granuloma formation, and sarcoidosis that "complements" the proposed immunopathogenic paradigm of this enigmatic disease. ■

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Household Air Pollution, Passive Smoking, and Lung Cancer
Do We Know Enough about This Conundrum?

The Global Burden of Disease (GBD) collaboration reported 2.2 million incident cases of lung cancer in 2017, a 37% increase from 2007 globally in 195 countries; a total of 1.9 million deaths; and 40.9 million disability-adjusted life-years in both sexes, although this was higher in males than in females (1). The lung cancer cases increased by 17% from 2007 to 2017 in high–sociodemographic index (high-SDI) countries, 62% in middle-SDI countries, and 49% in low-SDI countries, with a change in age structure, population growth, and age group being the primary factors for the increase (2). Several studies, including a study by Sir Richard Doll on British doctors published in 1976 (3), emphasize smoking as a primary driver of lung cancer incidence, with GBD studies reporting the relative risk of lung cancer from tobacco smoke being 3.4 at 10 pack-years and 6.5 at 20 pack-years (2). The attributable fraction of lung cancer mortality due to smoking (males, 75.4%; females, 36.6%) has been higher in males because of higher smoking prevalence than in women (1).

Ambient air pollution (AAP) (4) has been the other leading risk factor for lung cancer mortality. Other contributors to lung cancer include exposure to household air pollution (HAP); secondhand cigarette smoke (SHS); and occupational exposure to asbestos, nickel, chromium, arsenic, and radiation (5). Although many studies from high-income countries have reported that exposure to AAP and smoking is causally associated with an increase in mortality of cardiorespiratory diseases (6) and lung cancer, there is a lack of prospective evidence from low- and middle-income countries (LMICs), where HAP from burning solid fuel for domestic cooking and heating purposes in addition to AAP in cities is an area of significant health concern (7). In certain LMICs, up to 50% of the AAP is contributed by HAP from solid fuel burning and 30% from fossil fuel burning, of which 50% comes from coal burning (8). Globally, there has been a decline in the use of solid fuels for cooking from 53% (45–60%) in 1990 to 36% (30–43%) in 2020, and if the current trends continue, use will be about 31% in 2030; however, the total number of the population cooking with solid fuels was 2.8

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billion in 1990 and 2020, but it will have a very modest decline to 2.7 billion in 2030 (9). Both AAP and HAP contain carcinogens such as polycyclic aromatic hydrocarbons, including benzo[α]pyrene, a known carcinogen, and carbon-based particles that can adsorb several oxidants, such as ozone and reactive oxygen and nitrogen species (10, 11).

There is little doubt about the associations between smoking and air pollution, including HAP, with lung cancer; however, the main questions are whether the associations with SHS and HAP and lung cancer deaths are causal and, if yes, whether the excess deaths of lung cancer are caused by HAP and SHS. It is challenging to answer these questions with certainty in light of the evidence where many other risk factors are well established. The other question lies in the degree of risk posed by various types of solid fuel from wood, leaves, twig, charcoal, straws, and coal, because the types of emissions and their concentration from burning these various solid fuels are different.

In this issue of the *Journal*, Cheng and colleagues (pp. 1153–1162) analyzed a large prospective database of nonsmokers from 10 different geographical areas of China to report on the association of HAP and SHS with lung cancer mortality (12). Over a median 10.2 years of follow-up, 979 lung cancer deaths among 3,23,794 nonsmoking adults were reported. The study reported a 4% increase in lung cancer–related death for every 5 years of follow-up, with the risk being highest in the 40–50-year-old age group compared with the never smokers. A statistically significant *P* trend for the age group was reported; however, it is surprising to see lower risk in those older than age 50 years than in the 40–50-year-old age group, findings not aligning entirely with the GBD findings, which report the increase in age structure being one of the most critical factors for an increase in lung cancer. The study collected questionnaire-based data on the use of solid fuel from the previous three homes in which the participants lived; the authors report consistency in the baseline and follow-up, suggesting less recall bias. There were no direct exposure assessments for AAP or HAP in this cohort and hence no adjustment for AAP. We understand that air pollution exposure assessment in large cohorts is quite tricky, particularly when time and resources are constrained. Still, the findings are not free from bias, because important risk factors are not considered during the analysis phase (7). The authors have conducted several sensitivity analyses, including age, sex, and residence. They report a higher risk of lung cancer mortality in association with HAP exposure in men (hazard ratio, 1. 07; 95% confidence interval, 1.01–1.13) than in women (hazard ratio, 1.04; 95% confidence interval, 1.01–1.06). This is somewhat surprising, given that it is women in many LMICs who do most of the cooking and hence are exposed to higher concentrations of HAP.

In contrast, for both sexes, the proportions of the age-standardized mortality rate of lung cancer attributable to HAP from solid fuels reported by Cheng and colleagues are much higher (males, 21.7%; females, 29.9%) than GBD estimates for low-income countries where HAP is predominantly used (males, 4.0%; females, 5.4%) (2). A study of Chinese women reported that ever coal use was not associated with lung cancer; however, ever coal use with poor ventilation had a 69% higher risk and 20 or more years of using coal with poor ventilation had a 103% higher risk of lung cancer compared with no exposure to coal or poor ventilation (13). In reporting the lung cancer findings from epidemiological studies in LMICs, where the burden of HAP exposure is the highest, one should take into account that lung cancer is likely to be highly underdiagnosed because of a lack of proper health infrastructure. The participants living in the rural areas of LMICs use solid fuel for cooking and are mainly of poor socioeconomic status and may not be able to afford early diagnosis and treatment if diagnosed. Unsurprisingly, the study did not find any significant association between SHS and lung cancer. In China, more than two-thirds of the population are ever smokers. In practice, there are no restrictions on smoking in public places and in homes in front of other family members, which makes it very difficult to rule out individuals with no exposure to SHS (14).

It is too early to understand the full spectrum of diseases associated with exposure to HAP. Some of these large, prospective cohorts have tried to provide better estimates; however, they often have raised some serious public health concerns, which suggests that we need to develop policies for prevention rather than waiting to understand the full spectrum of diseases and mechanisms of how some of the HAP and SHS act. Cardiorespiratory diseases and lung cancer control should be targeted to improve global health. This is important if we are serious about reducing one-third of premature mortality from noncommunicable diseases by 2030, one of the key goals of the United Nations Sustainable Development Goals (15). ■

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Science-based Policy Recommendations for Fine Particulate Matter in the United States

The importance of reducing air pollution concentrations is clear: lower air pollution levels will lead to improvements in public health and exert co-benefits for climate actions. The American Thoracic Society (ATS) has a responsibility as the world's leading medical society dedicated to advancing global respiratory health to advocate for protective air quality standards that reflect the latest scientific understanding of the health risks of outdoor pollution exposures.

In the United States (U.S.), the U.S. Environmental Protection Agency (EPA) Administrator is responsible for making final decisions in regard to the National Ambient Air Quality Standards (NAAQS) for fine particulate matter ($PM_{2.5}$) as directed by the Clean Air Act. This decision is greatly assisted by technical and policy documents prepared by EPA staff, under the guidance of the Clean Air Science Advisory Committee (CASAC), and for which ATS provided substantive public comments.

Scientific Evidence for a Revised $PM_{2.5}$ Recommendation in the U.S.

ATS has long made science-based policy recommendations for the NAAQS for criteria pollutants (1). In 2019, ATS revised its recommendation for the annual $PM_{2.5}$ standard to 8 $\mu g/m^3$ and reaffirmed its recommendation of 25 $\mu g/m^3$ for the 24-hour standard. Meeting these recommendations would result in substantial health benefits compared with current air quality conditions (2).

The revised recommendation for the annual $PM_{2.5}$ standard was based primarily on epidemiological studies conducted among U.S. populations that observed increased risks for premature deaths associated with exposures below the current EPA standard (annual standard of 12 $\mu g/m^3$ and 24-h standard of 35 $\mu g/m^3$) and the previous ATS-recommended level (3–5). Valuable information from studies conducted in Canada, with lower ambient concentrations than the U.S., further supported the scientific rationale for the recommended level (6).

The 24-hour $PM_{2.5}$ standard is designed to protect the public from health risks associated with elevated short-term exposures. But interpreting results from epidemiology studies to inform decisions regarding the level of the 24-hour standard can be challenging. For example, acute health risks are most clearly associated with exposures occurring across multiple days while the averaging time of the standard is based on a single day. However, studies that have restricted the analysis to days with exposures below 25 $\mu g/m^3$ have demonstrated increased risk of mortality and morbidity on days with elevated levels of $PM_{2.5}$ and provide strong evidence in support of the ATS recommendation for the 24-hour standard (7, 8).

Comparing ATS Recommendations with WHO Guidelines

Air Quality Guidelines (AQGs) from the World Health Organization (WHO) represent an important guidepost for environmental and public health and provide governments a clear recommendation to protect people from the severe health effects of air pollution (9). The updated WHO AQGs for $PM_{2.5}$ are 5 $\mu g/m^3$ for annual values and 15 $\mu g/m^3$ for 24-hour values.

It is reasonable to ask why ATS doesn't adopt the WHO AQGs for its U.S. policy recommendations, even though it strongly supports their use at the global level as an aspirational target for providing clean air for all. The answer is that ATS recommendations apply specifically to the NAAQS established by the EPA under the Clean Air Act based on legal requirements unique to the U.S. The NAAQS are a legally binding standard that counties and states are required to attain through planning and management efforts. These standards are reviewed regularly and continue to be adjusted based on evidence primarily from U.S.-based studies.

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