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# THE TOXICOLOGY OF INHALED WOODSMOKE

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*In addition to developing nations relying almost exclusively upon biomass fuels, such as wood for cooking and home heating, North Americans, particularly in Canada and the northwestern and northeastern sections of the United States, have increasingly turned to woodburning as an alternate method for domestic heating because of increasing energy costs. As a result, the number of households using woodburning devices has increased dramatically. This has resulted in an increase in public exposure to indoor and outdoor woodsmoke-associated pollutants, which has prompted widespread concern about the adverse human health consequences that may be associated with prolonged woodsmoke exposure. This mini-review article brings together many of the human and animal studies performed over the last three decades in an attempt to better define the toxicological impact of inhaled woodsmoke on exposed children and adults; particular attention is given to effects upon the immune system. General information regarding occurrence and woodsmoke chemistry is provided so as to set the stage for a better understanding of the toxicological impact. It can be concluded from this review that exposure to woodsmoke, particularly for children, represents a potential health hazard. However, despite its widespread occurrence and apparent human health risks, relatively few studies have focused upon this particular area of research. More laboratory studies aimed at understanding the effects and underlying mechanisms of woodsmoke exposure, particularly on those individuals deemed to be at greatest risk, are badly needed, so that precise human health risks can be defined, appropriate regulatory standards can be set, and accurate decisions can be made concerning the use of current and new woodburning devices.*

## BACKGROUND AND OCCURRENCE

In developing nations, biomass fuels such as wood, animal dung, and crop residues are used extensively for home heating and cooking (International Institute for Population Science [IIPS], 1995; Smith, 2000). For example, three-quarters of all households in India use unprocessed biomass as their primary fuel for cooking, and among those homes, more than 90% use either wood or animal dung (IIPS, 1995). In countries such as India, daily air pollution exposures from cooking with biomass fuels typically exceed relevant health-based guidelines by at least 20-fold (Smith & Liu, 1994; Smith, 2000). It has been estimated that indoor air pollution in developing countries accounts for 2.2–2.5 million deaths annually (WHO, 1997). While biomass fuels are at the high end of the fuel ladder in terms of

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pollution emissions, they score low for combustion efficiency. Thus, effluents from these sources contain numerous toxic/carcinogenic components, such as formaldehyde and polyaromatic hydrocarbons (PAH), which at high exposure concentrations can cause serious health problems (Smith, 1987, 1993; Larson & Koenig, 1994; Nolte et al., 2001). Among the major respiratory illnesses, cooking smoke appears to increase the risk of chronic obstructive lung disease (Pandey, 1984; Malik, 1985; Perez-Padilla et al., 1996), lung cancer (Sobue, 1990; Franco, 1998), and respiratory infections (Pandey et al., 1989; Mishra & Retherferd, 1997; Kammen et al., 1998). In fact, a recent study in northern India noted an association between the use of wood and/or cow-dung cakes and an increased incidence of pulmonary tuberculosis in children (Gupta et al., 1997).

In addition to domestic woodburning in developing countries, over the past two decades, due to rising energy costs and the uncertain availability of petroleum and natural gas, homeowners in the United States and Canada have increasingly turned to the use of wood as an alternate heating fuel. Interestingly, most of the residential woodburning in the United States is done by people in the middle to upper-middle socioeconomic class. Increased usage of wood for home heating has been especially striking in the northeastern and northwestern United States (National Research Council, 1981). For example, the Washington State Department of Ecology estimated that during the 1980s wood was burned in 60% of all Washington households, with about 2.2 million cords consumed annually (Pierson et al., 1989). In Massachusetts, studies during this same time frame showed that 65% of all households surveyed used woodburning devices, and of those, 68% were in use all day (Tuthill, 1984). Between 1972 and 1989, sales of woodstoves increased 10-fold (by the late 1980s, the number of operating woodstoves was thought to exceed 11 million), and it is estimated that approximately 10% of the total space-heating input for the United States is from firewood (Lipfert & Dungan, 1983; Samet et al., 1987). While usage of wood for home heating and sales of woodburning devices declined after 1989, woodburning has resurged in the new millennium, again as a result of increasing energy costs.

In Canada, it is estimated that about 400,000 homes use wood as the primary heating fuel, and many others use fireplaces and woodstoves as supplementary sources of heat or for aesthetics. While the Atlantic provinces are more dependent upon wood for home heating than other locations, it is in British Columbia that smoke from residential woodburning poses the greatest threat to health (British Columbia Ministry of Environment, 1995). Here, inversions in weather patterns frequently warm the air on mountainsides, trapping cooler air and smoke at ground level in valleys and allowing the buildup of pollutants to high concentrations.

Increased usage of woodburning devices has resulted in greater public exposure to smoke-associated pollutants generated during combustion and an increased concern by local residents regarding the health effects associ-

ated with such exposure. Although legislative action mandating the reduction of residential woodsmoke levels is moving forward (Koenig et al., 1988), only a few states are currently affected by regulations (i.e., Colorado, Washington, Oregon), and legislation in other states will take several years to enact. Meanwhile, those most vulnerable to health impairment due to air pollutants, such as very young children, individuals with preexisting cardiopulmonary disease, asthmatics, and the elderly, will continue to be exposed both indoors and outdoors for prolonged periods of time to high concentrations of woodsmoke-generated pollutants (Koenig & Pierson, 1991).

## CHEMICAL CHARACTERIZATION AND POLLUTANT DISTRIBUTION

Woodsmoke is a complex mixture of numerous gases and respirable fine/ultrafine particles of varying inorganic/organic composition and diameter (Pierson et al., 1989; U.S. EPA, 1993; Nolte et al., 2001). Smoke generated from burning wood is thought to consist of over 200 chemicals and compound groups, which are contained in an effluent that is almost entirely in the inhalable size range (Cooper, 1980; U.S. EPA, 1993). Woodburning stoves, furnaces, and fireplaces emit significant quantities of toxic compounds, including respirable particulate matter (PM) with diameters <10 μm ($PM_{10}$), carbon monoxide (CO), nitrogen and sulfur oxides ($NO_X$ and $SO_X$), aldehydes, PAHs, volatile organic compounds (VOCs), chlorinated dioxins, and free radicals (Cooper, 1980; Dasch, 1982; Lao, 1983; Tuthill, 1984; Sexton et al., 1986; Traynor et al., 1987; Lachocki et al., 1989; Koenig & Pierson, 1991; Hildemann et al., 1991; Koenig et al., 1993; U.S. EPA, 1993; Larson & Koenig, 1994; Nolte et al., 2001).

Under normal usage conditions, woodburning devices create indoor pollution (Lao, 1983; Sexton et al., 1986; Traynor et al., 1987; Samet et al., 1987, 1988). It has been reported that both airtight and non-airtight stoves release fine/ultrafine-sized PM, CO, and PAHs directly within the indoor environment (Traynor et al., 1987). Concentrations of PM as great as 820 $\mu g/m^3$ (U.S. EPA standard for $PM_{10}$ is 150 $\mu g/m^3$ for a 24-h period, not to be exceeded >2% of the time) have been measured indoors from non-airtight stoves over a 24-h period (Traynor et al., 1987). In addition to that amount released directly inside the home, a large percentage (i.e., 70%) of outdoor woodsmoke from chimneys actually reenters the house and permeates neighboring dwellings (Pierson et al., 1989). Many circumstances, including improper installation, negative indoor air pressure, and downdrafts, facilitate entry of incomplete combustion products back into the home (Pierson et al., 1989; U.S. EPA, 1994). Since individuals typically spend 60–70% of their out-of-work time at home (Szalar, 1972; Chapin, 1974; Sexton et al., 1986), indoor woodsmoke potentially represents a major source for human exposure.

In addition to pollution created indoors, woodburning devices also contribute to outdoor air pollution (Butcher & Sorenson, 1979; Cooper, 1980;

Koenig et al., 1988, 1993; Koenig & Pierson, 1991). For example, aldehydes released into the ambient environment from woodburning have been measured at levels comparable to those emitted from power plants and automobiles (Lipari et al., 1984). Moreover, studies have demonstrated that, on a moderately cold winter day, 51% of the respirable air particulates in the Portland, OR, area were from residential wood combustion sources (Cooper, 1980). Investigations examining other parts of the northwest reported that residential woodsmoke in the Olympia, WA, area accounted for 50% (on clear days) to 85% (on polluted days) of airborne PM (Koenig et al., 1988). Additional studies in the same geographic area have demonstrated that 80–90% of the PM measured in the ambient air was due to use of woodburning devices during nighttime hours (Larson et al., 1992). Such studies have led to the conclusion that woodsmoke represents a more significant source of ambient PM, VOCs, and CO, than the sum total of all industrial point sources in the state of Washington (Koenig et al., 1988).

While most residential woodburning is currently associated with woodstoves, burning in fireplaces also contribute to elevated concentrations (both indoors and outdoors) of woodsmoke-associated pollutants. For example, studies have demonstrated that the levels of PAH and PM in homes with open fireplaces were approximately equal to those with non-airtight stoves, and substantially greater than those with airtight woodstoves (Maschandreas & Zabransky, 1980). Moreover, it has been reported that wood burned in an open fireplace yielded indoor PAH concentrations comparable to those of ambient urban air (Alfheim & Ramdahl, 1984). These same studies also reported that the mutagenicity of air samples collected from burning fireplaces exceeded the activity from samples emitted from airtight stoves. On the other hand, because airtight stoves burn wood in an oxygen-starved environment, organic chemicals are produced in greater variety in a woodburning stove than in a fireplace.

## HEALTH EFFECTS

Individually, many woodsmoke constituents have been shown to produce acute and chronic biologic effects and/or cause deleterious physiologic responses in exposed humans (Anderson et al., 1973; Speizer et al., 1980; Ramage et al., 1988; Koenig et al., 1988; Pierson et al., 1989; Koenig & Pierson, 1991; Schwartz, 1993). For example, CO at levels measured in homes using woodstoves (in the range of 1.2–43 ppm, compared to the indoor level of 5 ppm recommended by the American Society for Heating, Refrigeration, and Air Conditioning Engineers [ASHRAE] and the current outdoor standard of 9 ppm for an 8-h period) has been shown to produce carboxyhemoglobin and increase the incidence of angina among persons with cardiac disease (Anderson et al., 1973). Nitrogen oxides (primarily nitrogen dioxide and nitric oxide) bind to hemoglobin to produce methemoglobin and hematologic aberrations, affect the activity of several enzyme

systems, cause vascular membrane injury and leakage leading to edema, and may produce bronchoconstriction in asthmatics at low levels. The PAHs that are released into the environment adsorbed onto emitted PM are immunosuppressive in laboratory animals (White et al., 1994), as well as carcinogenic in animals and possibly humans (Koenig et al., 1988; Pierson et al., 1989). Aldehydes, mostly as formaldehyde and acrolein, measured indoors during operation of a woodburning device at concentrations ranging from 0.3 to 1 ppm (compared to ASHRAE recommended indoor levels of 0.1 ppm), are associated with upper airway irritation, headaches and other neurophysiologic dysfunctions, exacerbation of bronchial asthma, and possibly cancer (Kerns et al., 1983). In addition to the effects previously cited, other chronic health ailments have also been associated with exposure of humans to individual woodsmoke constituents. These include increased airway resistance, decreased vital capacity, increased respiratory symptoms (i.e., cough, wheeze, dyspnea), and infections in children (Koenig et al., 1988; Butterfield et al., 1989).

One of the most interesting components of woodsmoke pollution is PM (Butcher & Sorenson, 1979; Hytönen et al., 1983; Sexton et al., 1986; Traynor et al., 1987; Pierson et al., 1989; Hildemann et al., 1991; U.S. EPA, 2001). Woodsmoke-emitted respirable particulates (<3.5 μm), composed of a relatively equal mixture of ultrafine/fine (0.02–2.5 μm) and coarse (2.5–3.5 μm) particles (Sexton et al., 1986; Traynor et al., 1987; Hildemann et al., 1991) can penetrate into the deep lung, producing a variety of morphological and biochemical changes. A considerable body of epidemiologic evidence has associated short-term exposure to PM from a variety of sources with respiratory symptoms, increased use of asthmatic medication, hospital admissions, early mortality, exacerbation of preexisting medical conditions including a reduced likelihood of recovering from infectious diseases such as pneumonia, and an increased incidence and rate of infectious respiratory diseases in children (Schwartz, 1991, 1993; Pope, 1991; Kammen et al., 1998).

Although health effects associated with exposure to whole woodsmoke emissions are not as well studied as its individual components, a number of adverse health effects have been demonstrated. For example, exposure of laboratory animals to woodsmoke effluents decreased ventilatory frequency and ventilatory response to $CO_2$ (Wong et al., 1984), increased microvascular permeability and produced pulmonary edema (Nieman et al., 1988), caused necrotizing tracheobronchial epithelial cell injury (Thorning et al., 1982), possibly increased the lung cancer incidence in mice (Liang et al., 1988), increased levels of angiotensin-1-converting enzyme in the lungs (Brizio-Molteni et al., 1984), and compromised pulmonary macrophage-mediated immune mechanisms important in antimicrobial defense (Zelikoff et al., 1995a, 1995b), most likely via alterations in the integrity of the macrophage surface membrane or cytoskeletal components (Fick et al., 1984; Loke et al., 1984).

In humans, health effects seem to be related to host age at the time of woodsmoke exposure. In adults, effects include prolonged inhalation of woodsmoke contributed to chronic bronchitis (Rajpandey, 1984), chronic interstitial pneumonitis and fibrosis (Ramage et al., 1988), cor pulmonale, interstitial lung disease, pulmonary arterial hypertension (Sandoval et al., 1993), and altered pulmonary immune defense mechanisms (Demarest et al., 1979; Ramage et al., 1988).

While adverse effects of prolonged woodsmoke exposures on adults are notable, children appear to be at greatest risk. Exposure of preschool children living in homes heated with woodburning stoves or in houses with open fireplaces yielded these effects: decreased pulmonary lung function in young asthmatics (Koenig et al., 1993); increased incidence of acute bronchitis and severity/frequency of wheezing and coughing (Butterfield et al., 1989); and increased incidence, duration, and possibly severity of acute respiratory infections (Honicky et al., 1983, 1985; Rajpandey, 1984; Morris et al., 1990; Collings et al., 1990; Honicky & Osborne, 1991; Kammen et al., 1998). Even in those few epidemiological studies that failed to correlate woodsmoke exposure with respiratory disease/symptoms (Anderson, 1978; Tuthill, 1985; Browning et al., 1990), the authors concluded that woodsmoke pollution may have aggravated symptoms of respiratory disease and should not be disregarded as a possible contributing factor to increased respiratory infections in young children.

## THE IMMUNE SYSTEM AS A TARGET OF WOODSMOKE TOXICITY

In addition to the aforementioned health effects associated with inhaled woodsmoke and/or its components, many of the constituents have also been shown to alter pulmonary immune defense mechanisms in a persistent and often progressive manner (Jakab, 1977, 1992, 1993; Speizer et al., 1980; Hatch et al., 1981; Aranyi et al., 1983; Samet et al., 1987; Pierson et al., 1989; Burrell et al., 1992; Jakab & Hemenway, 1993; Zelikoff et al., 1999; Thomas & Zelikoff, 1999; Zelikoff, 2000). For example, studies have shown that in the absence of an inflammatory response, inhalation exposure of mice for 4 d to 15 ppm formaldehyde following bacterial challenge impaired intrapulmonary killing of *Staphylococcus aureus* 24 h after exposure; the same effect on lung antibacterial defenses was produced by formaldehyde at 1 ppm when exposure preceded, and was then continued after, bacterial challenge (Jakab, 1992). In the same study, $F_{c\gamma}$ receptor-mediated phagocytosis by alveolar macrophages recovered from mice exposed to 10 mg/m$^3$ carbon black and 5 ppm formaldehyde (4 h/d, 4 d) was progressively suppressed up to 25 d following exposure. In a later study by the same investigator (Jakab, 1993), coexposure of mice to carbon black (10 mg/m$^3$, 4 h/d, 4 d) and acrolein (2.5 ppm) suppressed intrapulmonary killing of *S. aureus,* impaired elimination of *Listeria monocytogenes* and influenza A virus, and enhanced intrapulmonary killing of *Proteus mira-*

*bilis;* it was suggested that the observed biologic effect was due to carbon particles acting as vehicles to carry acrolein into the deep lung. In addition, the same coexposure regime persistently suppressed alveolar macrophage-mediated tumor necrosis factor-α (TNFα) production and phagocytosis; phagocytic activity was significantly reduced at 1 through 11 d following exposure, while TNFα production was depressed after 4 d and reached control levels by d 20. Studies by this laboratory investigating the immunotoxicity of inhaled ambient PM (which could include particles generated from woodburning) demonstrated the ability of particulates <2.5 μm concentrated from New York City air to exacerbate an ongoing *Streptococcus pneumoniae* infection in PM-exposed rats (Zelikoff et al., 1999, in press). Thus, many respirable pollutants found in woodsmoke can offset the balance necessary for immunoregulation of the lung. This disruption in homeostasis may produce a cascade of detrimental secondary events, including pathogenesis and compromised host resistance which may lead to increased respiratory infections.

While only a limited number of studies have investigated the effects of whole woodsmoke emissions on pulmonary immunity, it appears that host defense and/or immune cell function is depressed in a manner similar to that produced by many of the individual woodsmoke constituents (Demarest et al., 1979; Fick et al., 1984; Loke et al., 1984; Zelikoff et al., 1995a, 1995b). For example, a single inhalation exposure of rabbits to smoke from the pyrolysis of Douglas fir wood produced an increase in the total number of recovered pulmonary macrophages and a transitory decrease in macrophage adherence to glass (Fick et al., 1984). Moreover, this same exposure regime decreased macrophage uptake of the gram-negative bacterial pathogen *Pseudomonas aeruginosa* in the absence of an inflammatory response or changes in macrophage viability. In another study, a single inhalation exposure of Douglas fir-generated woodsmoke altered macrophage morphology and membrane ultrastructure (Loke et al., 1984). Inhaled woodsmoke has also been reported to alter the chemotactic migration of bronchopulmonary lavaged human macrophages (Demarest et al., 1979).

The aforementioned studies have provided some evidence that inhalation of woodsmoke effluents can alter pulmonary immune defense mechanisms, and that the macrophage, a primary defense of the deep lung that provides a link between the nonspecific and specific defense systems of the respiratory tract, is the likely target for woodsmoke-induced immunotoxicity. However, some of the most compelling evidence demonstrating the ability of woodsmoke to modulate pulmonary immunocompetence comes from animal toxicology studies performed in this laboratory (Zelikoff et al., 1995a, 1995b). For these laboratory studies, 3-mo-old Sprague-Dawley rats were exposed repeatedly (1 h/d, 4 d) to a single concentration of woodsmoke (i.e., 750 μg $PM_{2.5}/m^3$) generated from red oak burned in a combustion furnace, originally developed for generating coal fly ash (Chen et al., 1990) and later adapted for woodburning (Figure 1).

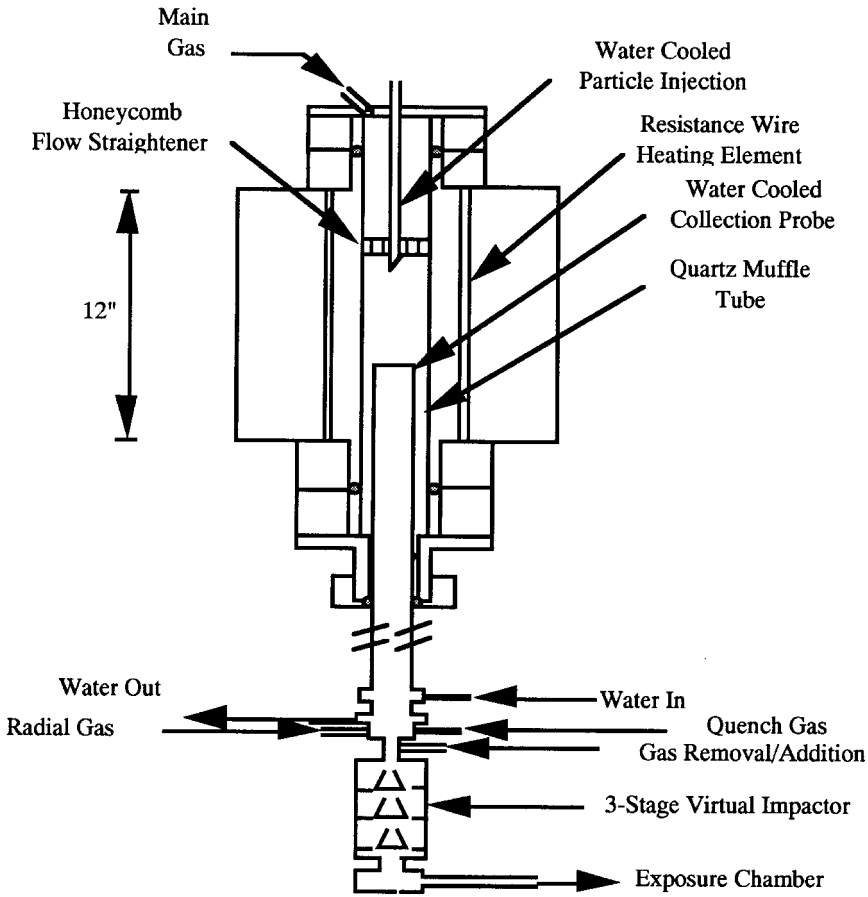


**FIGURE 1.** Combustion furnace for generating woodsmoke. The generation system consists of a feeder, laboratory-scale laminar-flow drop-tube furnace, and a collection probe. Wood dust is carried in a nitrogen gas stream and injected axially downward into the furnace, where the particles are ignited and burned in a narrow zone along the furnace axis. The temperature of combustion, as well as the bulk gas temperature, is controlled by the partial pressure of oxygen in the $O_2/N_2$ bulk gas mixture. At the exit of the collection probe, a three-stage virtual impactor was used to remove particles larger than 10 μm and the remaining particles and gas mixture then entered the exposure chamber.

Narrowly size-classified wood dusts (i.e., 53–63 μm) produced through mechanical grinding, were used for all experiments. The effluent concentrations of CO, PAH (measured as benzo[a]pyrene), $PM_{2.5}$, and $NO_X$ used in these studies were within the range of those measured indoors during non-airtight/airtight stove operation (Traynor et al., 1987). Mass median diameter of the emitted particles was 0.16 μm ($\sigma_g$ = 2.23), which is within the same particle size range shown to be released during the burning of oak wood in a residential fireplace (Hildemann et al., 1991).

At 3, 24, 72, and 120 h following the final woodsmoke exposure, rats were intratracheally instilled with the pneumonia-producing bacteria *Staphy-*

*lococcus aureus* to assess effects upon pulmonary clearance, or were sacrificed and their lungs either lavaged for recovery of pulmonary macrophages or fixed for histopathological examination (Zelikoff et al., 1995a, 1995b). Inhalation of woodsmoke emissions for 4 d (1 h/d) progressively reduced (compared to control) the in vivo clearance/killing of *S. aureus.* Effects of inhaled woodsmoke on intrapulmonary clearance appeared as early as 3 h following the final woodsmoke exposure and persisted for up to 5 d; killing/clearance was reduced to 60% of control values after 3 h and then progressively declined to 2% after 5 d. While the mechanisms by which woodsmoke may have acted to persistently suppress bacterial clearance are not yet clear, results from this part of the study demonstrated that short-term repeated inhalation of woodsmoke generated from the burning of a common hardwood used for home heating compromised pulmonary host resistance against an infectious, pneumonia-producing lung pathogen well after exposures ceased.

In this same study, both phagocytic activity and superoxide production by macrophages recovered from smoke-exposed animals were decreased (compared to control values) in a time-dependent manner. The persistent effects of short-term exposure to woodsmoke on $F_c$-dependent opsonized particle uptake were similar to previous studies that demonstrated a progressive decrease in $F_c$-receptor-mediated phagocytosis that began after 4 d and was persistent for up to 25 d following repeated coexposure to carbon black and the woodsmoke constituent formaldehyde (Jakab, 1992). It was concluded from this latter study that the observed onset delay and persistence of effects were due to formaldehyde desorption from the particle over an extended period of time, resulting in a slow accumulation of an internal dose, which, in turn, produced a continuous progressive effect. Given that woodsmoke is a mixture of gases and respirable particulates, a similar explanation could apply to the study with red oak effluents. Effects upon macrophage function along with those observed on bacterial clearance may help explain the increased incidence of respiratory infections observed in woodsmoke-exposed children, particularly those under 5 yr of age living in developing nations.

Even though information concerning the immunomodulating potential of inhaled woodsmoke is rather sparse (Demarest et al., 1979; Loke et al., 1984; Fick et al., 1984; Zelikoff et al., 1995a, 1995b), it appears that only a brief exposure to woodsmoke can alter intrapulmonary bacterial clearance and macrophage-mediated immunity. However, whether similar effects occur following long-term exposure, a scenario more reflective of the human situation, remains to be seen.

## SUMMARY

This mini-review has provided an overview of the health effects associated with exposure to woodsmoke and its individual constituents. In gen-

eral, combustion effluents from woodburning devices are increasing worldwide, and this has resulted in greater public exposure and increased concern by exposed individuals. While more studies are needed to determine the effects of long-term exposure, and the particular woodsmoke constituent(s) that may be responsible for the observed toxicities, it appears clear that inhalation of combustion products from wood can have a significant impact upon pulmonary homeostasis and/or exacerbation of ongoing disease processes, especially for those members of the population deemed most susceptible (i.e., young children, asthmatics, elderly, and individuals with ongoing cardiopulmonary disease).

Because of public outcry, a number of health-related agencies have offered some recommendations to individuals using woodburning devices, including consideration for your neighbors—that is, the smoke you generate also affects your neighbors "lungs"; burn cleanly and use only dry wood; avoid burning wood during hazy windless days and nights when temperature inversions might trap woodsmoke and other pollutants close to the ground; if possible, convert your woodburning fireplace to use natural gas or propane; and if your woodstove was manufactured before July 1988, replace it with one that is certified by the U.S. Environmental Protection Agency (British Columbia Ministry of the Environment, 1995; American Lung Association of Washington State, 1998; American Lung Association, 2000). Regarding the use of U.S. EPA-certified stoves, while it is true that these stoves generate only about half as much PM as uncertified ones (i.e., 4.0 vs. 10 μg PM/h, respectively), they still create as much particulate pollution as 12,000 houses heating with propane or natural gas.

Overall, more resources need to be devoted to woodsmoke research, particularly in the areas of air pollution measurements and adverse health effects, so as to better understand this continuing dilemma (American Lung Association, 2000).

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