Reuben M. Cherniak Lecture

When Smoke Gets in Your Lungs

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A major source of air pollution exposure in the developing world is smoke due to inefficient cooking with biomass fuels in poorly ventilated homes. Biomass fuel refers to any recently living plant- and/or animal-based material that is deliberately burned by humans as fuel, including wood, crop residues, and animal dung. The levels of exposure to particulate matter in such homes are often at least an order of magnitude higher than the highest concentrations that occur in the ambient air of the developed world. Because roughly half the world's population cooks daily with unprocessed biomass fuel, the potential public health impact is huge. The World Health Organization has estimated that indoor air pollution from solid fuel use is responsible for 2.6% of the total global burden of disease and between 1.5 and 2 million deaths each year, primarily due to acute lower respiratory infection in young children and chronic obstructive pulmonary disease in adult women. Major limitations of the existing epidemiologic literature include lack of actual exposure measurements, lack of longitudinal studies, inadequate exposure-response information, and few intervention studies. Ongoing research in Guatemala is attempting to address these data gaps.

Keywords: biomass smoke; global burden of disease; acute lower respiratory infection; chronic obstructive pulmonary disease

A major source of air pollution exposure in the developing world is smoke due to inefficient cooking with biomass fuels in poorly ventilated homes. The levels of exposure to particulate matter (PM) in such homes are often at least an order of magnitude higher than the highest concentrations that occur in the ambient air of the developed world (1, 2).

Biomass fuel refers to any recently living plant- and/or animal-based material that is deliberately burned by humans as fuel, including wood, crop residues, and animal dung (1). It has been estimated that roughly half the world's population cooks daily with unprocessed biomass fuel (3). Most of these people live in rural areas of lesser-developed countries (LDCs), where some four-fifths of households rely on biomass fuels as their major or only source of domestic energy for cooking and sometimes space heating (4).

Cooking with biomass fuels is generally done on unvented stoves typically consisting of such simple arrangements as three rocks, a U-shaped hole in a block of clay, or a pit in the ground (5). Combustion under such conditions leads to high emission factors that can lead to extremely high pollutant concentrations in the vicinity of the stove. Pollutant concentrations are further

exacerbated by the lack of ventilation that characterizes many of the kitchens in rural areas of developing countries.

Studies have shown that concentrations of pollution from cooking indoors with biomass fuels are commonly several thousand $\mu\text{g}/\text{m}^3$ of particulate matter with a diameter of 10 μm or less (PM_{10}) and, not infrequently, considerably higher values ranging from 10,000 to 20,000 $\mu\text{g}/\text{m}^3$ have been reported (6). These values are orders of magnitude higher than the U.S. Environmental Protection Agency national 24-hour standard for PM_{10} of 150 $\mu\text{g}/\text{m}^3$. In addition to PM, carbon monoxide (CO), nitrogen oxides, formaldehyde, and a number of toxic organic compounds (e.g., benzene; 1,3 butadiene; benzo[α]pyrene) are present in smoke from biomass combustion, depending on the type of fuel that is burned (7). In terms of emissions of PM and gases, the combustion of wood and other biomass is qualitatively similar to the burning of tobacco, although without the nicotine.

Because people in rural areas of LDCs often spend many hours a day cooking, average daily exposure is often considerable, particularly for women and children. The potential for exposure is further increased by common cultural practices. Infants and toddlers are often carried on the mother's back while she cooks so that from early infancy children spend hours breathing smoke from cooking or heating fires (8). In temperate climates and highland areas, people spend more time indoors to protect themselves from the cold, and the cold temperatures that characterize these areas require fires that burn over extended periods and tighter house construction for space heating (9, 10). Thus, both pollution levels and exposure times increase.

The public health impact of the relatively high exposures to PM in homes where cooking is done with inefficient, poorly ventilated stoves using biomass fuels is great. The comparative risk study undertaken by the World Health Organization and summarized in its annual report in 2002 found indoor air pollution from solid fuel use to be responsible for 2.6% of the total global burden of disease disability-adjusted life years, and between 1.5 and 2 million deaths each year (11). Indoor air pollution ranked eighth on the examined list of risk factors globally, ninth in premature deaths, and was the second most important environmental risk factor (after poor water/sanitation/hygiene). The estimates are based on metaanalyses of epidemiological studies of acceptable scientific quality, which at the time only included sufficient numbers for acute lower respiratory infection (ALRI), chronic obstructive pulmonary disease (COPD), and lung cancer (Table 1). The greatest burden of indoor air pollution-related premature deaths is in children with pneumonia exposed to biomass smoke (12). The greatest burden in adults is in nonsmoking women with COPD (12), but the process by which biomass smoke leads to this disease may begin in early childhood, or even *in utero*.

Acute lower respiratory infection is a leading contributor to the global burden of disease, accounting for 7% of the total

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TABLE 1. BIOMASS SMOKE-RELATED RESPIRATORY CONDITIONS

Evidence	Health Outcome	Group	RR*
Strong	ALRI	Children < 5 yr	3.2
	COPD	Women ≥ 30 yr	2.3
	Lung cancer (coal)	Women ≥ 30 yr	1.9
Moderate	COPD	Men ≥ 30 yr	1.8
	Lung cancer (coal)	Men ≥ 30 yr	1.5
	Lung cancer (biomass)	Women ≥ 30 yr	1.5
	Asthma	Children ≤ 14 yr	1.6
	Asthma	All ≥ 15 yr	1.2
	Tuberculosis	All ≥ 15 yr	1.5

Definition of abbreviations: ALRI = acute lower respiratory infection; COPD = chronic obstructive pulmonary disease; RR = relative risk.

* Values from Reference 11.

(13). Pneumonia is also the primary cause of death in children (2 million deaths in children younger than 5 yr) (13). The relative risk of ALRIs for children exposed to household biomass smoke has been quantified in a number of studies, the majority from developing countries, but also from the United States (14). Most of these studies have used a case-control design, although several cohort studies have been done. Taken together, these studies show a consistent association between solid fuel use and an increase of the risk of ALRI in exposed children. The overall estimate of the risk of ALRI from studies selected for the metaanalysis conducted by Smith and colleagues for the World Health Organization comparative risk assessment (11) was 2.3 (95% confidence interval [CI], 1.9–2.7), 1.8 for children younger than 5 years, and 2.5 for children younger than 2 years. The highest odds ratio (OR) was found in children carried on their mothers' backs while cooking (OR, 3.1; 95% CI, 1.8–5.3). An update of this metaanalysis was recently published with a total of 24 studies selected, including preliminary results for one randomized controlled trial (15). The overall pooled OR in this updated metaanalysis was 1.78 (95% CI, 1.45–2.18). Some evidence of an exposure–response relationship is available with an increased frequency of ALRI increase observed when PM₁₀ concentrations are greater than 2,000 mg/m³ (16). Impaired respiratory tract defense mechanisms, such as decreased mucociliary clearance and alveolar macrophage function, provide biological plausibility for the observed association between biomass smoke exposure and ALRI risk in children (14, 17).

COPD was the sixth leading cause of chronic morbidity and mortality worldwide in 1990 and is projected to rank third in 2020 (18). Cigarette smoking is the leading preventable cause of COPD in the developed world, but indoor biomass smoke exposure from inefficient burning of solid fuels may be the leading preventable cause among women in lesser developed countries. Because almost 3 billion people worldwide use biomass or coal as their main source of energy for cooking and heating, the population at risk worldwide is very large. Although cleaner energy sources are desirable, many of these people will continue to rely on biomass fuel for the short-term future. In addition, wood burning in home fireplaces and stoves remains prevalent in developed countries.

Only a few cross-sectional studies have measured lung function and these studies have showed an association between biomass fuel use and chronic airflow obstruction. For example, a recently published study from rural Mexico found that biomass use was associated with a 4% decrease in FEV₁/FVC (19). An increase in kitchen particulate concentration of 1,000 µg/m³ was associated with a reduction of 2% in FEV₁. A prevalence study of COPD in five cities of Colombia found that biomass stove use for 10 years or more was associated with COPD as defined by

post-bronchodilator FEV₁/FVC less than 0.70 (Global Initiative for Chronic Obstructive Lung Disease stage I or greater; OR, 1.5; 95% CI, 1.22–1.86) (20).

Case-control studies have consistently found an association between cooking with biomass fuel and chronic bronchitis or airflow obstruction (14). These studies are from developing countries, with the exception of a study from Spain (21). Taken together, the results of these studies show a strong association between cooking with biomass fuel and COPD among female never-smokers, with some evidence of an exposure–response relationship (e.g., hours of cooking per day and number of years cooking with biomass).

Longitudinal studies of the impact of biomass smoke exposure on the development of COPD are lacking, but one study did follow women with COPD associated with biomass smoke exposure in terms of mortality risk (22). Survival analysis over a 7-year follow-up period, adjusted for baseline FEV₁, O₂ saturation, body mass index, and age, showed that women with COPD associated with biomass smoke exposure had mortality rates similar to those of men with COPD due to tobacco smoking.

As part of the effort to update the comparative risk assessment of the impact of indoor air pollution from solid fuel use for a new round of the global burden of disease project, we have conducted a metaanalysis of studies that have investigated the association between biomass smoke exposure and COPD. Twenty-eight studies were selected (22 cross-sectional, 2 cohort, and 4 case-control) for the analysis; most of the studies used fuel type (n = 19) as the exposure and chronic bronchitis as the outcome (n = 20); only 4 studies measured lung function. The overall pooled odds ratio in this metaanalysis was 2.14 (95% CI, 1.78–2.58).

Intervention studies to prevent COPD from biomass smoke exposure are limited. A retrospective Chinese study found significant reductions in COPD incidence (relative risk of 0.58 in men, 0.75 in women) in homes where coal was used in improved stoves with chimneys, the effect increasing with time since adoption (23). This study used self-reported, doctor-diagnosed chronic bronchitis and COPD, which may underestimate prevalence in rural areas with low literacy and poor medical care access. Thus, although studies suggest lower biomass smoke exposure may be associated with lower COPD risk, two key questions remain: (1) Can prevention of COPD be achieved in these settings? And, (2) how much reduction in biomass smoke exposure is required to achieve useful benefit?

A multiinstitution collaborative research team has been conducting research on the respiratory health effects of wood smoke in the rural highlands of Guatemala for almost a decade. The study area covers about 25 km² and contains approximately 20 mostly Mam-speaking indigenous communities in the San Marcos region. This area is about 5 hours from Guatemala City and is one of the poorest districts in Guatemala. It was chosen as the site for the initial National Institutes of Health-funded RESPIRE trial because the members of the communities used open-fire stoves and there was little migration.

RESPIRE was a randomized stove intervention trial that recruited 534 households using open wood fires indoors for cooking and randomly assigned them to receive an improved stove with chimney, the *plancha* (Figure 1), or to continue using open fires. The aims of this trial were to examine the effect of the use of the improved stove with chimney on the incidence of ALRI in infants from birth to 18 months of age and to characterize in detail their exposure to biomass smoke. Personal 48-hour CO exposures were obtained every 3 months for the study children. At baseline before intervention, the control and intervention groups had similar child CO distributions (mean

Figure 1. The *plancha* is a wood-burning stove constructed from bricks and concrete blocks. It has a steel top-plate with three holes for pots and a metal chimney that directs the smoke outside the house. This stove was developed locally, is well accepted in the communities, and is built by local masons. Drawing by Nigel Bruce reproduced with permission.

values 2.4 ± 2.4 ppm and 2.5 ± 1.8 ppm, respectively) (24). A large reduction in exposure to 1.0 ± 2.3 ppm was observed in the intervention group. Adjusting for sex, age, season, and weekday, a model that included both personal and group-level exposure information estimated a 44% mean reduction (95% CI, -48 to -39%) in child CO associated with the improved stove intervention (25). Surveillance for ALRI was performed through weekly home visits by trained fieldworkers who referred cases to a study physician; all referred children had their arterial blood oxygen saturation measured by pulse oximetry. A respiratory syncytial virus (RSV) direct antigen test was performed on cases diagnosed by the physician as ALRI; chest radiographs were obtained on as many of these cases as possible. Preliminary intention-to-treat analysis of this randomized controlled trial found an ALRI rate ratio for intervention versus control of 0.84 (95% CI, 0.73–0.97; $P = 0.02$) for fieldworker-defined ALRI (24). There was an almost 40% reduction between groups over time for RSV-negative cases with hypoxia (oxygen saturation by pulse oximetry $< 87\%$; > 2 SD below the mean for well children at study altitude), with an OR of 0.62 (95% CI, 0.36–1.05; $P = 0.07$), a potentially important finding because these cases are likely to (1) be bacterial, and (2) have more severe disease, and hence the highest mortality. In contrast, there was no impact on hypoxic RSV-positive cases (OR, 1.01; 95% CI, 0.60–1.73).

CRECER is a longitudinal cohort study that is following more than 500 children, most of whom were former participants of RESPIRE, from age 3 to age 8 years. Because of loss of some of the original RESPIRE cohort, approximately 150 additional children from open-fire homes were recruited; after 18 months, these homes also received an improved stove. The primary aim of this study is to examine the effects of early lifetime wood smoke exposure (from birth to 18 months of age) on growth of lung function and the development of allergies and asthma. Quarterly home visits are being made to administer a respiratory questionnaire and to assess child CO exposure; semiannual visits are being made to administer allergy skin tests and spirometry. Preliminary results show that the improved stove was associated with decreased respiratory symptom reporting by the study children (26). Although no difference in allergic sensitization measured by a positive skin prick test to at least one out of six common aeroallergens was observed between

open-fire and *plancha* groups, the overall rate of sensitization was remarkably high, greater than 35%. Such a prevalence of atopy is what one would expect in a developed country population, not in a rural, impoverished population in an LDC.

Although the results of the metaanalysis described above demonstrate considerable evidence of an association between biomass smoke exposures and COPD, a major limitation is that exposure assessment is typically by self-report. In addition, there are no longitudinal studies that allow quantification of the effect of biomass smoke exposures on the rate of decline in lung function. Moreover, there are no studies of the efficacy of improved chimney stoves to slow the rate of decline in lung function in biomass smoke-exposed women as exist for smoking cessation. To address these data gaps, longitudinal cohort studies are needed. We are attempting to take advantage of the existing infrastructure from our ongoing research in Guatemala to establish a cohort of nonsmoking women, half from homes where cooking is done indoors with open fires and half from homes with improved chimney stoves, for longitudinal follow-up. Our primary hypothesis is that greater biomass smoke exposure is associated with more rapid decline in lung function. Our secondary mechanistic hypothesis is that inhalation of biomass smoke causes oxidative stress and lung inflammation that can lead to airway remodeling.

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