking adults and exposed 21 to sidestream smoke for 15 minutes at a CO concentration of 45 ppm. In the

11 participants not sensitive to secondhand smoke, spirometric test results before and after exposure were unchanged; small, but statistically significant, effects were found in the 10 participants sensitive to secondhand smoke.

In the only study of the dose-response relationship between secondhand smoke exposure and lung function, Danuser and colleagues (1993) exposed 10 persons with hyperreactive airways and 10 healthy persons matched for age and gender to five increasing levels of secondhand smoke at 2, 4, 8, 16, and 32 ppm of CO for two minutes each. Among participants with hyperreactive airways, the FEV<sub>1</sub> fell an average of 6.5 percent after a 2 ppm exposure of CO, and fell further with higher levels of exposure (-5.6 percent at 4 ppm of CO, -7.1 percent at 8 ppm, -8.2 percent at 16 ppm, and -8.7 percent at 32 ppm). The FEV<sub>1</sub> level did not drop among the healthy participants at any level of exposure.

Chronic effects of secondhand smoke exposure on lung function have been examined primarily in cross-sectional studies (Trédaniel et al. 1994; Coultas 1998; Carey et al. 1999; Chen et al. 2001) and in a few cohort studies (Jaakkola et al. 1995; Abbey et al. 1998; Carey et al. 1999). Carey and colleagues (1999) published a meta-analysis of 15 cross-sectional studies and found a 1.7 percent mean deficit (95 percent CI, -2.8 to -0.6) in the FEV<sub>1</sub> level associated with secondhand smoke exposure. In addition, they conducted a cross-sectional investigation of secondhand smoke exposure, classified by salivary cotinine and FEV<sub>1</sub> levels, among 1,623 British adults aged 18 through 73 years (Carey et al. 1999). Comparing the top with the bottom quintiles of cotinine levels among lifetime nonsmokers, the researchers observed small decrements in FEV<sub>1</sub> levels that were larger in men than in women, -90 milliliters (mL) (95 percent CI, -276–96) and -61 mL (95 percent CI, -154–32), respectively. Chen and colleagues (2001) examined the effects of secondhand smoke exposure among 301 Scottish lifetime nonsmokers and found an inverse dose-response relationship between self-reported levels of secondhand smoke exposure at work (“none, little, some, a lot”) and FEV<sub>1</sub> levels. Compared with persons who were unexposed at work, “a lot” (Chen et al. 2001, p. 564 [the term was not defined by the authors]) of secondhand smoke exposure was significantly associated with a lower FEV<sub>1</sub> (-254 mL [95 percent CI, -420 to -84]).

Only three cohort studies have assessed secondhand smoke exposure and lung function (Jaakkola et al. 1995; Abbey et al. 1998; Carey et al. 1999). In 1980, Canadian researchers enrolled 117 lifetime nonsmokers from Montreal aged 15 through 40 years

and followed them through 1989 (Jaakkola et al. 1995). The investigators assessed cumulative exposures at enrollment, exposures at follow-up, and exposures at home and at work during the three days before completing the questionnaire. During the eight years of follow-up, the researchers did not find a significant association between secondhand smoke exposure and the rates of decline of FEV<sub>1</sub> and forced expiratory flow between 25 and 75 percent of the forced vital capacity (FVC). Researchers also did not find significant associations for cumulative secondhand smoke exposures up to the start of the study.

In a study of the effects of ambient air pollution on lung function, Abbey and colleagues (1998) followed 1,391 lifetime nonsmokers and former smokers from California for 16 years who were 25 years of age and older at enrollment in 1977. Secondhand smoke exposure was assessed from self-reports of the number of years the participants had lived or worked with a smoker. Among women, a small but nonsignificant decline in the ratio of FEV<sub>1</sub> to FVC (-0.2 percent [95 percent CI, -0.5–0.1]) was associated with living with a smoker for 10 years through 1993. A similar decline was observed for men who had worked with a smoker for 10 years through 1993 (-0.5 percent [95 percent CI, -1.2–0.1]). Moreover, although quantitative data were not reported, the authors stated that concomitant secondhand smoke exposures ( $\geq 1$  hour per day for at least one year at work or at home in 1987, 1992, or 1993) resulted in stronger effects of particulate pollution on lung function in men but not in women.

In a population-based sample from Britain in 1984 and 1985, Carey and colleagues (1999) enrolled 1,623 lifetime nonsmokers and former smokers aged 18 through 73 years and followed them for 7 years. Living with a smoker at enrollment and at follow-up was not associated with an accelerated FEV<sub>1</sub> decline (25 mL [95 percent CI, -20–70]).

## Evidence Synthesis

The effects of acute and chronic secondhand smoke exposure on lung function have been examined in experimental and observational studies, respectively. In experimental studies, some persons with asthma consistently had a small decline in the FEV<sub>1</sub> following secondhand smoke exposure. Small decrements in lung function are coherent with the far greater impairment of lung function observed with active smoking (USDHHS 2004). However, evidence for the dose-response relationship between secondhand smoke exposure and the FEV<sub>1</sub> decline is

limited. In the only relevant study, a dose-response relationship was not found (Danuser et al. 1993). The available evidence from experimental studies on the relationship between acute exposure to secondhand smoke and a decline in the FEV<sub>1</sub> suggests that the subgroup of persons with asthma is at risk from secondhand smoke.

The cross-sectional studies documented an association between chronic secondhand smoke exposure and a small decrement in lung function (Carey et al. 1999). However, these findings provide limited support for a causal relationship because the temporality between exposure and lung function decrement cannot be established with this study design, and most of these studies lack information on dose-response relationships. Although the small effect in these observational studies is coherent with larger decrements in lung function level associated with active smoking (USDHHS 2004), the small overall effect may actually reflect a larger decrement in a susceptible subpopulation. However, this hypothesis has received limited attention (Chen et al. 2001). The lack of an effect of secondhand smoke exposure on lung function decline in a small number of longitudinal studies further suggests that chronic secondhand smoke exposure may have little or no effect on lung function in the general population, but the effect in possibly susceptible subgroups has not been examined.

## Conclusions

1. The evidence is suggestive but not sufficient to infer a causal relationship between short-term secondhand smoke exposure and an acute decline in lung function in persons with asthma.

2. The evidence is inadequate to infer the presence or absence of a causal relationship between short-term secondhand smoke exposure and an acute decline in lung function in healthy persons.
3. The evidence is suggestive but not sufficient to infer a causal relationship between chronic secondhand smoke exposure and a small decrement in lung function in the general population.
4. The evidence is inadequate to infer the presence or absence of a causal relationship between chronic secondhand smoke exposure and an accelerated decline in lung function.

## Implications

Although acute secondhand smoke exposure is associated with small decrements in lung function among persons with asthma, the magnitude of the effect is, on average, small. Moreover, the characteristics of a one-time exposure in the experimental studies do not reflect a real-life exposure repeated over months and years. Future experimental studies of the effects of secondhand smoke exposure need to create better simulations of real-world situations, but these studies cannot address chronic effects on lung function, functional status, quality of life, and health care utilization.

Experimental and observational studies document small decrements in lung function. These findings provide a rationale for conducting observational studies to examine the larger effects of secondhand smoke exposure on lung function in potentially susceptible subgroups, such as persons with asthma (see "Respiratory Diseases" in the next section).

## Respiratory Diseases

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### Asthma

Asthma is a heterogenous and complex disorder characterized by chronic airway inflammation and reversible airflow obstruction (National Heart, Lung, and Blood Institute 1997; Floreani and Rennard 1999). Since the 1992 U.S. EPA risk assessment report (USEPA 1992), a number of published studies have

examined the role of involuntary smoking in causing asthma (etiologic) and in exacerbating asthma (morbidity) among adults. These studies have been reviewed for this report (Coultais 1998; NCI 1999; Weiss et al. 1999). The aim of the etiologic studies has been to determine the association between involuntary smoking and the new diagnosis of asthma among adults. However, because asthma often begins during

infancy or childhood (Chapter 6, Respiratory Effects in Children from Exposure to Secondhand Smoke), it may be difficult to truly establish adult-onset asthma and distinguish it from a failure to recall the onset of childhood asthma (see the next section). In contrast to studies of causation, morbidity studies have examined the role of involuntary smoking in causing symptoms, worsening lung function, causing or increasing the use of medication, increasing health care utilization, and worsening the quality of life in persons with asthma.

### Etiologic Studies

Asthma is diagnosed by six years of age in approximately 80 percent of the cases (Yunginger et al. 1992), and available data suggest that by early adulthood, 30 to 50 percent of persons with childhood asthma become asymptomatic (Barbee and Murphy 1998). In etiologic investigations of adult-onset asthma, it may thus be difficult to differentiate adult-onset asthma from childhood asthma that is recurrent in adulthood because of exposure to secondhand smoke or to another environmental agent (Weiss et al. 1999). Investigation of the relationship between secondhand smoke exposure and adult-onset asthma may be further complicated by the "healthy smoker effect" (Weiss et al. 1999, p. 891), that is, the self-selection of persons with better respiratory health to be active smokers compared with those who remain nonsmokers. This effect might explain the avoidance of exposure to secondhand smoke by some persons susceptible to the development of asthma. The resulting bias would tend to underestimate the association between secondhand smoke exposure and adult-onset asthma.

Greer and colleagues (1993) examined the association between workplace exposure to secondhand smoke and a new onset of asthma among a non-smoking population of 3,577 Seventh-Day Adventists from southern California followed between 1977 and 1987. The mean age at enrollment was 56.5 years. During the 10-year follow-up period 78 participants developed asthma, and workplace exposure to secondhand smoke was a significant risk factor (RR = 1.5 [95 percent CI, 1.2–1.8]) after controlling for gender, education, a history of obstructive airway disease before 16 years of age, and ambient ozone levels.

In a cross-sectional study of 4,197 lifetime nonsmoking Swiss adults 18 through 60 years of age, Leuenberger and colleagues (1994) found that self-reports of physician-diagnosed asthma were

associated with involuntary smoking (OR = 1.39 [95 percent CI, 1.04–1.86]), defined as any secondhand smoke exposure in the past 12 months. They also found a dose-response relationship between the total number of hours of secondhand smoke exposure per day and a risk of physician-diagnosed asthma.

Flodin and colleagues (1995) conducted a population-based, case-control study in Sweden that included 79 persons with adult-onset asthma, defined as the onset of symptoms consistent with asthma after 20 years of age and bronchial reactivity measured by methacholine challenge or bronchodilator responsiveness. Secondhand smoke exposure at work was associated with an increase in the risk of asthma (OR = 1.5 [95 percent CI, 0.8–2.5]) similar in magnitude to the findings of Greer and colleagues (1993) and Leuenberger and colleagues (1994).

Because active cigarette smoking has been associated with an increased risk of developing occupational asthma attributable to IgE-inducing agents (Venables and Chan-Yeung 1997), and secondhand smoke exposure has been associated with higher IgE levels (Oryszczyn et al. 2000), it is plausible to hypothesize that involuntary smoking may also contribute to the development of occupational asthma in nonsmokers. Although workplace exposures to secondhand smoke have been associated with asthma among adults (Greer et al. 1993; Flodin et al. 1995), no investigations have reported on the interaction of secondhand smoke exposure at the workplace with specific occupational agents.

In 1993, Hu and colleagues (1997) surveyed 1,469 young adults aged 20 through 22 years from Los Angeles and San Diego (California) to determine the prevalence of asthma in this population. Parental reports obtained in 1986 as part of a school-based smoking prevention program were used to determine exposures to secondhand smoke. Maternal and paternal smoking were associated with the young adults ever having had physician-diagnosed asthma (OR = 1.6 [95 percent CI, 1.1–2.3] and 1.3 [95 percent CI, 0.9–1.8], respectively). Similar results were found for current asthma with maternal smoking (OR = 1.6 [95 percent CI, 1.0–2.1]). Hu and colleagues (1997) also found a dose-response relationship with the amount smoked and the number of parents who smoked. The highest risk of having a physician-diagnosed asthma (OR = 2.9 [95 percent CI, 1.6–5.6]) and current asthma (OR = 3.3 [95 percent CI, 1.7–6.4]) was associated with smoking by both parents compared with smoking by neither parent.

## Morbidity Studies

Trédaniel and colleagues (1994) summarized results of the effects of secondhand smoke exposure on respiratory symptoms and lung function from four observational studies of patients with respiratory allergies and from five experimental studies of patients with asthma. The authors concluded that “Conflicting evidence exists on the association in asthmatic patients between ETS exposure and appearance of symptoms and functional abnormalities (including change in bronchial responsiveness)” (p. 181). Weiss and colleagues (1999) reached similar conclusions in their review of 2 observational studies and 12 experimental studies of secondhand smoke exposure and an exacerbation of asthma.

## Experimental Studies

Results of 10 chamber studies of secondhand smoke exposure in persons with asthma were extensively reviewed in the Cal/EPA report (NCI 1999) and summarized earlier in this chapter (see “Biologic Basis” and “Lung Function”). Methodologic limitations of experimental studies examining the relationship between secondhand smoke exposure and asthma morbidity reflect the inability to replicate real-life exposure conditions and the failure of health outcome measures (e.g., symptoms or lung function) to adequately assess asthma morbidity. Consequently, observational studies provide the best evidence for assessing asthma morbidity associated with secondhand smoke exposure.

## Observational Studies

Study designs that have been used to examine secondhand smoke exposure and asthma morbidity include population-based, cross-sectional surveys (Mannino et al. 1997); clinic-based, cross-sectional studies (Jindal et al. 1999); case-control studies (Tarlo et al. 2000); and prospective cohort studies (Jindal et al. 1994; Ostro et al. 1994; Sippel et al. 1999). In a nationally representative sample of 43,732 U.S. adults who participated in the 1991 National Health Interview Survey (NHIS), Mannino and colleagues (1997) examined the relationship between any self-reported secondhand smoke exposure during the previous two weeks and the exacerbation of any chronic respiratory disease (asthma, chronic bronchitis, emphysema, and chronic sinusitis) in the two weeks before the survey. In a multiple logistic regression model that adjusted for age, gender, race, socioeconomic status (SES), living alone, season, and region of the country, exposure

to secondhand smoke was significantly associated with the exacerbation of any chronic respiratory condition among lifetime nonsmokers (OR = 1.44 [95 percent CI, 1.07–1.95]).

Jindal and colleagues (1999) measured bronchial hyperresponsiveness and bronchodilator use in a sample of 50 women with asthma aged 20 through 40 years followed at a chest clinic in India. Exposure to secondhand smoke was assessed with questions on smoking by the husband, by other family members, and by coworkers. Compared with no exposure, secondhand smoke exposure was associated with significantly greater bronchial hyperreactivity and with continuous bronchodilator use (39 percent of exposed women and 26 percent of unexposed women [ $p < 0.05$ ]).

Tarlo and colleagues (2000) conducted a case-control study of 36 patients with an asthma exacerbation within 24 hours of completing the study questionnaire, and 36 persons similar in age with asthma but without an exacerbation. Of the 36 patients with an exacerbation, 21 were adolescents or adults (aged 13 through 55 years) and 15 were children (aged 7 through 12 years). The study documented that exposures to secondhand smoke during the previous year were reported more frequently by cases (39 percent) than by controls (17 percent) ( $p < 0.03$ ).

To assess the clinical consequences of secondhand smoke exposure on patients with asthma, Jindal and colleagues (1994) enrolled 200 lifetime nonsmoking patients with asthma aged 15 through 50 years from a chest outpatient clinic in India, and then followed them for one year. Patients were categorized by whether or not they had been exposed to secondhand smoke. Exposed patients had more acute episodes of asthma, emergency department visits, absences from work, parenteral bronchodilator use, and steroid use. In addition, exposed patients had a greater impairment of lung function ( $FEV_1/FVC = 68.7$  percent) than unexposed patients ( $FEV_1/FVC = 78.4$  percent).

Ostro and colleagues (1994) studied 164 persons with asthma with a mean age of 45.5 years from a clinic in Denver, Colorado. For up to three months, they recorded daily information about symptoms, medication use, physician and emergency room visits, and indoor exposures to secondhand smoke. Using a statistical approach appropriate for these daily data, the researchers estimated risks for symptoms resulting from exposure to secondhand smoke: moderate or worse shortness of breath (OR = 1.35 [95 percent CI, 0.84–2.15]), moderate or worse cough (OR = 1.15 [95 percent CI, 0.97–1.36]), and restricted activity (OR = 1.61 [95 percent CI, 1.06–2.46]).

Sippel and colleagues (1999) enrolled 619 patients with asthma aged 15 through 55 years who were members of a large health maintenance organization. Health outcome data were collected during a 30-month period. Compared with patients without secondhand smoke exposure, exposed persons with asthma had a greater utilization of hospital services (i.e., urgent care, emergency room, and hospitalization) (OR = 2.34 [95 percent CI, 1.80–3.05]). In addition, persons with asthma who were exposed to secondhand smoke had lower quality of life scores compared with unexposed patients.

### Evidence Synthesis

Earlier reviews of secondhand smoke exposure and the etiology of adult-onset asthma found the evidence for causality to be inconclusive because of methodologic limitations and the small number of studies (Trédaniel et al. 1994; Coultas 1998; Weiss et al. 1999). Although only a few new studies have been published since these reviews, there is a consistent (albeit weak) association between secondhand smoke exposures at home or in the workplace and a 40 to 60 percent increase in the risk of asthma in exposed adults compared with unexposed adults. Moreover, cross-sectional and longitudinal studies have consistently found this association, and results from longitudinal studies provide support for the temporality criterion of causality. One study documented a dose-response relationship between the number of parents smoking in the home and the risk of asthma among young adults. Because a causal link between active smoking and adult-onset asthma has not been established (USDHHS 2004), the coherence criterion for secondhand smoke currently cannot be fulfilled. However, because the pathogenesis of asthma is complex and coherence between active smoking and secondhand smoke exposure may be too restrictive, researchers should not expect a full parallel between the effects of active and involuntary smoking in asthma.

Both experimental and observational study designs have examined secondhand smoke exposure and asthma morbidity. The small particles and irritant gases in secondhand smoke would be anticipated to adversely affect the hyperresponsive airways of persons with asthma and contribute to lung inflammation, as postulated for air pollution generally (Bascom et al. 1995, 1996). Inconsistent results from experimental studies may be explained in part by a number of methodologic differences and limitations (Weiss et al. 1999). However, these studies provide “evidence that individual asthmatics and groups of asthmatics do

respond to levels of ETS that do not elicit responses in healthy volunteers” (Weiss et al. 1999, p. 894). Several published observational studies of secondhand smoke exposure and asthma morbidity were not included in earlier reviews (Trédaniel et al. 1994; Coultas 1998; Weiss et al. 1999). Taken together, these observational studies provide evidence that exposure to secondhand smoke worsens asthma in adults, findings that are consistent with the effects of active smoking (USDHHS 2004).

### Conclusions

1. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and adult-onset asthma.
2. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and a worsening of asthma control.

### Implications

There is a need for additional research on the etiologic relationship between secondhand smoke exposure and adult-onset asthma. Although the available evidence for asthma morbidity suggests that the elimination of secondhand smoke exposure would improve asthma control in adults, no clinical trials have addressed this issue. Despite the evidence on secondhand smoke exposure and poor asthma control, a substantial proportion (43 percent) of persons with asthma presenting for emergency care were exposed to secondhand smoke at home (Dales et al. 1992), suggesting a need for greater awareness among patients and physicians of this relationship.

## Chronic Obstructive Pulmonary Disease

COPD is a nonspecific term, defined differently by clinicians, pathologists, and epidemiologists, each using different criteria based on symptoms, physiologic impairment, and pathologic abnormalities (Samet 1989). The hallmark of COPD is the slowing of expiratory airflow measured by spirometric testing, with a persistently low FEV<sub>1</sub> and a low ratio of FEV<sub>1</sub> to FVC despite treatment. Although chronic bronchitis and emphysema are classically associated with the term COPD, they do not invariably involve chronic airways obstruction. Recent evidence suggests that changes in the structure and function of the bronchioles may be fundamental to the development of

smoking-induced COPD (Wright 1992; Thurlbeck 1994). Active cigarette smoking is the single most important risk factor for COPD (USDHHS 2004), with 85 to 90 percent of COPD-related mortality attributable to active cigarette smoking (Thun et al. 1997a,b). However, other risk factors such as second-hand smoke, occupational exposures, and genetic factors may also contribute to COPD.

Using survey data from three national health and nutrition examination surveys, Whittemore and colleagues (1995) determined the prevalence of COPD (self-reports of physician-diagnosed chronic bronchitis or emphysema) among 12,980 lifetime nonsmokers aged 18 through 74 years. Overall, 3.7 percent of men and 5.1 percent of women reported physician-diagnosed COPD, and the prevalence increased with age and with a low SES. Although this study was limited to self-reports of COPD and lacked information on secondhand smoke exposure, these results provide evidence that COPD occurs among nonsmokers, and that risk factors other than active cigarette smoking (such as secondhand smoke exposure) may contribute to the development of COPD in nonsmoking adults.

Results from the Third National Health and Nutrition Examination Survey provide further evidence that COPD occurs in nonsmokers (Coultais et al. 2001). Among 5,743 persons aged 45 years and older, 3.1 percent reported having physician-diagnosed COPD; of these, 1.6 percent of the men and 12.2 percent of the women were lifetime nonsmokers. Furthermore, 12 percent of the entire sample had spirometric evidence of airflow obstruction that was undiagnosed; 10.5 percent of the men and 27.5 percent of the women with undiagnosed airflow obstruction were lifetime nonsmokers. The factors contributing to airflow obstruction in nonsmokers are uncertain, and secondhand smoke exposure may have a role.

The presence of COPD can be measured in numerous ways, including self-reported measures (e.g., symptoms and physician diagnoses), physician diagnoses (e.g., hospitalizations and mortality), and spirometric criteria. All of these measures have been used to investigate the relationship between secondhand smoke exposure and the etiology of COPD. The discussion that follows summarizes the results from each type of investigation.

### **Etiologic Studies**

Published investigations examining the etiologic role of secondhand smoke exposure in COPD use different definitions of COPD, including self-reports

(Robbins et al. 1993; Dayal et al. 1994; Leuenberger et al. 1994; Piitulainen et al. 1998; Forastiere et al. 2000), hospitalizations for COPD (Lee et al. 1986; Kalandidi et al. 1987), COPD mortality (Hirayama 1981; Sandler et al. 1989), and lung function (Dennis et al. 1996; Berglund et al. 1999). Most of the studies that used self-reports relied on recalled physician diagnoses, and all but one (Forastiere et al. 2000) combined asthma, chronic bronchitis, and emphysema to define COPD.

In a cohort study conducted from 1977 to 1987 of 3,914 adults aged 25 years and older, Robbins and colleagues (1993) used self-reported symptoms and physician diagnoses (asthma, chronic bronchitis, and emphysema) to define airway obstructive disease (AOD). They found that secondhand smoke exposures at home and at work during both childhood and adulthood were significantly associated with AOD (RR = 1.7 [95 percent CI, 1.3–2.2]).

Leuenberger and colleagues (1994) conducted a cross-sectional survey of 4,197 Swiss adults 18 through 60 years of age. The investigators examined the relationship of respiratory symptoms and diseases to self-reports of secondhand smoke exposure at home and at work during the previous 12 months. Reports of chronic bronchitis were significantly associated with secondhand smoke exposure (OR = 1.7 [95 percent CI, 1.3–2.2]).

In a population-based study of air pollution, Dayal and colleagues (1994) used a case-control design to examine the association between secondhand smoke exposure and obstructive respiratory disease. A total of 219 lifetime nonsmokers reported a history of physician-diagnosed asthma, chronic bronchitis, or emphysema, and were matched by age, gender, and neighborhood to 657 persons without these diagnoses. Although exposure to less than one pack of cigarettes per day was not significantly associated with obstructive respiratory disease (OR = 1.2 [95 percent CI, 0.8–1.7]), exposure to one or more packs per day was significantly associated with obstructive respiratory disease (OR = 1.9 [95 percent CI, 1.2–2.9]).

Forastiere and colleagues (2000) conducted a cross-sectional survey of 1,938 nonsmoking women from four areas in Italy. Out of 1,212 women who reported that they had ever been married to a smoker, 711 were still exposed to the husband's smoking. After adjusting for age, area, and education, the husband's smoking was not significantly associated with self-reported COPD (OR = 1.75 [95 percent CI, 0.88–3.47]).

In contrast to the general population studies, Piitulainen and colleagues (1998) examined the effects of secondhand smoke exposure in a group

susceptible to developing emphysema: 205 non-smokers with a severe alpha-1-antitrypsin deficiency. The researchers found that exposures of 10 or more years to secondhand smoke, compared with no exposure, were significantly associated with chronic bronchitis (OR = 1.6 [95 percent CI, 1.3–2.4]), defined as a daily cough with phlegm at least three months per year.

There have been two case-control studies of hospital admissions for COPD and secondhand smoke exposure (Lee et al. 1986; Kalandidi et al. 1987). In a hospital-based, case-control study of 10 hospital regions in England conducted from 1977 to 1982, Lee and colleagues (1986) found a small increase (OR = 1.3 [95 percent CI was not provided]) in risk for chronic bronchitis with the highest category of secondhand smoke exposure, but this estimate was based on only two cases. Kalandidi and colleagues (1987) studied 103 ever-married women aged 40 through 79 years who, on two separate occasions—first, during routine history-taking, and again categorically at the study interview—denied ever smoking and who were admitted to an Athens, Greece, hospital with a diagnosis of chronic obstructive lung disease. The control group comprised 179 ever-married non-smoking women who were visiting the hospital. Compared with women whose husbands had never smoked, women whose husbands smoked one pack per day or less had an increased risk of COPD (OR = 2.6 [90 percent CI, 1.3–5.0]); those whose husbands smoked more than one pack per day had an OR of 1.5 (90 percent CI, 0.8–2.7).

Two cohort studies examined the association between COPD mortality and involuntary smoking (Hirayama 1981; Sandler et al. 1989). In a population-based cohort of 91,540 nonsmoking Japanese housewives aged 40 years and older, Hirayama (1981) determined that from 1966 to 1979, there were 66 deaths from emphysema and asthma. Compared with women married to nonsmokers, women whose husbands were former smokers or smokers of 19 cigarettes or fewer per day had a 29 percent increased risk of death from emphysema or asthma, and women whose husbands smoked 20 or more cigarettes per day had a 49 percent increased risk. The gradient of risk from smoking by the husbands was not statistically significant. Because the number of deaths was small, these results were not statistically significant. Another study (Sandler et al. 1989) determined the causes of death for White residents of Washington county, Maryland (United States), who had died between 1963 and 1975. The researchers examined associations with secondhand smoke exposure

among 10,799 residents who had reported in 1963 that they were lifetime nonsmokers with household smoking exposures. There was an increased risk of death from emphysema and bronchitis in women (RR = 5.7 [95 percent CI, 1.2–26.8], n = 13) but not in men (RR = 0.9 [95 percent CI, 0.2–5.3], n = 6).

Some studies on involuntary smoking and COPD examined the relationship between lung function level and involuntary smoking (Trédaniel et al. 1994; Kerstjens et al. 1997). Results of several cohort studies published since 1994 (and reviewed in the section on “Lung Function” earlier in this chapter) suggest that secondhand smoke exposure does not increase the average rate of lung function decline (Jaakkola et al. 1995; Abbey et al. 1998; Carey et al. 1999). Although longitudinal data on the effects of active or involuntary smoking and the development of COPD are not available from childhood through adulthood, evidence suggests that the development of COPD in adults may result from impaired lung development and growth and a premature onset of and/or an accelerated decline in lung function (Fletcher et al. 1976; Samet and Lange 1996; Kerstjens et al. 1997). In utero airway development and alveolar proliferation until 12 years of age are critical to the mechanical functioning of the lungs, and impaired lung growth in utero from an exposure to maternal smoking may begin a process that leads to the development of COPD. Exposure to secondhand smoke in infancy and childhood and active smoking during childhood and adolescence contribute to impaired lung growth, which in turn limits the maximum level of lung function attained (Kerstjens et al. 1997; USDHHS 2004) and may increase the risk for developing COPD. The impact of involuntary smoking during adulthood on lung function and the risk for developing COPD remain controversial (Trédaniel et al. 1994). However, because studies have established that active cigarette smoking in adulthood leads to an accelerated decline in the FEV<sub>1</sub> and ultimately to the development of clinically apparent COPD among susceptible smokers, involuntary smoking is considered a biologically plausible risk factor.

Trédaniel and colleagues (1994) reviewed the available evidence on exposure to secondhand smoke and adult non-neoplastic respiratory diseases, citing 18 publications on lung function and secondhand smoke exposure published between 1977 and 1992. Of these 18 publications, 8 found no effect of secondhand smoke exposure on lung function and 10 demonstrated small decrements in lung function. Noted limitations of the available studies include a lack of information on potential confounders and on

childhood exposures to secondhand smoke. Further, when detected, the magnitude of the decrement associated with secondhand smoke exposure was small (see the section on “Lung Function” earlier in this chapter), raising questions about the clinical relevance to COPD. This conclusion is further strengthened by the results from Piitulainen and colleagues (1998), who found no effect of secondhand smoke exposure on lung function level among 205 participants with a severe alpha-1-antitrypsin deficiency.

Spirometry is the main physiologic measure of airway obstruction and was used as a measure of COPD in some investigations (Dennis et al. 1996; Berglund et al. 1999). To investigate selected indoor air pollutants and their association with AOD, Dennis and colleagues (1996) conducted a case-control study of 104 women with airways obstruction (mean age 63 years) and 104 controls from three hospitals in Bogota, Colombia. Airways obstruction was defined as a  $FEV_1/FVC$  of less than 70 percent and a  $FEV_1$  of less than 70 percent of predicted value. In a multiple logistic regression model that adjusted for smoking and wood and gasoline use, exposure to smoking by the husband was significantly associated with airway obstruction (OR = 2.04 [95 percent CI, 1.1–3.9]).

In a cohort study, Berglund and colleagues (1999) conducted spirometry on 1,391 adult lifetime nonsmokers and former smokers from California who were younger than 80 years of age. Obstructive impairment was defined as a  $FEV_1$ /maximum vital capacity of less than 65 percent or a  $FEV_1$  of less than 75 percent of predicted value. Secondhand smoke exposure was based on self-reports and defined as at least one hour per day for at least one year. Ever having a secondhand smoke exposure was significantly associated with airways obstruction (RR = 1.44 [95 percent CI, 1.02–2.01]).

### Morbidity Studies

Compared with the numerous investigations of the health effects of secondhand smoke exposure in persons with asthma, there are only a few investigations of the health effects in persons with COPD. One study used a nationally representative sample of 43,732 U.S. adults who participated in the 1991 NHIS (Mannino et al. 1997). These researchers examined the relationship between secondhand smoke exposure and any chronic respiratory disease exacerbation (asthma, chronic bronchitis, emphysema, and chronic sinusitis) in the two weeks before the survey. In a multiple logistic regression model that adjusted for age, gender, race, SES, living alone, season, and region of the country, there was a significant association among

lifetime nonsmokers exposed to secondhand smoke with the exacerbation of any chronic respiratory condition (OR = 1.44 [95 percent CI, 1.07–1.95]).

### Evidence Synthesis

Investigations of COPD in nonsmokers are limited. Results from a nationwide, population-based survey in the United States suggest that 3 to 5 percent of nonsmokers may be affected (Whittemore et al. 1995). However, these results were based on self-reports of COPD and smoking status, and thus may be overestimates. In another U.S. survey, only 0.5 percent of nonsmokers reported a physician-diagnosed history of COPD, but 5.2 percent had undiagnosed airflow obstruction measured by spirometry (Coultas et al. 2001).

Using diverse methods to define COPD (including self-reported physician diagnoses, hospitalizations, mortality, and lung function diagnoses), a number of studies have consistently identified involuntary smoking as a risk factor for COPD among nonsmokers. Active smoking is a well-established cause of COPD, and there is a substantial understanding of the mechanisms by which tobacco smoke damages the lung to produce COPD. However, studies that have relied on self-reported diagnoses are limited by the inclusion of physician-diagnosed asthma in their definition of COPD. Furthermore, self-reports of smoking status may misclassify current and former smokers as lifetime nonsmokers, resulting in a biased association between secondhand smoke exposure and COPD. The magnitude of these reported associations has been consistent but the risk estimates are weak, ranging from 1.2 to about 2.0, which is a plausible range of association given the exposure levels. Few investigations have examined the dose-response relationship between secondhand smoke exposure and the risk of COPD. Evidence from a limited number of cohort studies documents that secondhand smoke exposure precedes the COPD diagnosis, thus meeting the temporality criterion.

Finally, little is known about the effects of secondhand smoke exposure on respiratory symptoms, lung function, health care utilization, or the quality of life of patients with COPD. An analysis of the 1991 NHIS data showed that among lifetime nonsmokers and current smokers, secondhand smoke exposure was associated with exacerbations of chronic respiratory diseases during the two weeks before their interview (Mannino et al. 1997). The analysis did not specifically separate COPD from the other chronic respiratory diseases that were considered.

This review indicates a surprisingly high prevalence of airflow obstruction among nonsmokers and associations of indicators of airflow obstruction with secondhand smoke exposure. These findings need a targeted follow-up with designs that incorporate state-of-the-art approaches for exposure assessment and longitudinal tracking of lung function.

### Conclusions

1. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and risk for chronic obstructive pulmonary disease.
2. The evidence is inadequate to infer the presence or absence of a causal relationship between secondhand smoke exposure and morbidity in

persons with chronic obstructive pulmonary disease.

### Implications

Although limited data suggest that COPD is not uncommon among nonsmokers, there is a need for epidemiologic studies that use objective measures of airflow obstruction to establish the prevalence of this condition in nonsmokers. Excluding persons with asthma and using methods to minimize diagnostic misclassification (e.g., questionnaires and spirometric measures) will strengthen future etiologic studies. Investigations need to explore the association between secondhand smoke exposure and health outcomes such as symptoms, functional status, quality of life, and health care utilization in patients with COPD.

## Conclusions

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### *Odor and Irritation*

1. The evidence is sufficient to infer a causal relationship between secondhand smoke exposure and odor annoyance.
2. The evidence is sufficient to infer a causal relationship between secondhand smoke exposure and nasal irritation.
3. The evidence is suggestive but not sufficient to conclude that persons with nasal allergies or a history of respiratory illnesses are more susceptible to developing nasal irritation from secondhand smoke exposure.

### *Respiratory Symptoms*

4. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and acute respiratory symptoms including cough, wheeze, chest tightness, and difficulty breathing among persons with asthma.
5. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand

smoke exposure and acute respiratory symptoms including cough, wheeze, chest tightness, and difficulty breathing among healthy persons.

6. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and chronic respiratory symptoms.

### *Lung Function*

7. The evidence is suggestive but not sufficient to infer a causal relationship between short-term secondhand smoke exposure and an acute decline in lung function in persons with asthma.
8. The evidence is inadequate to infer the presence or absence of a causal relationship between short-term secondhand smoke exposure and an acute decline in lung function in healthy persons.
9. The evidence is suggestive but not sufficient to infer a causal relationship between chronic secondhand smoke exposure and a small decrement in lung function in the general population.

10. The evidence is inadequate to infer the presence or absence of a causal relationship between chronic secondhand smoke exposure and an accelerated decline in lung function.

#### *Asthma*

11. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and adult-onset asthma.
12. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and a worsening of asthma control.

#### *Chronic Obstructive Pulmonary Disease*

13. The evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and risk for chronic obstructive pulmonary disease.
14. The evidence is inadequate to infer the presence or absence of a causal relationship between secondhand smoke exposure and morbidity in persons with chronic obstructive pulmonary disease.

## Overall Implications

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This review clearly points to the need for further research. The evidence for adverse respiratory effects in adults has identified a large number of health outcomes for which the data are suggestive of but not sufficient to infer a causal relationship attributable to secondhand smoke exposure. The evidence reviewed in Chapter 2 (Toxicology of Secondhand Smoke) indicates multiple mechanisms by which exposure to secondhand smoke causes injury to the respiratory

tract. In addition, researchers have established active smoking as a primary cause of many adverse respiratory effects in adults. However, the number of studies on secondhand smoke is limited, and there is a need for research that examines the types and magnitude of risk for adverse respiratory health effects caused by exposure to secondhand smoke.

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