Published in final edited form as:
Curr Allergy Asthma Rep. ; 18(12): 65. doi:10.1007/s11882-018-0820-8.

Agriculture Occupational Exposures and Factors Affecting Health Effects

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Abstract

Agriculture environments contain a variety of inflammatory aerosols that may increase risk for lung inflammation and disease in exposed individuals. In addition, epidemiological studies have also identified protective effects of rural environments and farming exposures. In this review, we will discuss recent literature published since 2016 that investigates the impact of differing agricultural exposures on respiratory health. Discussions include the impact of farming modernization, education and personal protective equipment usage amongst workers, timing and duration in mediating lung health outcomes, and population studies investigating the association between exposure and risk for numerous lung diseases.

Keywords

agriculture; work exposure; health effects; factors affecting

Introduction

Occupational and environmental exposures in agriculture settings are known to elicit lung inflammatory responses and increase risk for numerous lung diseases. Conversely, certain exposures have been identified as protective against allergy/atopy, lung cancer, and other ailments. It is clear that the diversity of organic aerosols and other environmental contaminants in different farming environments account for a portion of these differing respiratory responses, while timing and duration of these exposures is also important in driving lung health outcomes. Furthermore, changes in farming practices including farm modernization, education, and health risk awareness may also impact respiratory health outcomes in exposed individuals. Herein we provide a background of agriculture work exposures and respiratory disease risk, with a focused review of literature published since 2016.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent: This article does not contain any studies with human participants or animals performed by any of the authors.

Methods

PubMed literature searches were performed as follows: Years searched: 2016 – 2018, journal articles (searches performed May – June 2018) Terms Searched: “agriculture work exposure disease”, “agriculture lung disease”, “farming exposure lung disease”, “occupational lung disease agriculture”, “occupational lung disease farming”, “occupational respiratory disease farming”, “agriculture exposure respiratory disease” Selection: Articles were selected from the above search results based on topic fit. Exclusions included articles related to animal respiratory health and disease (with the exception of preclinical animal models studying human disease conditions); studies of emerging pathogens with farming as a pathogen source, including influenza and mycobacterium tuberculosis, with exception for documented or modeled disease association in humans; non-agricultural occupation-associated exposures causing lung disease, e.g. mining; agriculture exposure-associated diseases unrelated to the lung, e.g. gastrointestinal diseases; review articles.

Historical records of the recognition of dangers associated with farming work

The earliest history of identification of dangers associated with working in certain professions comes from Egyptian papyrus and Hippocrates. Hippocrates identified colic due to lead exposure and later many cultures around the world began to understand the risks associated with mining and other professions (reviewed in [1]). Agriculture operations and associated risks were first noted by Swedish writer Olaus Magnus. In his book (published in 1555), Magnus documented the “damage to the vital organs of threshers from inhaling the grain dusts” [2]. Later, Bernardino Ramazzini, an Italian physician also wrote about dangers of inhaling the grain dust (reviewed in [3]). The negative health effects of exposure to grain dust and other on-site contaminants in agriculture work settings have remained a major focus of current research.

Development of industrial-scale farming and health impacts

In the 20th century, increases in the global population coupled with higher demand for food (protein source) has profoundly influenced the food production system. In order to produce large amounts of food with greater feed efficiency and by using smaller land area, concentrated animal feeding operations (CAFOs) began to evolve [4]. These more efficient production systems have adopted industrial production principles and have led to maximized production and profits. However, these changes have come at a cost. CAFOs are known to generate and store many contaminants on-site. Most of these contaminants are either animal origin (manure, urine and gas) or feed components, pesticides, or other noxious materials.

Airborne organic dust (OD) that contains particulate matter of varying sizes, microbes and microbial products such as lipopolysaccharides (LPS), peptidoglycan (PGN), fungal cell wall components and viral particles pose risk for the development of a variety of respiratory and other symptoms. Although a large number of gases in farm work settings have been identified, methane (CH_4), ammonia (NH_3), hydrogen sulfide (H_2S), carbon monoxide (CO) and carbon dioxide (CO_2) pose greater health risks for both workers and animals (reviewed in [5]). In addition, a large number of volatile organic compounds (VOCs) present in the CAFO environment are known to produce unpleasant odor contributing to negative health effects and affect the communities that live in the neighborhoods surrounding the CAFOs [6].

Health impacts of working in various agriculture and animal production facilities are many-fold, and the majority of the symptoms indicate respiratory exposure to irritants. Full-time barn workers, veterinarians and residents near CAFOs are exposed to various contaminants and report symptoms ranging from irritation of mucus membrane, eyes, nasal congestion and runny nose, wheezing, coughing and dyspnea, asthma, asthma-like symptoms, exacerbation of pre-existing asthma, chest tightness and exercise intolerance. Particularly, barn workers experience annual decline in their lung function (reviewed in [7]).

Occupational contaminants present in the work setting with their physical, chemical and biological properties and concentration create a complex exposure driving a host innate inflammatory response. Since varieties of contaminants are involved, understanding how these multiple factors interact is an emerging challenge.

Pesticide exposure

Pesticide is a term that is broadly used to encompass all agents that are used against the crop pests such as insecticides, fungicides or herbicides. Hence, pesticides form major occupational contaminants in modern agriculture and animal production systems as well as in floristry, veterinary medicine, wood and building material protection and in gardens. A recent review [8] summarizes how organophosphate (OP) exposure causes airway reactivity and asthma. It is alarming to note that high levels of pesticides are found in the homes of farming families [9]. Pesticide exposure occurring via dermal, digestive, or respiratory routes results in reduced lung function [10], wheezing [11], higher incidences of lung cancer [12], chronic bronchitis and chronic obstructive pulmonary disease (COPD) [13], coughing, rhinitis, asthma and other respiratory symptoms [14]. Respiratory inflammatory mechanisms of pesticide exposure are being examined using animal models (reviewed in [15]).

Zoonotic Disease Risk

Working in agriculture and animal production environments is a risk factor for acquiring one or more zoonotic pathogens. Workers who spend time in the vicinity of animals, urine, manure, feed, soil and contaminated water are at the risk of contracting fungal infections, pathogens with antibiotic resistance genes, tuberculosis, campylobacteriosis, brucellosis, cryptosporidiosis and giardiasis, drug resistant staphylococcus spp., salmonellosis, horse flies, influenza virus, *Escherichia coli* and a number of other pathogens. Some of these agents cause acute and or chronic respiratory symptoms and are a significant public health concern (reviewed in [16]).

Innate immune mechanisms of organic dust exposure

Innate inflammatory mechanisms of exposure to dust in the agriculture work environment has been studied using human volunteers, laboratory animals and various *in vitro* models (reviewed in [15]). We used a unique rat model of human occupational exposure and demonstrated that a single eight-hour exposure induces lung inflammation and airway reactivity, and a 20 day exposure dampens airway reactivity [17]. Using strains of mice that either carried or lacked a functional Toll-like receptor 4 (TLR4), we showed that barn exposure-induced lung inflammation, but not airway reactivity, is dependent on a functional *tlr4* gene. Next, several other researchers have demonstrated the role of protein kinase C (PKC) [18], TLR9 [19], TLR2 [20], MyD88 [21], and Nucleotide-binding and oligomerization domain 2 (NOD2) [22] indicating the involvement of several innate signaling pathways in responding to organic dust exposure. Our recent work examined various kinome (set of protein kinases) signaling pathways in human airway epithelium and monocytic cell lines and concluded that the innate inflammatory response to organic dust involves several overlapping signaling pathways [23].

What factors impact agriculture work exposure effects?

It is known that agriculture on-site contaminants not only impact workers, but affect families and other residents in the vicinity. A number of factors such as a farm size and type, animal density, feed type, floor space, grower or finisher stage pigs, ventilation, farm location, local weather patterns, residential area location and many more factors are likely going to influence the exposure to contaminants and health effects.

Rural residence/farming proximity

A recent study utilized the SPIROMICS cohort to assess the relationships between rural residence, urban residence, and agriculture-related occupation/exposure, and prevalence of COPD incidence and exacerbations [24]. Investigators identified that individuals living in a rural residence had increased odds of experiencing COPD exacerbations compared to those living in urban environments, while self-reported asthma diagnoses were significantly less prevalent in individuals from rural regions than urban regions. Furthermore, when considering agriculture exposure in this population, agriculture exposures independently increased odds for total and severe COPD exacerbations; when these exposures were considered in multivariate analyses, they attenuated the association identified between rural living and exacerbations. They did not, however, entirely explain the relationship between rural residence and COPD exacerbation incidence risk, suggesting other factors are also at play. This study was corroborated by investigations in the Netherlands where the impact of residential proximity to livestock farms on exacerbations in COPD and asthma patients were assessed. Here, investigators found increased exacerbation rates in COPD patients, but not asthma patients, when patients lived in areas of concentrated livestock farming [25]. Another study performed in the Netherlands utilized the VGO study (Dutch acronym for “Farming and Neighbouring Residents’ Health”; a project designed to assess whether residence in the vicinity of livestock farming has negative health impacts). VGO data from 2012 were used to assess the impact of residence proximity to livestock farms found a significant positive association between ammonia emissions within 500 meters of livestock farms and allergic rhinitis in COPD patients [26]. However, authors noted a significant protective effect of livestock farming proximity and reported respiratory symptoms among patients, leading to somewhat inconclusive findings. Adding to these findings, living in a community with high density of livestock farming in the Netherlands also was associated with reduced contact with general practitioners and respiratory symptom reporting [27]. Although, when considering individuals living less than a half kilometer from poultry farming operations having greater than 14,000 animals, authors identified significant increases in general practitioner contacts for respiratory-related diagnoses or infections.

Further considering livestock farming proximity, investigations in the Netherlands also assessed the impacts of living within a kilometer of one or more livestock farms on lung health outcomes in non-farming residents [28]. From this study, it was identified that individuals living in close proximity to livestock farming experienced reduced lung function outcomes, and also experienced temporal-based effects, whereby lung function reductions were found to correlate with increased week-average ambient ammonia levels. Of note, spatial effects identified were particularly prominent in atopic individuals. In another investigation evaluating a Pennsylvania population, residential proximity (within 3 miles) to industrialized food animal productions was also found to be associated with increased odds of asthma-related hospitalizations and oral corticosteroid use [29].

Early life/childhood farm exposures and disease risk

While a study performed using the Agricultural Health Study recently identified that early life exposure to farming environments was associated with strong protective effects against atopy in adulthood, early farming exposure was found to provide little to no protection against asthma in adults [30]. However, a study performed using the European Community Respiratory Health Survey II identified a respiratory protective effect of living on a farm within the first 5 year of life, including significantly decreased odds ratios for adult atopic asthma, atopic rhinitis, or any atopic sensitization as compared to individuals living in an inner city in early life [31]. There were no associations found with non-atopic asthma. Interestingly, this study also found that women who lived in a farm environment during early life also had significantly higher FEV_1 compared to those living their first 5 years in an inner city environment. Another investigation assessed the impact of early life farm exposure with or without current farm exposure and no farm exposure in altering incidence of asthma or hay fever in adults living in Saskatchewan, Canada. In this investigation, women with early farming exposure (in first year of life) had reduced risk of both hay fever and asthma as an adult, while men reporting currently living on a farm (with no early farming exposure) had increased asthma prevalence, and no significant protective effects of early farming exposure on hay fever or asthma incidence [32]. Pesticide exposure was not found to modify asthma or hay fever prevalence in this cohort.

Indoor endotoxin levels found in a US farming population were compared with adult asthma incidence using a cohort from the Agricultural Health Study [33]. Here, investigators found a significant positive association between indoor endotoxin levels and odds of asthma. Interestingly, this association was more marked in individuals that were not born on a farm, although a significant (although weaker) association between endotoxin levels and asthma still existed in individuals who were born on a farm. This study also identified that these associations were unrelated to atopy, as endotoxin levels increased incidence risk for both atopic and non-atopic asthma, and endotoxin levels were not associated with allergic rhinitis symptoms in the past year.

Concerning the effects of the farming environment on child health, a recent investigation assessed the impacts of indoor dusts found in the homes of children from Amish and Hutterite families, who utilize traditional versus industrialized farming practices, respectively. In this study, the dusts from the Amish family homes, but not Hutterite homes, elicited protection against an *in vivo* model of allergic asthma [34]. These *in vivo* data corroborated findings of significantly decreased asthma and allergic sensitization in the Amish children that corresponded with increased endotoxin levels in the collected Amish home dust samples. A study of Argentinean children between 13–14 years also identified protection against odds of wheeze and allergic rhino-conjunctivitis in children who had contact with farm animals and/or resided on a dairy farm [35]. Another investigation utilized the Canadian National Longitudinal Survey of Children and Youth to assess how living on a farm impacted respiratory health in children. Here, children who entered the study in 1994–5 with no asthma diagnosis were followed until they turned 25 years old [36]. Over 14 years, the incidence of asthma in children who lived on a farm was significantly lower than those living in a non-rural environment (10.18% versus 16.50%), with a 44% reduction in asthma incidence based on a multivariate analysis. These findings were further corroborated by a study performed in urban and rural children in southeast China, where investigators found that living in a crop-farming family at less than 1 years old resulted in about an 80% risk reduction for asthma in children surveyed at 13 – 14 years [37]. This study also identified a significantly reduced incidence of asthma in children having high indoor endotoxin levels. On the other hand, a recent report of findings from the United States 2008 Minority Farm Operator Childhood Agricultural Injury Survey (M-CAIS) identified that children (ages 0 – 19 years) who were working on their household farms had significant increased prevalence of asthma (13%) compared to children who were not participating in the farming operations (9%) [38]. Investigators also found that asthma prevalence differed by sex, age, measures of socioeconomic status, and farm operator race. Furthermore, early-life organophosphate pesticide exposures were recently identified to be associated with reduced lung function in children. Using the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) cohort, investigators found that urine levels of several organophosphate metabolites, measured between 6 months and 5 years of age, were negatively associated with lung function measures taken at 7 years [39].

Farming modernization, PPE, and preventive efforts

Efforts are ongoing to assess how farming modernization, education practices, access to personal protective equipment (PPE), and implementation of other safety measures in farming environments are impacting incidences of occupational injuries and disease. With regards to farm modernization, in a study of 575 dairy farmers, it was found that working in modernized farms was associated with a decreased prevalence of COPD, as compared to individuals working in traditional dairy farms [40]. Specific modernized farm characteristics that were associated with decreased incidence of COPD included separation of house/residence and cowshed, having a loose bovine housing system instead of a tie stall system, and having larger farms, measured by area and herd size. It was further identified that dairy workers who smoked tobacco and worked in a traditional dairy farm setting had a synergistic increase in risk for COPD development, suggesting that modernization may alter multiple-exposure effects.

With regards to education, perceptions, and PPE usage, numerous studies have identified discrepancies between knowledge/education regarding the harmful effects of aerosols in farming environments, protective effects of respiratory protection, and regular usage of these PPE. In a small cohort study assessing respiratory symptoms and PPE perceptions and usage in 24 poultry farm workers from small farms in North Carolina, while greater than 75% of workers asked whether they “wear respiratory protection” indicated respiratory PPE as important, less than half of the individuals reported commonly or ever utilizing respiratory protection [41]. Several respondents elaborated on difficulties in respiratory PPE usage, indicating that paper dust masks were subject to clogging and/or becoming too damp from perspiration, while half-face masks were described as being too hot to wear, or too costly. These findings regarding inconsistent respiratory PPE usage were corroborated in a recent large-scale study utilizing the 2011 Farm and Ranch Safety Survey, where farm operators were assessed for respiratory use and asthma incidence [42]. In this study, less than 40% of farm operators reported utilizing respirators (defined as respirator or dust mask usage) in the past year. Farm operators with asthma were more likely to wear respirators than farmers without asthma (47% versus 35%), and amongst operators with asthma, approximately two-thirds of those with work-related asthma reported respirator use, while only 44% of operators with non-farm-related asthma used respirators. Farm operators reporting pesticide use were over 3 times more likely to use respirators, with about 55% reporting use within the past year. In this study, crop farmers were more likely to use respirators than livestock farmers.

The finding of increased respirator usage amongst crop vs. livestock farmers in the 2011 Farm and Ranch Safety Survey study [42] may be supported by outcomes identified in another recent study investigating the perceptions and knowledge of farm operators in the Midwestern US regarding respiratory PPE. In this study of nearly 300 farm operators, greater than 95% of farm operators were aware that use of respiratory PPE (defined as respirators/masks) would reduce dust-related exposures [43]. However, respondents reported using PPE for dust exposures less than 50% of the time. Collectively, about 25% of respondents indicated they disagreed or did not know that continual dust exposure could result in COPD. Further, about 15% did not agree that dust exposures occur from animal confinement settings and 40% were unaware that dusts in these environments contain respirable toxins. The top reason reported for lack of PPE use was that the respondent would “forget.” Reasons cited for not wearing PPE included that the masks were “uncomfortable” or “not necessary”, and individuals indicating “other” reasons for not using PPE indicated lack of respirator availability, or that they considered respiratory use to be ineffective. In another investigation where pulmonary function and PPE usage was assessed in 80 Latino thoroughbred workers, similar results were found [44]. Here, nearly 80% of participants reported having respiratory symptoms, while 94% of workers indicated they infrequently used dust masks.

Taken together, these investigations highlight numerous opportunities for intervention to improve the health and safety of farm workers. Potential improvements include continued modernization practices to reduce exposure risks, as well as attempts to increase education and awareness of the risks of respirable dusts in farming exposures, including how these hazardous exposures may increase lung disease risk.

Population-level Assessments of Occupational Disease Risk

Lung Cancer

Numerous recent studies have assessed the impact of farming occupational exposures on lung disease risk. Building upon previous epidemiological evidence for a protective effect of farming occupations and lung cancer risk, a recent study utilizing the Agriculture and Cancer (AGRICAN) cohort has identified that cattle exposure duration was inversely related to lung cancer risk, with a trend towards decreased lung cancer risk in horse farmers as well [45]. Interestingly, the protective effects of cattle exposure were only identified in individuals who had early life (infancy) exposure to cattle, as opposed to first exposure being occupational, and was associated with protection specifically against lung adenocarcinomas. Swine and poultry farming did not exhibit similar protective effects, and there was a significant positive association between lung cancer risk and number of pigs in swine farming. Another investigation assessing the impact of occupational endotoxin exposure and lung cancer risk also identified a protective effect for farming exposures. In this ICARE Study (Investigation of occupational and environmental causes of respiratory cancers; a French population-based study), high exposure settings, including dairy, cattle, swine, and poultry farms, were associated with reduced risk for disease even decades after exposures ceased, with greater exposure durations also associated with greater reductions in lung cancer risk [46]. Similar to the findings of the AGRICAN cohort, the strongest inverse relationships were with lung adenocarcinomas.

Asthma/Allergic Rhinitis

A recent investigation utilized the 2011 Farm and Ranch Safety survey to evaluate potential associations between farming and incidence of allergic rhinitis [47]. In addition to identifying higher prevalence of allergic rhinitis among farm operators compared to the general population, in this study authors also reported a significant positive association between pesticide use and lifetime allergic rhinitis and combined asthma and lifetime allergic rhinitis.

A cross-sectional survey assessing asthma diagnosis and symptoms incidence in residents of Telemark, Norway identified increased odds ratios for wheezing and asthma diagnosis in individuals falling within the occupational category that included agriculture/fishery workers and craft/related trade workers [48]. Although, no associations were identified amongst those with the specific occupation designation of “agricultural labour.”

A study assessing how occupation modifies risk for disease amongst farmers in Poland identified that during 2000 – 2014, 12% of the reported occupational diseases were bronchial asthma and about 5% were allergic rhinitis [49]. Interestingly, the mean age of farmers that had asthma and/or allergic rhinitis diagnoses was significantly higher than that of the general population having the same diagnoses. However, these authors and others have cited that underreporting of occupational diseases is likely prevalent, and incidences of occupational respiratory diseases may be much higher than reported. Similarly, an investigation into the associations between farming and “united airway disease” in eastern North Carolina identified that while 35% and 66% of farmers/workers reported lower and upper airway symptoms, respectively, only 1% and 7% of the farmers had a physician diagnosis of rhinitis or asthma, respectively [50]. Furthermore, there was a significant association between upper and lower airway diseases in these farmers/workers; authors argue that considering this “united airway disease” may lead to improved early diagnosis and treatment options to prevent airway health problems in agriculture workers.

Another study also identified a high prevalence of reported respiratory symptoms but low levels of diagnosed disease. In this study of 372 Irish farmers, 62% of participants reported chronic respiratory symptoms, with 40% reporting upper respiratory symptoms [51]. Yet, only 13% of the farmers had a previous diagnosis of airways disease. Interestingly, in this cohort, greater than 60% of the participants were never-smokers, and there was no significant difference in the proportion of individuals reporting respiratory symptoms among smokers and non-smokers.

Interstitial Lung Disease

A retrospective study was performed to identify how pigeon breeding modifies risk for hypersensitivity pneumonitis and other interstitial lung diseases. Using records from the Danish Racing Pigeon Association identifying nearly 7,000 pigeon breeders and compared with over 276,000 matched individuals from the Danish population, authors identified significant positive associations between pigeon breeding and hypersensitivity pneumonitis and other interstitial lung diseases, with a 56% overall increased risk [52]. In particular, the adjusted hazard ratio for hypersensitivity pneumonitis was 14.36 compared to the general population.

COPD

A cross-sectional study of farmers in France identified significantly increased risk for COPD in cattle breeders, poultry farmers, pig breeders, and farmers having at least two livestock types, as compared to non-farming workers [53]. Although, authors also identified variability in findings based on geographic region and criteria utilized to define COPD (Global Initiative for Chronic Obstructive Lung Disease [GOLD] versus Quanjer reference equation [LLN]).

Cardiorespiratory Disease

In results reported from the National FINRISK 2007 study (a nationwide survey conducted in Finland for monitoring risk factors for chronic disease), individuals working in agriculture industries were at greater risk for heat-related cardiorespiratory symptoms (odds ratio of 2.27 as compared to industry work) [54].

Summary

Working and/or living near CAFOs is a risk factor for development of various respiratory diseases due to exposure to a variety of contaminants including organic dust, pesticides and zoonotic pathogens. Host innate response to exposure involves complex and overlapping signaling pathways. The complex exposure and host responses result in many challenges to develop effective therapies. Several factors such as rural residences, early life exposures, use of protective equipment, and worker education influence exposure effects. An integrated system of development of better therapies through biomedical research, design of engineering controls to regulate contaminants and agriculture safety education of stake holders will likely reduce farm contaminant-induced respiratory disease burden.

Acknowledgement:

Dr. Nordgren's research is supported by NIEHS (R00ES025819). Dr. Charavaryamath's research is funded through a startup grant from Iowa State University and CDC-NIOSH pilot grant (5 U54 OH007548).

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