Pollutants in the workplace: Effect on occupational asthma

Kevin J. Kelly, MD,[a] and Jill A. Poole, MD[b] *Chapel Hill, NC, and Omaha, Neb*

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Pollutant and allergen exposures encountered at the workplace can cause or exacerbate asthma, and these potential pollutants are numerous, varying, and often underrecognized. Commonly, these causative pollutants are associated with a specific immunologic response, referred to as occupational sensitizers, and are broadly classified as high-molecular-weight (HMW) and low-molecular-weight (LMW) agents.[1] HMW agents include vertebrate and invertebrate animal, plant, bacterial, and fungal exposures commonly encountered in farming, laboratories, office buildings, health care, and processing/harvesting environments. LMW agents, such as diisocyanates, wood dusts, chemicals, biocides, and acid anhydrides, are usually encountered in painting, industrial, health care, cleaning, and hairdressing work. Pollutants can also induce asthma in the absence of a specific immunologic response that can be observed after high-level exposure referred to as irritant-induced occupational asthma.[1] The collapse of the World Trade Center, which created exposure to very high concentrations of highly irritating dusts, gases, and fumes, is an example of irritant-induced occupational asthma experienced by emergency first responders.[1] In this brief review the current perspective and paradigm shifts of workplace pollutants focused on latex and farm sensitizers with occupational asthma are examined (Fig 1).

INDOOR AIR POLLUTANTS: THE LATEX ALLERGY EXAMPLE

Despite more than 400 occupational sensitizers identified to induce allergy or asthma in workers, specific predictive testing has been less than satisfactory, with false-negative and false-positive results. Advances in the molecular diagnosis of sensitization to occupational exposures show promising results, with latex allergy as one example of a successful approach.[2] Diagnosis of occupational allergy is made by a combination of medical history, physical examination, positive methacholine challenge result or bronchodilator responsiveness, determination of IgE-mediated sensitization to HMW allergens, and possibly basophil activation testing to LMW chemicals and HMW allergens. Diagnostic testing is complicated by the numerous HMW proteins recognized in various indoor air pollutant environments. In the example of latex allergy, more than 250 peptides have been identified, yet only 15 allergens from *Hevea brasiliensis* latex (Hev b 1-15) are included in the official allergen list of the World Health Organization and International Union of Immunological Societies Allergen Nomenclature database. Unfortunately, current serologic testing for latex-specific IgE demonstrates a sensitivity of 35% to 76%[3] but with high specificity.

A promising alternative to latex challenge testing is use of component-resolved diagnostic reagents and cloning of recombinant latex allergens. The "spiking" of rHev b 5 into the ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) greatly improved the diagnostic capacity of the ImmunoCAP test and serves as a model for improved testing in diagnosing other pollutant-induced asthma.[2] For example, patterns of reactivity to rHev b 1 and rHev b 3 identify up to 86% of patients with spina bifida and latex allergy. Similarly, reactivity of specific IgE to rHev b 5, rHev b 6.01, and rHev b 6.02 is the most accurate predictor of a positive inhalation challenge test response to latex allergen.[4] This pattern of reactivity to allergen components in patients with latex-mediated disease demonstrates superior diagnostic capacity compared with ImmunoCAP. The global success of reduction of latex allergy in health care workers by reducing environmental contamination of latex allergens carried on cornstarch powder has been nothing short of a remarkable achievement.[4]

OUTDOOR AIR POLLUTANTS: AGRICULTURE EXPOSURES

In the past 20 years, the protective role for early-life farming exposures in reducing the development of asthma has been established, and animal modeling studies demonstrate that exposure to these dust extracts before and during allergic sensitization and challenge reduces airway hyperreactivity and eosinophilia.[5] However, this paradigm of early-life farm exposures as protective against asthma development does not explain the observations in adults that occupational agriculture exposure can cause or exacerbate asthma.

Among farm operators with farm work–related asthma, 33% had asthmatic exacerbations while doing farm work, suggesting that farm exposure is a risk factor for worsening asthma disease.[6] The agriculture exposure is complex and characterized by its abundance and wide variety of gram-positive and gram-negative bacteria, fungi, particulates, gases, pesticides, and allergens. All of these complex factors, which can be either HMW or LMW agents, can sensitize or irritate the airway response toward allergic or nonallergic asthmatic disease. The timing and magnitude of the exposure plays a significant role because greater endotoxin levels, which serve as a surrogate measure of bacterial burden, have been associated with lower lung function in asthma cases among adult farmers.[7] Interestingly, this relationship is

From [a]the Department of Pediatrics, Division of Allergy/Immunology/Rheumatology, University of North Carolina, Chapel Hill, and [b]the Department of Medicine, Section of Allergy, Division of Pulmonary, Critical Care, Sleep and Allergy, University of Nebraska Medical Center, Omaha.

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Corresponding author: Jill A. Poole, MD, University of Nebraska Medical Center, Department of Pulmonary and Critical Care, Sleep and Allergy Division, 985990 Nebraska Medical Center, Omaha, NE 68198-5990. E-mail: japoole@unmc.edu.

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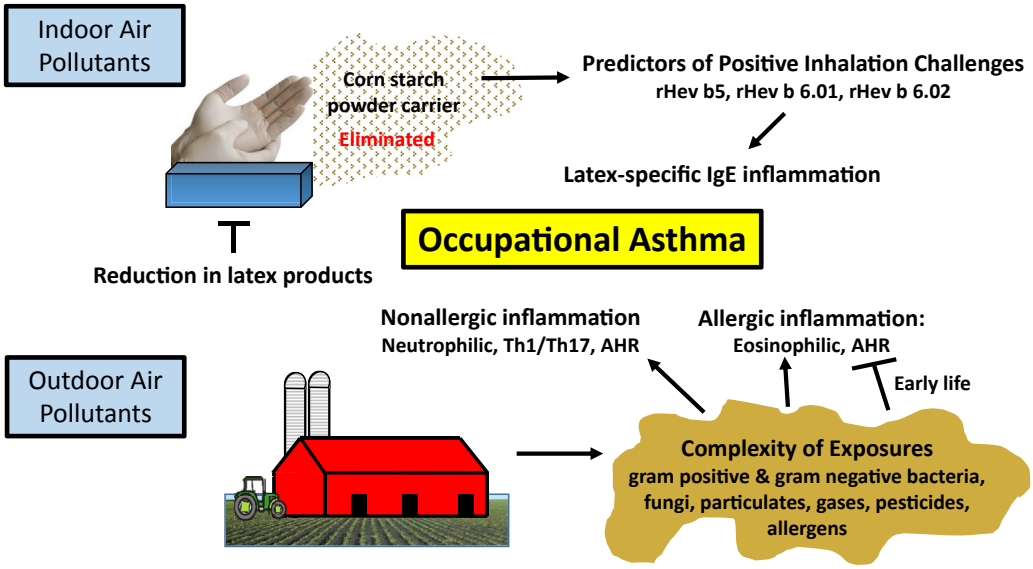

FIG 1. Indoor and outdoor air pollutants affect occupational asthma. Latex, an indoor air pollutant, is an HMW allergen mediating IgE sensitization that is potentiated through a corn starch carrier, with recent advances in component diagnostic testing to demonstrate specificity to occupational asthma. Agriculture exposures are complex outdoor air pollutants that can mediate occupational asthma through nonallergic and allergic mechanisms, with early-life exposure demonstrating protection against allergic asthma. *AHR,* Airway hyperresponsiveness.

modified by early-life farm exposures because those not born on a farm had greater rates of asthma compared with adult farmers who were born and raised on a farm.[7] Similarly, exposure to swine and dairy confinements are risk factors for new-onset nonallergic asthma and worsening lung function over time, whereas being born and raised on a farm reduces this risk.[7]

Finally, the use of various types of pesticides, including but not limited to organophosphorus pesticides,[8] should be highlighted because pesticides are LMW agents that can be important independent risk factors to explain workplace-exacerbated asthma among exposed adults.

The mechanisms to explain occupational asthma and workplace-exacerbated asthma in farming occupations are not well defined. Nonallergic asthma tends to prevail over allergic asthma, but atopy can be found in these asthmatic patients. Microbial components within agricultural dust extracts activate pathogen recognition receptor signaling pathways to elicit strong inflammatory responses marked by neutrophil and T_H1/T_H17 lymphocyte influx, as well as trigger airway hyperresponsiveness.[7] Neutrophilic inflammation has also been associated with airway dehydration in asthmatic patients, which is hypothesized to contribute to bronchoconstriction. Endotoxins can also enhance histamine release caused by allergens and potentiate eosinophilic inflammation.[9]

Large prospective longitudinal studies of adult agriculture workers are warranted to better understand the pathogenesis of asthma associated with agriculture work. Comprehensive exposure assessments incorporating molecular techniques to move the field toward the ultimate goal of understanding the occupational "exposome"[10] will be necessary. It will also be important to identify how the changing demographics of this industry, with racially/ethnically diverse workers and a potential expansion of female workers, might affect asthma outcomes. Finally, the nonuniform use of respirators within agricultural work contributes to workplace asthma, and education for respiratory use should clearly be considered by health care providers.

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