HHS Public Access

Author manuscript

J Asthma. Author manuscript; available in PMC 2017 June 01.

Published in final edited form as:

J Asthma. 2016 June ; 53(5): 471–477. doi:10.3109/02770903.2015.1116089.

Occupational agriculture organic dust exposure and its relationship to asthma and airway inflammation in adults

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Abstract

Objective—Recent studies have made advances into understanding the complex agriculture work exposure environment in influencing asthma in adults. The objective of this study is to review studies of occupational agricultural exposures including dust, animal, and pesticide exposures with asthma in adult populations.

Data Sources—PubMed databases were searched for articles pertaining to farming, agriculture, asthma, occupational asthma, airway inflammation, respiratory disease, lung disease, pesticides and organic dust.

Study Selections—Studies chosen were published in or after 1999 that included adults and asthma and farming/agricultural work or agricultural exposures and airway inflammatory disease measurements.

Results—The data remains inconclusive. Several retrospective studies demonstrate agricultural work to be protective against asthma in adults, especially with increased farming exposure over time. In contrast, other studies find increased risk of asthma with farming exposures, especially for the non-atopic adult. Mechanistic and genetic studies have focused on defining the wide variety and abundance of microorganisms within these complex organic dusts that trigger several pattern recognition receptor pathways to modulate the hosts' response.

Conclusion—Asthma risk depends on the interplay of genetic factors, gender, atopic predisposition, type of livestock, pesticide exposure, and magnitude and duration of exposure in the adult subject. Longer exposure to occupational farming is associated with decreased asthma risk. However, studies also suggest that agricultural work and multiple types of livestock are independent risk factors for developing asthma. Prospective and longitudinal studies focusing on genetic polymorphisms, objective assessments, and environmental sampling are needed to further delineate the influence of agriculture exposure in the adult worker.

Keywords

farm; immunology; lung; innate; adaptive

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Introduction

Agriculture is a major global industry. Since 2009, it has accounted for 35% of employment worldwide (1). In the United States alone, 3.2 million people are currently farming (2). In this occupation, workers may be exposed to multiple types of livestock and crops, as well as animal feed, pesticides, solvents, engine exhausts, dusts, and microbes (3, 4, 5). With recurrent inhalation of these potentially hazardous materials, adult agriculture workers are at risk for respiratory diseases such as asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), and hypersensitivity pneumonitis (HP) (5, 6-13). Numerous studies in children demonstrate a strong protective effect of growing up around agriculture environments against the development of atopy and asthma (14, 15). However even among children, the data is dependent on exposures. A study performed in Iowa found that children who lived on farms tended to have decreased atopy, but those children living on a farm that raised swine had increased prevalence of asthma (44-56%) as compared to non-farming rural children (33.6% prevalence) (16).

The impact of agricultural exposures in asthma and allergy in adult populations is complex and less clear. This article aims to review the current literature on new-onset and exacerbated adult asthma and airway inflammation as it is related to farming exposures. Understanding the asthma phenotypes, airway inflammatory profile, and mechanisms involved in disease development might lead to strategic strategies to reduce risk factors and preventative and/or therapeutic approaches to protect adult agricultural workers from adverse airway disease consequences.

Methods

PubMed databases were searched for articles pertaining to farming, agriculture, agricultural, asthma, occupational asthma, airway inflammation, respiratory disease, lung disease, organic dust, and pesticides. Studies chosen were published in or after 1999 that included adults and asthma and farming/agricultural work or agricultural exposures and airway inflammatory disease measurements.

Results

Is farming protective against new-onset or exacerbations of adult asthma?

Several studies demonstrate that environmental agriculture exposures protect adult populations from the reporting of asthma and/or asthma symptoms. Douwes et al. (17) retrospectively compared New Zealand subjects who had never been exposed to a farming environment to subjects who were current farmers. A questionnaire, based on the survey from the European Community Respiratory Health Survey (ECRHS) (18), was sent to 2509 families who had farming exposure to dairy, beef, sheep, crop, and/or orchards as well as to 1001 nonfarming families in the same rural area (17). In subset analysis of the adult population (average age of 48.9 and 42.6 years in the farming and nonfarming groups, respectively) differences in respiratory risk were discovered. When compared to the non-farmers with no childhood exposure, current farmers had reduced risk of shortness of breath (odds ratio [OR]: 0.63; confidence interval [CI]: 0.47-0.84; $p < 0.01$), wheeze (OR: 0.80; CI:

0.65-0.99; p < 0.01), asthma medication use (OR: 0.68, CI: 0.51-0.9; p < 0.01), or ever having asthma (OR: 0.69, CI: 0.56-0.85; p < 0.01) (17). The authors interpreted this to be an intermediate risk reduction of asthma symptoms with active farm exposure. Among the adults who had childhood farming exposure but no current farm exposure, there was no or only slightly reduced risk (shortness of breath OR 0.97, CI 0.65-1.44; wheeze OR 1.01, CI 0.75-1.34; asthma medication use OR 0.78, CI 0.51-1.19; ever having asthma OR 0.87, CI 0.63-1.19) (17). This study suggests that ongoing exposure to farming environments in adulthood reduces the risk of current respiratory symptoms as opposed to history of childhood exposure with no active farm exposure.

Thoan et al. specifically evaluated ongoing livestock exposure (4). Adults age 16-66 years (at baseline) were examined in 1993-1994 and grouped by occupation: dairy farmers, nondairy agricultural workers (including farmers with other types of livestock and non-livestock farmers), and a control group (agricultural administrative workers). Subjects completed a medical questionnaire based on surveys from the American Thoracic Society and the ECRHS, an occupational questionnaire about their working status and exposure to hay or straw and animal feed, and underwent spirometry testing. These investigations were repeated in 1999 and 2006, with the addition of oximetry testing in 2006. Researchers found that farmers who *formerly* worked with hay, straw, or animal food had higher prevalence of respiratory symptoms than those who *currently* have exposure to these materials (4). Specifically, *former* workers had increased self-reported asthma (OR: 8.37; CI: 1.78-39.25 and OR: 5.69; CI: 1.53-17.04, for hay or straw and animal food, respectively) and doctor-diagnosed asthma (OR: 7.51; CI: 1.59-35.41 and OR: 4.56; CI: 1.36-15.33, for hay or straw and animal food, respectively) as compared to administrators (4). While *current* workers has less risk of self-reported (OR: 1.20; CI: 0.21-6.28 and OR: 0.50; CI: 0.09-2.84, for hay or straw and animal food, respectively) and doctor-diagnosed asthma (OR: 0.93; CI: 0.15-5.81 and OR: 0.26; CI: 0.03-2.39, for hay or straw and animal food, respectively) (4).

The Douwes et al. study (17) also investigated how duration of occupational farming may play a role in determining asthma risk. Researchers found that the more years spent farming, the less likely a subject was to report symptoms of asthma or use of asthma medication. The relationship was inversely dose-dependent until approximately 40-50 years of age, whereby asthma prevalence plateaued at approximately 13% prevalence (17).

Eduard et al. (19) showed a protective effect of farming against atopic and nonatopic adult asthma. They compared rates of asthma in 2106 Norwegian farmers to 727 urban and 351 rural subjects in neighboring towns. The study population was pooled from adults 21-69 years old, who were independently studied in 1998, 1991, and 1988, respectively (19). Asthma prevalence was determined by questionnaires and defined as physician-diagnosed asthma. Presence of atopy was defined by one positive radioallergosorbent test (RAST) for IgE to birch, timothy grass, or house dust mites. The authors found a decreased prevalence of atopic and nonatopic asthma among farmers (OR: 0.52; CI: 0.36-0.75) and among rural residents (OR: 0.77; CI: 0.45-1.3) as compared to their urban counterparts (19). They found no difference in atopy status among the farming population (OR: 1.0, CI: 0.76-1.4) and rural population (OR: 0.89, CI: 0.58-1.4) in comparison to the urban population (19). This later

observation promotes the concept that occupational exposure to agriculture work, independent of atopy, is mediating asthma risk reduction.

A US study by Hoppin et al. (20) supports both decreased prevalence and decreased incidence of adult asthma in farmers. This prospective cohort study compared data from the Agricultural Health Study (AHS) of pesticide users in Iowa and North Carolina to data from the general public via the National Health and Nutrition Examination Survey (NHANES). Ever having asthma and adult-onset asthma were both less prevalent among the AHS group as compared to the NHANES group (Prevalence Ratio [PR]: 0.54; CI: 0.49-0.59, and PR: 0.65; CI 0.57-0.74, respectively) (20). However, in the AHS group, wheezing was more prevalent (PR: 1.66; CI 1.51-1.82) (20). As the study evaluated patients at two separate 5 year intervals, researchers were also able to evaluate for new cases of asthma. The incidence rate in the AHS population was 2.1 (per 1000 person-years) versus 4.0 (per 1000 person-years) in the NHANES population (20). This study supports decreased asthma, both new-onset and ever asthma, in adult farmers.

Henneberger et al. (21) utilized the AHS data, but evaluated only the 925 adults with active asthma, as defined by having at least 1 episode of wheezing or whistling in the past 12 months and having a breathing problem in the same time period. It was discovered that 22% (N=202) of these pesticide applicators had asthma exacerbations in the past 12 months, defined by a visit to the emergency room or doctor for an episode of wheezing or whistling in the past 12 months (21). Two pesticides (glyphosate and paraquat) were inversely associated with asthma exacerbation (OR: 0.5; CI 0.3-0.8, and OR: 0.3; CI: 0.1-0.9, respectively) (21). However, it was unclear if farmers were less-responsive to these pesticides or if they had stopped using them due to symptoms.

Is farming a risk factor for new-onset or exacerbations of adult asthma?

In contrast to the concept that occupational farming is protective against asthma, several studies have shown that adult exposure to farming increases the likelihood of developing asthma or asthma-like symptoms. The ECRHS was a large, multicenter prospective study that included 15 637 participants across 14 industrialized countries that was completed in two parts (18, 22, 23). An initial survey was conducted in 1991-1993 and then any persons with positive respiratory symptoms on their questionnaire, as well as 20% random sample of the study population to serve as the control group, were re-contacted to undergo more detailed questioning, clinical exams, spirometry, and methacholine challenges The second part, conducted from 1998-2003 involved contacting the initial participants for a follow up survey and repeat investigations (18, 22, 23). Using data from the ECRHS, Kogevinas et al. (23) prospectively investigated asthma risk, defined as bronchial hyperresponsiveness and reported asthma symptoms or medication, across multiple occupations. Amongst occupational groups, farmers had the highest risk of asthma (OR: 2.62; CI: 1.29-5.35) when compared against a reference group of professionals, clericals, and administrators (23). Another study across occupations was conducted by Karjalainen et al (24), who aimed to understand how many new cases of adult asthma were attributable to work. Through national registries, employed Finns with no known asthma, ages 25-59 were identified and followed from 1986-1998 at 3-5 year intervals. New cases of asthma were identified via

reimbursement programs for asthma medications. The occupation group consisting of agriculture, forestry, and commercial fishing was at increased risk of new-onset asthma (Relative Risk [RR]: 2.12; CI 1.99-2.26 for men; RR: 1.84; CI 1.76-1.92 for women), as compared to the administrative reference group (24). Both of these studies advocate that adults in farming or similar occupations are at increased risk for developing asthma.

A longitudinal, prospective study in Denmark by Omland et al. (25) followed farming school students for 5 years to observe for new-onset asthma with a control group of rural students who were not enrolled in farming school. Participants' ages at enrollment ranged from 16-26 years with a mean age of 19.2 years. Students participated in an annual health assessment questionnaire and telephone interview. If at least 1 symptom indicative of asthma was reported, the farming student and a subject from the control cohort both underwent physical exam, spirometry, tests for bronchial hyperresponsiveness, and allergy skin pick tests. Overall, the authors discovered 122 new cases of asthma with agricultural school students comprising 88% (N=107) and non-farming students comprising 12% (N=15) of new asthma cases (25). There was no difference in the proportion of atopy among the two groups, but the type of animal exposure was found to be an important factor in the risk of asthma. Specifically, the highest risk was for raising hogs (OR: 3.37; CI: 1.63-6.97) and cattle (OR: 2.47; CI: 1.14-5.34) (25).

Others have also shown that exposure to livestock might represent an important risk factor with reporting asthma symptoms. Eduard et al. (3) enrolled adults currently farming in Norway, and grouped farmers by farm product produced to assess and compare health conditions. When compared to non-atopic crop farmers, non-atopic farmers working with multiple types of livestock were more likely to have asthma (OR: 1.9; CI: 1.1-1.3) (3). In contrast, atopic farmers with multiple types of livestock were less likely to have asthma (OR: 0.32; CI: 0.11 to 0.97) as compared to atopic crop farmers (3). This apparent dichotomy underscores the complex interplay underlying the adult response to agriculture exposures, and suggests that pathways involved in asthma risk in non-atopic individuals might confer protective effects for atopic individuals.

The organic materials workers handle when raising livestock may play a substantial role in exposures that contribute to adult farmers increased risk of respiratory disease. The aforementioned study by Thaon et al. (4) found that all farmers had higher risk of wheezing if ever handling hay or straw (OR: 3.49; CI: 1.43-8.54) or if ever handling animal feed (OR: 2.4; CI: 1.14-5.04) compared to agricultural administrators. Comparing the spirometry data from 1994 to 2006, they investigated annual changes in respiratory function and found a greater decline in FEV_1 (-16.4±30.0 milliliters per year [mL/yr]) and in FEV_1/FVC (-0.21±0.64 percent per year [%/yr]) in dairy farmers as compared to the changes in FEV_1 and FEV_1/FVC for the control group (-8.2±23.0 mL/yr and 0.005±0.57 %/yr, respectively) (4). This study suggests that symptoms may be the result of exposure to the dairy cows themselves or perhaps it is exposure to the hay, straw, and animal feed that comes with livestock farming that is contributing.

Pesticide use in farming may contribute to asthma risk. Using data from the AHS study, Hoppin et al (26) evaluated male private pesticide applicators who were age 20 years and

older, but excluded those with asthma diagnosed prior to age 20 years. In this subset of 19 704 farmers, 441 (2.2%) reported adult-onset asthma (26). Cumulative years of pesticide use did not show any contribution to atopic or non-atopic asthma, but a high pesticide exposure event increased a subject's risk of either type of asthma by almost double (OR: 1.98; CI 1.3-2.99 for atopic asthma; OR: 1.96; CI 1.49-2.56 for non-atopic asthma) (26). Moreover, investigating individual pesticides, it was discovered that more pesticides were associated with allergic asthma (N=12) than non-allergic asthma (N=4) (26). Subset analysis of female farmers yielded similar prevalence of 2.7% adult onset of 702 cases of the 25 814 women in the study (27). However in the female population, use of any pesticide on the farm was associated with increased risk of atopic asthma (OR: 1.46; CI: 1.14-1.87) (27). Consistent with the study of male farmers, in analysis of individual pesticides, more pesticides were associated with atopic asthma (N=10) in female farmers than with non-atopic asthma (N=1) (27). In focusing specifically on worsening existing asthma, Henneberger et al. (21) discovered 2 pesticides (pendimethalin and aldicarb) with a positive association for asthma exacerbations, but only in the farmers who reported history of allergies (21). These studies help to illustrate the complex interplay of internal environment (i.e. atopy, gender) with external environment (i.e. specific pesticides).

A study by Stoecklin-Marois et al. (28) demonstrates that many other complexities may contribute to asthma risk. In the MICASA study, 843 male and female Californian farmworkers aged 18-55 years were interviewed in person. Asthma prevalence was determined based on the American Thoracic Society (ATS) and NHLI Division of Lung Diseases (DLD) questionnaire (ATS-DLD-78 questionnaire) and acculturation (i.e. adoption of culture traits of another group) was measured based on the Acculturation Rating Scale for Mexican-Americans II (ARSMA-II) (28). Results showed an overall low asthma prevalence of 6%; however, the total number of years worked in agriculture was associated with asthma (OR: 1.04; CI: 1.00-1.09) (28). In subset analysis, medium/high acculturated male farmers had no increased risk of asthma, but medium/high acculturated female farmers had a higher prevalence of asthma (OR: 6.06; CI: 1.40-26.29) (28). Gender differences, duration of time in agriculture, and assimilation to culture may be additional factors that contribute to asthma risk.

Refer to Table 1 for a summary of the studies highlighted in this article and respective conclusions regarding asthma risk in adult farmers.

How do studies analyze farming exposures?

Agriculture environmental exposures are complex and vary based upon geographical location, type and size of farming operation, and time of year. Although endotoxin has been recognized as a key component within these environments (6, 29), several recent studies have sought to determine whether other components may be responsible for mediating disease consequences found within these environments. For example, evaluations of random samples of personal exposure obtained from 127 Norwegian farms over a period of 5 years revealed particulates including total dust, fungal spores, bacteria, endotoxins, and ammonia (3); however, none of these exposures were associated with asthma symptoms independently

(3). The study authors inferred that the combination of factors probably contribute to increased asthma risk.

Inhalation of nonbacterial irritants likely adds to risk of respiratory disease. Gases and fumes originate mostly from animal manure (ammonia, methane, hydrogen sulfide, and carbon dioxide) and stored feed (nitrogen dioxide and carbon dioxide) (10). When acutely inhaled in high concentrations, these gases can lead to conditions such as silo filler's disease or bronchiolitis obliterans (10). However, chronic exposure to these gases, even at low levels, can lead to lung inflammation, which has been implicated in contributing to chronic lung disease (10). Analyzing the particulate within agricultural dust, Peters et al. (30) demonstrated that the majority of cowshed dust was composed of arabinogalactan, a plant compound. Mice sensitized with dust extract or arabinogalactan and subsequently treated with intranasal application of dust obtained from a cowshed responded similarly (30). Specifically, both treatment groups had decreased eosinophilic airway infiltration, reduced IL-5 and IL-13 production, and decreased IgE levels in bronchiolar lavage fluid (30). Mice treated with arabinogalactan alone showed less bronchial hyper-reactivity to methacholine as compared to sham-treated mice (30). The authors suggested that arabinogalactan provides a protective response against eosinophilic/atopic asthma, while other components (i.e. endotoxin, peptidoglycan/muramic acid, ammonia) lead to increased respiratory risk.

A wide variety and abundance of microorganisms have been shown from culture-independent studies of organic dust samples collected from various farming environments using gas chromatography-mass spectrometry, polymerase chain reaction (PCR), denaturing gradient gel electrophoresis (DGGE), and shotgun metagenomics sequencing techniques (31-33). Collectively, these studies reported abundance of gram-positive and gram negative bacteria components that included several dominant bacterial families within the hog barn: *Bacteriodes*, *Lactobacillus*, *Clostridium, Ruminococcus*, and *Eubacterium* (31-33).

How do farming exposures elicit airway inflammatory responses?

To provide mechanistic insight, animal models utilizing organic dust samples have complemented these component investigation studies. Namely, several Toll-like receptor (TLR) pathways that recognize components of bacteria including endotoxin (TLR4), muramyl dipeptides/peptidoglycan (TLR2), and bacterial DNA (TLR9) have been implicated in mediating swine confinement facility organic dust-induced airway inflammation (34-36). It was also shown that the adaptor protein myeloid differentiation factor 88 (MyD88), which is utilized by all TLRs (except TLR3) and IL-1R/IL18R, plays a central role, because mice deficient in MyD88 were nearly completely protected against swine facility dust extract-induced acute airway inflammatory responses (35). Scavenger receptors might also represent an important pathway as researchers reported that scavenger receptor A (CD204) deficient mice had increased airway inflammatory consequences to organic dust extract treatment (37). Next, a study of swine confinement workers in Canada found that polymorphisms of the TLR2 gene were associated with improved lung function; polymorphisms in the TLR4 gene were not associated with lung function changes (38). Another study of swine confinement workers in Canada by Senthilselvan et al. (29) showed that after 5 hours of confinement exposure, non-atopic healthy adults with TLR4 SNPs had

less reduction in the percentage across-shift change of FEV1 from baseline as compared to age- and sex-matched adults with wild-type TLR4 genes. However, this relationship was dose dependent as it was only found for “high” concentrations of endotoxin (≥1550 EU/m3) (29).

Progress has also been made in understanding the innate and adaptive immune response to organic dust via murine and human studies. Poole et al. (39) demonstrated through murine modeling that repeated intranasal exposure to swine confinement facility dust induces a mixed T helper cell (Th)1 and Th17 immune response. Subsequently, a Dutch study confirmed a dominant Th1/Th17 response in mice following exposure swine barn dust, but also with flower bulb, onion, and cattle farm dust extracts (40). They also found increased frequency of IL-17 and IFN-γ expressing T cells in agriculture workers (N=33) as compared to non-agriculture workers (N=9) (40). Furthermore, within this study, farm dust extract reduced Th2 responses in a house dust allergy rodent model (40). In addition, two independent research groups utilizing similar animal models demonstrated increased frequency of activated lung macrophages ($CD11c^{+}/CD11b^{+}$) following repetitive exposure to swine facility organic dust extracts (41, 42). Refer to Table 2 for a summary of the important mediator responses and implicated receptor pathways associated with organic dust exposure.

Discussion

Does farming cause or contribute to adult asthma or protect against asthma?

As summarized in Table 1, the data remains inconclusive. The retrospective studies by Douwes (17) and Eduards (19) collectively suggest that exposure to farming environments in adulthood reduces the asthma risk. Eduards et al. (19) found decreased asthma prevalence in farmers as compared to rural and urban groups, which was independent of atopy status. Moreover, their study reveals that living in a rural location alone does not appear to be sufficient to reduce asthma risk. In addition, decreased asthma prevalence was also found in the longitudinal AHS study (20). However, the so-called “healthy worker effect” might be an important alternative explanation for the protective asthma effect ascribed to farm work. The “healthy worker effect” proposes that if a farmer experiences symptoms of asthma, they would select themselves out of the population and thereby, only healthy workers would remain in the working population (43). This effect would be difficult to recognize and account for in retrospective studies. This possibility was highlighted in the study by Thaon et al. (4). The authors suggested that symptomatic agriculture workers, who formerly handled such materials in 1994, selected themselves out of this type of work by the time the group was re-evaluated in 2006.

In contrast, several studies also showed increased risk of asthma with farming. In the large ECRHS study and Finland study, agricultural workers had the highest risk of asthma amongst occupations (23, 24). Moreover, working with livestock has been associated with increased risk of adult asthma (3, 4, 25). However, it is not clear if the livestock animals or the associated exposures of hay, straw, animal feed, bacteria, or organic dust is influencing the asthma risk in adults (3, 4, 30-33). In addition to these multiple external variables,

Eduard et al (3) demonstrated an important internal variable: the dichotomous role of atopy in farmers with several types of livestock.

Did farming increase the amount of new onset asthma cases?

The data here supporting or refuting farm exposure as causing new onset asthma remains inconsistent. The study by Omland et al. (25) of farming school students showed increased adult-onset asthma in this population, especially those with swine and cattle exposure. The Finnish study showed an increase in new cases of asthma within workers in the agriculture, forestry, and commercial fishing group (24). Conversely, Hoppin et al's AHS study showed a decrease in asthma incidence in the farming population (20); however, the AHS only included farmers who apply pesticides and did not classify them based on type of agriculture (20).

Conclusion

The occupation of agriculture represents a complex exposure environment for farm workers, and the resultant airway disease outcomes depend on the interplay of genetic factors, gender, atopic predisposition, type of livestock, pesticide exposure, and magnitude and duration of exposure in the adult subject. Retrospective and cross-sectional studies have supported that farming exposure can decrease the risk of asthma in the adult subject with longer exposure duration to occupational farming further decreasing asthma risk (17, 19, 20). However, the healthy worker effect might be missed in the retrospective study designs as evident by a longitudinal study demonstrated that agricultural work is an independent risk factor for developing asthma (4). Multiple types of livestock exposure appear to increase asthma risk, particularly for the development of nonatopic asthma (19). Prospective and longitudinal studies of adult populations focused on genetic polymorphisms and objective lung function assessments coupled with environmental sampling are suggested to further define risk factors for occupational-exposed adult farmers to ultimately reduce asthma disease burden.

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Table 1

Summary of the studies in adult subjects highlighted in this review that supports occupational farming exposures as either a risk factor for asthma or as a protective factor against asthma.

Study	Farming as Risk Factor for Asthma	Farming as Protective Against Asthma	No Effect
Douwes et al. (17)			
Current livestock and crop farmers		X	
Thaon et al.(4)			
Dairy	X		
Non-dairy livestock			X
Eduard et al. (19)			
Atopic asthma		X	
Nonatopic asthma		X	
Hoppin et al.(20, 26, 27)			
AHS study group		X	
Pesticide use	Atopic > Non-atopic		
HPEE	X		
Kogevinas et al. (23)			
All farmers	X		
Omland et al. (25)			
Swine	X		
Cattle	X		
Eduard et al. (3)			
Atopic with ≥ 2 livestock		X	
Nonatopic with ≥ 2 livestock	X		
Karjalainen et al. (24)			
Men and women	X		
Stoecklin-Marois et al. (28)			
Acculturated farm men			X
Acculturated farm women	X		

HPEE= High Pesticide Exposure Event.

Table 2

Important components within agriculture-related organic dust environmental samples and the associated immunological responses and implicated pattern recognition receptor pathways.

Important components identified within organic dust samples (3, 30-33)
Gram positive bacteria Lactobacillus Clostridium Ruminococcus Eubacterium
Gram negative bacteria Bacteriodes Eubacterium
Fungal spores
Arabinogalactans
Organic dust associated mediator responses (30, 39-42)
Increase in inflammatory responses
TNF-α
IL-6
IL-8
Th1/Th17 microenvironment
Activated macrophages
Decrease in atopic responses
IL-5
IL-13
IgE (in BALF)
Th2
Pattern recognition receptor pathways implicated in organic dust responses (29, 34-38)
TLR2
TLR4
TLR9
MyD88-dependent pathway
CD204 (scavenger receptor A)

TNF= tumor necrosis factor; IL= interleukin; Th= T helper cell; Ig= immunoglobulin; BALF= bronchoalveolar lavage fluid; TLR= toll-like receptor; MyD= myeloid differentiation.