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Pulmonary Health Effects of Agriculture

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Abstract

Purpose of review—Occupational exposures in the agricultural industry are associated with numerous lung diseases, including chronic obstructive pulmonary disease, asthma, hypersensitivity pneumonitis, lung cancer and interstitial lung diseases. Efforts are ongoing to ascertain contributing factors to these negative respiratory outcomes and improve monitoring of environmental factors leading to disease. In this review, recently published studies investigating the deleterious effects of occupational exposures in the agricultural industry are discussed.

Recent findings—Occupational exposures to numerous agricultural environment aerosols, including pesticides, fungi, and bacteria are associated with impaired respiratory function and disease. Increases in certain farming practices, including mushroom and greenhouse farming, present new occupational exposure concerns. Improved detection methods may provide opportunities to better monitor safe exposure levels to known lung irritants.

Summary—In the agricultural industry, occupational exposures to organic and inorganic aerosols lead to increased risk for lung disease amongst workers. Increased awareness of respiratory risks and improved monitoring of agricultural environments are necessary to limit pulmonary health risks to exposed populations.

Keywords

occupational exposures; agriculture; pulmonary health

Introduction

Production agriculture produces a variety of dusts, vapors and fumes that can cause respiratory symptoms and disease. Examples of exposures include: organic dusts from livestock barns and confinements, grain dusts, and pesticides. These exposures can lead to increased rates of COPD, asthma, hypersensitivity pneumonitis, interstitial lung disease, and possibly lung cancer. While evidence is mixed regarding the pulmonary health effects of agricultural exposures, this review will highlight recent findings relating to the detrimental consequences of agricultural exposures with regards to COPD, asthma, hypersensitivity

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pneumonitis (HP), and interstitial lung disease. Ongoing evaluation of lung cancer risk with agricultural exposures will also be reviewed.

COPD

COPD is an obstructive lung disease that presents with increased shortness of breath, cough and wheezing. Using standards set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [1], COPD is diagnosed by spirometry with obstruction (FVC/FEV_1 ratio of <70) that is not fully reversible with bronchodilators. Although the vast majority of COPD is caused by smoking, up to 30% of COPD is caused by occupational exposures. COPD caused by occupational exposures has increased respiratory morbidity, including lower quality of life and functional status [2]. Agricultural exposures that can cause COPD are diverse. In concentrated animal feeding operations, workers are exposed to gases including ammonia and hydrogen sulfide; organic dusts that contain bacterial products such as peptidoglycan and lipopolysaccharide, fungal spores and particulate matter. All of these components can cause airway irritation and inflammation and over time can lead to airway obstruction. Other agricultural exposures include grain dusts, diesel exhaust particles, pesticides and herbicides.

A recent report showcased the cause-effect relationship of occupational exposures and COPD by assessing disease prevalence in a cohort of non-smoking dairy farmers [3]. In this cross-sectional study, dairy farmers were found to have increased prevalence of respiratory symptoms including cough, phlegm, and dyspnea, as compared to office workers. The rates of COPD were also higher; 10.7% of dairy farmers were found to have COPD, versus 2.7% in office workers. A survey performed in Saskatchewan revealed increased respiratory symptoms (chronic cough, chronic phlegm, shortness of breath, wheeze) in rural dwellers exposed to diesel fumes, fungicides, molds, or dusts [4]. Similarly, a report compared data collected between 2005-2010 from the Agricultural Health Study (a cohort of farmers and their spouses from North Carolina and Iowa) with data from the National Health and Nutrition Examination Survey [5]. Here, numerous respiratory symptoms were increased amongst those living on a farm, including wheeze, cough and phlegm. In the MICASA study performed on hired farm workers in California, a worse FEV_1/FEV_6 ratio was associated with more years in agriculture work [6]. Finally, Borlee and colleagues found that COPD patients living near farms had increased respiratory symptoms including wheeze and use of inhaled corticosteroids [7].

Direct and indirect pesticide exposures also present a risk for long-term respiratory diseases including COPD. DDT (1,1,1-trichloro-2,2-bis[4-chlorophenyl]ethane) was banned worldwide in 2004 (subsequent to its discontinued use and/or banning beginning in the 1970’s). Still, recent results from the Canadian Health Measures Survey highlight the potential long-term harmful effects of this chemical that can persist in soil for decades [8]. In this report, DDT or its breakdown product DDE (1,1-bis-[4-chlorophenyl]-2,2-dichloroethene) were still readily detectable in nearly all participants (not selecting for pesticide use/exposure); while DDE plasma levels dose-dependently correlated with FEV_1 reductions.

There are important potential confounders to consider when assessing COPD and other respiratory health risks with agricultural exposures. Socioeconomic status is a possible confounder in literature analyzing agriculture and pulmonary health effects, where findings of increased respiratory disease in farming communities could be linked to low socioeconomic status [4,9,10]. A recent report investigating the relationship between socioeconomic status and COPD in rural Poland revealed that farmers with COPD have smaller farm area than healthy farmers—indicating a relationship between lower socioeconomic status and COPD risk [10]. The Saskatchewan survey also observed lower household income to be related to cough, shortness of breath, and phlegm [4]. Interestingly, recent data suggest that some individuals are genetically less susceptible to the deleterious effects of agriculture exposures. Polymorphisms in two genes, TLR2 and NOS3, were found to have independent associations with lung function specifically in individuals working in swine operations (as opposed to nonfarming rural dwellers), where certain polymorphisms in these genes are protective against airway disease in these high-exposure settings [11,12].

Asthma

Agricultural work is associated with both occupational asthma and work-exacerbated asthma. Occupational asthma is caused by conditions at work, while work-exacerbated asthma is preexisting asthma that is made worse by working conditions. Asthma presents with coughing, wheezing, and chest tightness. It is diagnosed by spirometry that shows obstruction that is completely reversible with bronchodilators. Agricultural exposures early in life have traditionally been shown to decrease the rates of asthma in the children of farmers. Paradoxically, there is an increase in non-atopic asthma in livestock workers [13]. As agricultural practices change to concentrated animal feeding operations (CAFO), the exposures may no longer be protective, with higher rates of childhood asthma reported in children that live near CAFO’s [14].

Airborne allergens of multiple origins (e.g. fungi, animal) may contribute to allergic sensitization and asthma in farm workers. Ongoing investigations are aimed at better defining exposures experienced by farmers to learn how specific exposures lead to respiratory illness. In a recent study, Air samplers were used at pig, corn, poultry, and mushroom farms to size-selectively determine the fungal exposures of workers in these environments [15]. In this study, β-D-glucan sample levels correlated with total fungal spores and culturable fungi, as well as small (< 1 μm) fragments of *Alternaria* and *Botrytis* —fragments that could deposit in the lungs and lead to disease. No current occupational fungal exposure limit exists for agriculture; these findings reveal the possible utility of tracking β-D-glucan levels as an indicator for occupational exposures. Similarly, a recently developed PCR-based platform that identifies allergenic fungi levels in the environment may provide a means of determining actionable levels on a large-scale basis [16]. Potential animal allergens are also being explored as possible exposure indicators. In one investigation, dusts were collected from pig, dairy, and mink farmers in Denmark and bovine allergen levels were measured to determine if exposure levels were linked with allergy in farmers and non-farmers [17]. While bovine allergen levels were high in dairy farms, sensitization to the allergen was actually low in farmers. The authors conclude that while bovine allergen sensitization may be an issue for farmers with occupational asthma, the association between allergen level and symptoms remains unclear from this investigation, requiring additional studies.

Exposures to pesticides may also increase asthma risk. In the AGRICAN French cohort, occupational crop exposure as well as pesticide use were associated with increased risk for allergic asthma but not non-allergic asthma [18]. Agricultural Health Study findings indicate that exposure to certain pesticides, as well as certain farming activities are inversely related to risk of exacerbation in workers with active asthma, while a positive association is seen with certain pesticide exposures in workers with asthma as well as allergy [19]. The Saskatchewan survey found exposures to fungicides to be a significant predictor of chronic phlegm among farm residents [4]. In a study of adolescent Egyptian agriculture workers applying the organophosphate insecticide chlorpyrifos, the adolescent pesticide applicators had higher prevalence of reported wheeze compared to age-matched non-applicators [20]. At 5 months into the study (near the end of spraying season), increased cumulative urinary TCPy (3,5,6-trichloro-2-pyridinol; a chlorpyrifos metabolite) was associated with reduced FEV_1 and FVC spirometric measures. At 9 months, TCPy had returned to baseline and spirometric measures were no longer associated with TCPy levels, suggesting an acute effect of the insecticide on lung function.

Hypersensitivity pneumonitis

Hypersensitivity pneumonitis (HP) is also known as farmer’s lung and extrinsic allergic alveolitis. Patients typically present with chronic cough, dyspnea on exertion, fatigue, anorexia and weight loss. Pulmonary function testing shows restriction and an impaired diffusing capacity. CT scans reveal patchy ground glass opacities in the middle and lower lung zones as well as micronodules.

Certain farming environments clearly increase risk for hypersensitivity pneumonitis, including previously unrecognized or newer farming practices. Hypersensitivity pneumonitis has recently been associated with greenhouse farming—an agricultural practice that is increasingly common. In an epidemiological survey performed in Northeastern China, it was found that nearly 6% of greenhouse farmers were diagnosed with HP [21], along with nearly a quarter of subjects exhibiting upper respiratory tract infection symptoms, 19% exhibiting bronchial asthma, and 17% with COPD. In this study, risk factors for farmer’s lung included high humidity, large greenhouse size and low greenhouse height, greenhouse ventilation frequency greater than once in 4 hours and less than 30 minutes ventilation durations. Exposure to moldy materials and microorganism concentration in the near-surface soil of the greenhouse were also contributors. A recent analysis revealed that the standardized endotoxin exposure limit of 90 EU/m^{-3} was exceeded in 30% of samples from Danish flower greenhouses obtained during various seasons and tasks [22]. Mushroom farming is another increasingly popular farming practice that may present respiratory health risks. In a study of mushroom workers in Ireland, a high prevalence of respiratory symptoms was found, with approximately two out of three workers reporting work-related symptoms including cough, wheeze, and chest tightness [23]. Workers indicated improvement of symptoms while away from the workplace, and mushroom growers were most likely of all workers to have symptoms associated with airways disease (OR = 9.2). A recent case report reviewed the treatment of an adult male who presented with HP after working in mushroom production [24]. It was determined that Shiitake mushroom spores were the causative agents of the individuals HP, as eliminating the patient's exposure to the mushrooms alleviated his clinical symptoms.

Efforts are ongoing to ascertain safe practices and exposure level monitoring, and improved diagnostic criteria to prevent and detect occupational respiratory diseases like HP. A multilevel analysis performed by Gbaguidi-Haore, et al. assessed numerous studies to ascertain the factors contributing to agricultural HP in eastern France [25]. This study revealed that climatic conditions, particularly increased humidity, along with dense packing of hay were correlated with increased concentration of HP-causing microorganisms (e.g. *Absidia corymbifera*, *thermophilic actinomycetes*) in the hay. These findings point to less dense hay packing practices, hay drying, and use of respiratory protection (e.g. N95 or FFP3 respirators) when handling potentially moldy hay as means of preventing occupational HP.

Interstitial lung disease

Idiopathic pulmonary fibrosis is a progressive interstitial lung disease of unknown origin. It presents with insidious increases in dyspnea on exertion over a period of years, sometimes associated with a dry cough. "Velcro" crackles are heard over the lower lung fields. It is diagnosed by restriction on PFT's and an impaired diffusing capacity along with interstitial fibrosis on high resolution CT scan.

There is growing evidence that idiopathic pulmonary fibrosis can be linked to agricultural exposures. In 2000, a multi-center case-control study performed between 1989 – 1993 assessed the relationship between occupational factors and IPF [26]. Farming (OR = 1.6) and exposure to livestock (OR = 2.7) were two occupational factors found to be associated with increased odds for IPF. In 2006, Taskar and Coultas performed meta-analysis on numerous case-control studies performed since 1990 (including the study by Baumgarter, et al.) and found that agriculture/farming (OR = 1.65) and livestock exposures (OR = 2.17) were associated with significantly increased odds of presenting with IPF [27]. These findings led the authors to propose that IPF may actually be a diverse disorder caused by various occupational and environmental exposures. A recent Egyptian study showed increased risk (OR = 3.34) of IPF in female farm workers with occupational exposures to animal feeds, dusts, and pesticides significantly increasing their risk for IPF [28]. These findings suggest a link between occupational dust exposures and IPF. In another recent study in Korea, it was shown that dust-exposed workers (where dust exposure included wood, metal, sand, stone, diesel, or chemical exposure-related occupations) are more likely to develop early onset of IPF and have a longer history of symptoms prior to diagnosis. Dust exposed individuals also had a higher mortality (OR = 1.81) [29].

Another interstitial lung disease recently associated with agricultural exposures is pneumoconiosis. Characterized by inflammation and fibrosis, occupational pneumoconiosis is caused by the inhalation of inorganic dusts, which settle in the lungs and lead to alveolar inflammation and lung tissue remodeling. Pneumoconiosis presents with shortness of breath and is diagnosed by the presence of patchy dust macules or nodules in the lungs evident upon chest X-ray. In 2009, Schenker, et al. reported on findings of pneumoconiosis during lung autopsies of young Hispanic male farmworkers in California who died of causes unrelated to respiratory health [30]. Compared to non-farmworkers, these individuals had significantly higher prevalence of mineral dust small airways diseases, chronic bronchitis-like pathology, and pneumoconiosis.

Approximately 32% of agriculture workers had pneumoconiosis (macules or nodules) compared with only 8% of the non-farmers ($p = 0.003$), with an OR of 5.36 for pneumoconiosis with agricultural work after controlling for age and cigarette smoking. With the inclusion of interstitial fibrosis as a feature of pneumoconiosis, prevalence increased to nearly 42% in farmworkers compared to almost 19% in non-farmers ($p < 0.0001$). While findings are clearly complex, Schenker describes in a 2010 review that while reports studying the effect of inorganic dusts and pneumoconiosis are limited, current evidence meets criteria for a causal relationship between mineral dust exposures and the disease, supporting further investigations [31]. Particularly in dry regions with agricultural based economies, inhalable mineral dust levels can easily exceed occupational exposure limits, as shown in a survey of respirable dust and quartz concentrations from a sandy soiled farm in South Africa [32]. Thus, assessing occupational risks associated with these inorganic dust exposures is warranted.

Lung cancer

The association between agriculture exposures and lung cancer is complex and debated. In the Agricultural Health Study cohort, increased lifetime exposure days to the pesticide diazinon amongst male pesticide applicators corresponded to elevated lung cancer risk (RR = 1.60; p= 0.02) with a similar trend present based on intensity-weighted lifetime exposure days [33]. Regarding lung cancer histological subtypes, lifetime exposure days was significantly associated with adenocarcinoma. On the other hand, another analysis of the Agricultural Health Study also indicated a decrease in lung cancer risk with livestock and poultry production [34]. Here, increasing herd/flock size correlated with a decreased lung cancer risk in livestock farming, and the association between livestock/poultry farming persisted after controlling for smoking status. As a possible explanation to these contradictory findings, It is hypothesized that exposure to endotoxins by farmers involved in animal farming may be protective against lung cancer [35]. Lending support to this hypothesis, a study investigating cancer incidence among Finnish farmers from 1995 to 2005 found that dairy farming decreased risk of lung cancer, while dairy farmers’ risk increased with a switch to alternate types of farming (e.g. crop or beef) [36]. Similarly, an analysis on members of the United Farm Workers of America in California from 1973 – 2000 found farmers to be at reduced risk for lung cancer [37]. In a study assessing cancer risk in California farm workers from 1988 – 2010, less lung cancer was found in farm workers compared to a non-Hispanic white population assessed [38]. On the other hand, a study comparing farmers to non-farmers in the Province of Vercelli in Italy, farmers had increased risk of numerous cancers including lung cancer (OR = 1.59), with males having a higher lung cancer risk than females [39] The AGRICAN cohort study from France summarizing data collected from 2005 – 2009 reported no significant changes in lung cancer risk for farm owners and agriculture workers [40].

Conclusion

Modern agriculture leads to a wide variety of respiratory exposures. Here, we have provided a review of the recent literature describing the negative health consequences of various agricultural occupations, including crop and animal farming and pesticide application. The summarized reports reveal potential respiratory hazards associated with these occupations, including increased risk for COPD, asthma, HP, and interstitial lung disease. Additionally, new insight into exposure limits and respiratory disease detection are described. Together, these findings should be utilized in the development of safe work practices, identifying hazardous exposure levels and defining appropriate exposure limits in the agricultural workplace.

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Key Points

- Production agriculture produces a variety of dusts, vapors and fumes that can cause respiratory symptoms and disease.
- Agricultural exposures can lead to the development of several diverse lung diseases, including: COPD, asthma, hypersensitivity pneumonitis, and interstitial lung disease.
- Agricultural exposures can also worsen symptoms caused by preexisting lung disease.
- Clinicians should inquire about agricultural exposures while trying to determine the etiology of unexplained respiratory symptoms.