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Rural PM_{10} and Respiratory Health

In this issue of *AnnalsATS*, James and colleagues (pp. 947–954) present a retrospective cohort study demonstrating that higher levels of particulate matter with aerodynamic diameter of less than 10 μm (PM_{10}) are associated with increased healthcare use for respiratory disorders (1). This is not a new finding and a large body of evidence shows that ambient air pollution exposure causes significant respiratory morbidity and mortality, including exacerbations of asthma and chronic lung disease (2–4). However, the bulk of studies have focused on the urban environment, where pollutant levels are highest and are dominated by combustion-derived pollutants with well-understood pulmonary effects. Here, the authors have turned their attention to an understudied population and pollution source, determining health effects in a rural community in the San Luis Valley of Colorado.

The study includes all respiratory-related emergency room and urgent care visits to the regional healthcare center of the San Luis Valley in individuals more than 5 years old, from 2003 to 2012. The authors define their outcome based on *International Classification of Diseases, Ninth Revision* (ICD-9) codes for asthma, pneumonia, acute respiratory illness, and chronic obstructive pulmonary disease with bronchitis. Daily mean pollutant levels were obtained from an air quality monitor in the San Luis Valley, located in close proximity to the main residential area of the community. To investigate the effect of different time windows of exposure, the authors examined 1-, 3-, and 5-day moving averages of PM_{10} from presentation, as well as individual mean day exposures up to lag day 4. In postulating that there may be threshold values for adverse effects, they also investigated effects for pollutant cut-points at 50 $\mu g/m^3$ and 100 $\mu g/m^3$.

The authors report that higher PM_{10} levels were associated with increased emergency room and urgent care visits for respiratory-related disorders. The associations were particularly strong for asthma-related diagnoses: for each 15 $\mu g/m^3$ increase in 3-day and 5-day averaged ambient PM, there was an associated 3.1% increase in hospital visits for patients with asthma. When they examined the relationship for binary pollutant cutoffs, they found significant associations for both 50 $\mu g/m^3$ and 100 $\mu g/m^3$ levels of PM_{10}. Of note, both of these threshold values are well below the U.S. Environmental Protection Agency national ambient air quality 24-hour standard of 150 $\mu g/m^3$ (5).

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One could conclude from this study that the current national ambient air quality standard for PM_{10} does not protect against a significant number of adverse health effects in rural communities. If true, this would be an important finding because these particles are derived from largely "natural" sources, which are thought to be less harmful (6). Some have argued that these natural sources of PM do not need to be a focus of prevention efforts (7). Whereas urban ambient air pollutants and fine particulates are derived predominantly from byproducts of fossil fuel combustion and are enriched in components such as polycyclic aromatic hydrocarbons and transition metals, rural "coarse" air pollutants are composed primarily of wind-borne crustal elements resuspended from the earth's surface. In addition to these suspended dust particulates, rural particulates can also contain organic debris, endotoxins, pollens, and toxic trace elements from engine exhaust and pesticides (8).

Both the chemical and morphologic composition profiles of pollutants likely determine pathogenicity. PM_{10} is comprised of two distinct particle subtypes with different size characteristics. The larger coarse particles (PM with aerodynamic diameter of 10–2.5 μm, $PM_{2.5-10}$), which are believed to predominate in rural PM, tend to deposit in the upper airway and tracheobronchial tree. Fine PM (PM with aerodynamic diameter of less than 2.5 μm, $PM_{2.5}$) can travel throughout the respiratory tract and deposit down to the alveoli (9). Upon deposition, PM can induce oxidative stress and epithelial damage, altering the immunologic response and contributing to airway remodeling.

PM_{10} is the only pollutant that is monitored in the San Luis Valley, which makes it difficult to separate the relative effects of mixed-pollutant exposure. It is impossible to distinguish coarse from fine PM, or to determine the relative contribution from other pollutants, such as nitrogen oxides, ozone, and sulfur dioxide.

In addition to this source of uncertainty in exposure assessment, air pollutant measurements in the study were derived from only one monitor. Because of its large size, PM_{10} tends to have a short residence time in the air and high spatial heterogeneity, which was not at all captured by the study design. This leads to substantial exposure misclassification for participants who live or work at significant distances from monitoring stations. In an area where regional large dust storm events predominate, this source of measurement error may be less significant. In fact, there was a high correlation of the PM_{10} levels between the two air pollution monitors in the San Luis Valley, albeit the stations were only 2 miles apart.

This observational study has other notable limitations due to outcome misclassification, selection bias, residual confounding, and the inability to infer causation. The reliance on ICD-9 codes to capture cases leads to a substantial risk for disease miscategorization. Although the authors were able to capture all emergency room and urgent care visits in the area, they missed individuals with less severe disease who were treated as outpatients and those who were treated elsewhere. In excluding children less than 5 years old from the study, they omitted a vulnerable population that not only had the highest rate of respiratory visits in their study but also may be more affected by pollution due to their immature immune system, narrower airways, and higher minute ventilation. Importantly, with no access to individual-level data regarding the patients studied, the authors are unable to adjust for confounders such as ethnicity, sex, tobacco use, socioeconomic status, and disease severity.

Despite these limitations, the findings from this study highlight the potentially significant health effects of rural pollutants. In the setting of climate change and current land use practices, the amount of globally aerosolized dust has doubled in the past century and is expected to continue to increase (10). Many areas are seeing an increasing frequency and severity of dust storms, such as the massive storm in northern India that killed hundreds in early May. As this study demonstrates, even lower levels of nonurban PM_{10} are associated with adverse respiratory effects.

Attention to preventing the health effects of rural air pollutants remains important, even while more studies are needed to determine the relative pathogenicity of constituent pollutants, biologic pathways, and susceptible populations. ■

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Immunosuppression and Heterogeneity in the Sepsis Volume–Outcome Relationship

Sepsis is a common cause of critical illness, affecting over 2 million Americans annually, and it is the leading cause of death in hospitalized patients (1, 2). Patients with underlying immune dysfunction are particularly susceptible to sepsis-related morbidity and mortality (3). Early identification of septic patients, followed by prompt administration of antibiotics and appropriate hemodynamic resuscitation, improves sepsis outcomes, but many patients do not receive optimal sepsis care (4). The precise mechanisms underlying this quality gap are multifactorial.

One important organizational factor is case volume, in that patients have better outcomes at hospitals that care for greater numbers of patients. This volume–outcome relationship is well documented in a variety of critical illness syndromes, and sepsis is no exception (5, 6). Physicians and hospitals with higher case volumes may provide more evidence-based sepsis care, thereby improving outcomes (7). In effect, management within a high-volume center is a system-level "treatment" for sepsis that is associated with lower morbidity and mortality, raising the

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