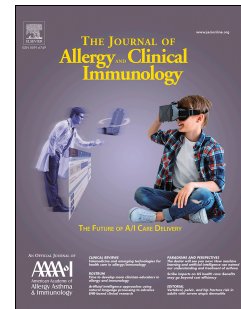


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From the farm to the big city: emerging health effects of agricultural emissions on asthma

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Title: From the farm to the big city: emerging health effects of agricultural emissions on asthma

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26 The 2018 *Lancet* Commission on Pollution and Health recognized that exposure
27 to pollution is “the largest environmental cause of disease and premature death in the
28 world today”(1). With increasing economic development in low- and middle-income
29 countries, the burden of rising levels of air pollution on respiratory health in large sectors
30 of the global population was largely unexplored. In the current issue of the *Journal of*
31 *Allergy and Clinical Immunology*, Wang et. al. report their findings on the association
32 between asthma prevalence and average exposure to particulate matter less than or
33 equal to 2.5 μm (PM_{2.5}) and its individual constituents [black carbon (BC), organic
34 carbon (OC), sulfate, ammonium (NH₄⁺) and nitrate] from The World Health
35 Organization’s Study on global AGEing and adult health (SAGE) cohort (2). This large
36 cross-sectional study includes survey data from over 45,000 adults from low- and
37 middle-income countries including China, Ghana, India, Mexico, Russia, and South
38 Africa. Most studies use PM mass concentration as their metric of exposure, but given
39 the heterogenous makeup of PM, recent evidence suggests that individual components
40 of PM may be more harmful than others, such that the true impact of PM on asthma
41 may be missed by focusing on PM mass concentration alone (3). In addition to
42 confirming that exposure to elevated levels of PM_{2.5} were associated with increased
43 odds of self-reported asthma, they found that each of the five individual constituents
44 measured were also associated with increased odds of asthma. Of the components
45 examined, NH₄⁺ was associated with the highest adjusted OR of asthma for every
46 increase of one SD in NH₄⁺ (aOR 1.28 (95%CI: 1.17, 1.41). A counterfactual analysis

was applied to estimate the number of preventable asthma cases associated with each $PM_{2.5}$ component by hypothetically setting pollutant concentrations to the 5th percentile of the range of measured levels. Using this approach, they found that reduction of black carbon, sulfate and NH_4^+ in $PM_{2.5}$ were associated with the largest decrease in asthma cases; reduction of NH_4^+ had the largest effect seen among the five constituents, with a 22% decline (95%CI: 18.64%, 25.84%) in asthma cases, suggesting that NH_4^+ exposure may be particularly harmful for asthma.

This study has several strengths, including the large size of the cohort, approximately equal distribution of urban and rural sites and multinational design with inclusion of low and middle-income countries, which have not been sufficiently represented in previous studies. Importantly, this study excluded children and did not take into account the relationship between cumulative exposure to $PM_{2.5}$ over the lifetime and odds of asthma. It is conceivable that the reduction in asthma incidence observed may be an underestimation of the true effect. Other limitations of the study include the lack of data on age of asthma onset, asthma severity, health care expenditures attributable to pollutant exposure, and the presence or absence of co-morbid COPD. PM exposure over the 3-year period of observation is less relevant to the discussion of asthma incidence in adults who had onset of asthma in childhood. The relationship between asthma prevalence and exposure to PM components may have been confounded by the presence of COPD as the two diseases can occur together and the symptoms of both diseases are often similar and difficult to distinguish from one another.

The finding that NH_4^+ exposure may be particularly harmful for asthma is supported by emerging literature on the detrimental effects of ammonia (NH_3) emissions on human health, including increased mortality (4) and premature death (5). NH_3 can drift long distances and react with atmospheric sulfur dioxide and nitrate oxidants in urban areas to form NH_4^+ , a component of $\text{PM}_{2.5}$ that then settles as smog. PM elicits bronchospasm and increased mucus production, which are hallmarks of asthma (**Figure 1**). Globally, NH_3 emissions are largely (90%) attributable to agricultural sources such as animal manure and crop fertilizer and, to a lesser extent, to burning of fossil fuels (6). Due to increased demand for animal products worldwide and use of chemical fertilizers, agricultural NH_3 emissions have greatly increased since the 1960s, resulting in greater contribution of NH_3 to $\text{PM}_{2.5}$ (5), outpacing the contribution of the primarily fossil fuel-derived nitrogen oxides (NO_x). A global analysis found that from 1990-2013, reactive nitrogen (N_r) constituents of $\text{PM}_{2.5}$ pollution increased the most in areas with rapid economic development including Asia, South America, and South Africa (5).

The findings of Wang et. al. specifically expands our understanding of the role of NH_4^+ on asthma prevalence in individuals from low and middle-income countries that have experienced large increases in N_r -rich $\text{PM}_{2.5}$. A Danish study of preschool aged children reported a positive association between NH_3 , NH_4^+ and combined exposure and diagnosis of asthma, but the association was lost after adjusting for region (7). The authors concluded that NH_3 may be associated with asthma prevalence in children, but the relationship may have been confounded by other unmeasured factors associated with proximity to sources of NH_3 emissions. Another study showed that ambient air NH_3 concentration was associated with reduced lung function, but not asthma symptoms or

medication use, in children living in the agricultural region of Yakima Valley, Washington, home to numerous concentrated animal feeding operations (CAFOs) (8). Close residential proximity to CAFOs was associated with increased odds of self-reported asthma, nasal allergies, uncontrolled asthma, use of asthma medications and reduced FEV₁ (9).

In contrast to European countries, agricultural operations have been subjected to little regulation of emissions by the U.S. Environmental Protection Agency through programs like the Clean Air Act, which sets National Ambient Air Quality Standards but does not regulate NH₃ emissions. Therefore, agricultural operations are not required to measure and report NH₃ emissions, resulting in a lack of data on NH₃ sources in the U.S. (10). The current standards regulate for sulfur dioxide, PM, nitrogen dioxide, carbon monoxide, ozone, and lead but not agricultural emissions such as NH₃ and the greenhouse gases methane, carbon dioxide and nitrous oxide. Gu et. al. estimated that reducing NH₃ emissions as a strategy for reducing PM_{2.5} is much more cost effective than reducing NO_x emissions and accounts for a fraction of the economic cost associated with pollution-related mortality (5). Some of the proposed solutions to the NH₃ problem include reducing the use of nitrogen fertilizer and improved strategies for management of livestock manure, with some success in European countries. Solutions focused on NH₃ abatement in U.S. agricultural environments are likely to encounter political barriers, and these would need to be complemented with continued efforts to reduce fossil fuel use and PM_{2.5} precursors in industrial and urban areas.

The full scope that NH₃ emissions have on both the environment and our health has yet to be elucidated, including the role of NH₃/NH₄⁺ exposure in asthma and COPD

development, morbidity, and costs to healthcare systems. Greater than 92% of pollution-related deaths occur in low-income and middle-income countries (1) that are also experiencing rapid economic development and urbanization, trends that have also increased greenhouse gas emissions and accelerated the climate crisis. It is imperative that we as researchers educate and collaborate with policymakers to prioritize our understanding of how the complex mixtures we breathe influence human health while we develop strategies to protect our environment. Innovative and cost-effective strategies to reduce NH_3 emissions to reduce the burden of $\text{PM}_{2.5}$ are only a first step in a global effort to protect human health.

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