

The role of farm exposures in occupational asthma and allergy

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Agriculture is very diverse. Farmers commonly grow several different crops, and may also raise animals. They are exposed to a variety of antigens from plants, animals, insects and molds, to which they may become allergic. However, several large epidemiological studies conducted recently in various regions of the world indicate that the prevalence of asthma and allergy is no higher in farmers than in other populations. There is increasing evidence that growing up on a farm may protect against developing asthma and allergic rhinoconjunctivitis. *Curr Opin Allergy Clin Immunol* 1:151–156. © 2001 Lippincott Williams & Wilkins.

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Abbreviation

FEV₁ forced expiratory volume in 1 s

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Introduction

Farming is a complex industry. Agricultural products include meat animals, dairy products, poultry, soybeans, grains, fruit, nuts, vegetables and flowers. Inhalation exposures occur in a variety of farm settings, including fields, grain storage bins, barns, silos, confined animal feeding operations and greenhouses. Agents present in these settings consist of the crops and farm animals themselves as well as bacteria, fungi, insects and viruses. Dust from grain and confined animal feeding operations is rich in endotoxin, a potent inflammatory agent. People who live on farms, including small children, are regularly exposed to these substances. Farms are becoming larger and more specialized in many parts of the world, intensifying exposures that can cause respiratory disorders. Agricultural environments are associated with a number of different respiratory tract disorders that include asthma and allergic rhinitis as well as disorders that can have similar symptoms, including acute bronchitis, chronic bronchitis and the asthma-like syndrome [1,2]. This article focuses on recent investigations designed to answer questions concerning the prevalence of asthma and allergy in farmers and children raised on the farm, as well as studies concerning specific farm exposures associated with asthma and allergic rhinoconjunctivitis.

Is the prevalence of occupational asthma and allergy higher in farmers than in the general population?

A number of epidemiological studies have been conducted in order to assess the prevalence of asthma and allergic rhinitis in individuals who work on the farm. The majority of such studies have used self-administered questionnaires containing questions about wheezing, chest tightness and physician-diagnosed asthma to determine if asthma is present [3]. In some cases, subjects were also assessed using spirometry. Allergy was most often determined only by using information from questionnaires. Although the data from this research answer important questions concerning the prevalence of the problems of interest, they cannot be used to demonstrate a temporal connection between exposure and outcome because of the cross-sectional design of the studies.

Several larger studies have been conducted in recent years in several different countries looking at the prevalence of asthma, wheezing and allergic rhinitis symptoms in groups of farmers (Table 1). A cross-sectional study of 4793 crop farmers from Denmark,

Table 1. Prevalence of asthma, wheezing and allergic rhinitis in farmers 1990–2000

First author	Type of farming	Location	Farmer subjects (n)	Control subjects (n)	Asthma (%)	Wheezing (%)	Allergic rhinitis (%)
Monsó <i>et al.</i> [4••]	Grains, vegetables, root crops, oil plants, fruits, nuts, flowers, livestock	Denmark, Germany, Spain, Sweden	4793	None	3.3	14.9	14.4
Masley <i>et al.</i> [7•]	Grains, livestock	Saskatoon, Canada	1047	336	5.2 farmers 6.1 controls	9.1 farmers 6.1 controls	10.0 farmers 11.5 controls
Wilkins <i>et al.</i> [8]	Corn, wheat, oats, soybeans, cattle, hogs	Ohio, USA	1793	None	None reported	8.1	Not reported
Kimbell-Dunn <i>et al.</i> [9•]	Corn, wheat, oats, vegetables, fruit, bees, cattle, hogs, poultry, horses, goats, deer	New Zealand	1706	None	11.8	20.4	28.4
Dalphin <i>et al.</i> [10]	Dairy cattle, hay	Doubs, France	265	149	5.3 farmers 3.4 controls	8.7 farmers 4.7 controls	31.1 farmers 35.6 controls
McCurdy <i>et al.</i> [11]	Rice	California, USA	464	None	7.1	8.8	25.7

Germany, Sweden and Spain was performed to assess the prevalence of respiratory symptoms [4••]. Many of the farmers also raised animals as part of their farming operation. The prevalence of asthma ranged from 1.8% in Germany to 4.7% in Denmark. Overall, 14.9% of the farmers reported wheezing and 14.4% reported nasal allergy, values that are similar to those for the general European population [5,6]. Flower growing, but not livestock exposure or grain handling, was a risk factor for asthma. No association was found between nasal allergy symptoms and various types of farming in the regions studied.

A cross-sectional study of health of 1185 rural households was conducted in southern Saskatchewan, Canada [7•]. The study site is a semi-arid prairie used mainly for raising small grains, hogs and cattle. Again, a relatively low prevalence of asthma was reported, in that only 5.9% of men and 4.6% of women reported ever having asthma, compared with 6.5% of children and young adults in Canada [12]. There was no significant difference in the prevalence of asthma between the farming and non-farming households, which argues against farming causing asthma in this population. The prevalence of hay fever was no higher in adults from farming households than in adults from non-farming rural households. No analysis was reported concerning specific farm exposures and the prevalence of asthma, wheezing or hay fever.

A cross-sectional study of chronic respiratory symptoms was recently conducted in male Ohio cash grain farmers [8]. From the 1793 completed questionnaires, it was determined that only 8.1% of the farmers reported wheezing. The number of cattle and hogs on the farm, a measure of the intensity of exposure, was inversely related to the prevalence of wheezing. The value for wheezing in this population is much lower than the

value of 25.7% reported in another survey conducted in the United States [5]. The low prevalence of cigarette smoking in the farming population may help to explain this observation. The healthy worker effect could also help to explain the lower prevalence of wheezing in these farmers. In this group of farmers, acres of alfalfa hay and pet allergy were the only factors positively associated with wheezing. Exposure to cows, which has been implicated in causing asthma in Scandinavian farmers, and exposure to hogs, which has been associated with asthma in a small group of Danish farmers, were not associated with wheezing or chronic cough in this population [13,14].

Farmers in New Zealand raising a variety of crops and livestock were examined for the prevalence of asthma and allergy in a recent study utilizing self-administered questionnaires [9•]. The asthma prevalence was found to be 11.8% overall, compared with 15% in the general population. However, the prevalence of asthma was found to be significantly higher in horse breeders/groomers, pig farmers, poultry farmers and those handling oats. Those raising bees and deer reported a higher than expected prevalence of hay fever symptoms.

Dalphin and colleagues [10] described a population of dairy farmers and non-exposed subjects in France in terms of the prevalence of asthma and respiratory symptoms. An allergological evaluation was conducted using the determination of serum total IgE levels, the Phadiatop test and skin prick tests. The prevalence of self-reported asthma was 5.3%, which was not statistically different from the general population. Only two of the 15 asthmatic farmers appeared to have disease resulting from IgE-mediated mechanism. Wheezing was more common in the farmers than in the reference population, however.

McCurdy and colleagues [11] studied California rice farmers, and determined that the prevalence of physician-diagnosed asthma was 7.1% and that of wheezing was 8.8%. These values are higher than those reported in some, but not all, studies of the prevalence of asthma in the United States [6,15]. Mean forced expiratory volume in 1 s (FEV₁) and forced vital capacity were at expected values in the rice farmers. Hay fever was reported in 25.7% of the rice farmers, which is a value higher than that found in the general population [15]. There was a positive association between the risk of hay fever and the number of years spent working in rice drying/storage activities.

Other methods have been used to study the prevalence of asthma in farmers. Finland is one of the countries where asthmatic farmers and other workers undergo detailed assessments designed to determine whether or not their asthma has an occupational aetiology. A review of occupational asthma, as documented in the Finnish Registry of Occupational Diseases, included farmers and individuals with a variety of other occupations [16]. It was determined that the incidence rate of asthma was higher in farmers, veterinarians and animal husbandry workers than in most other occupational groups. It was concluded that cases caused by animal epithelia, hairs and secretions or flours, grains and fodders accounted for 60% of the total cases of occupational asthma.

A recent study [17] addressed the question of whether or not farmers were more likely to die from asthma than other Swedish workers. The investigators found a significantly increased mortality rate among male farmers, a difference that persisted after adjustment for smoking. Interestingly, the prevalence of asthma is lower in Sweden than in many developed countries [5]. The usage of medical facilities by individuals with asthma was found to be significantly lower in farmers in a French study [18]. It is possible that this observation applies to other countries, and that reduced access to medical care secondary to geographical or social factors could help explain the higher mortality rate secondary to asthma in Swedish farmers. The contribution of occupational exposures to fatal asthma in farmers is poorly understood.

In summary, the studies described above demonstrate associations between some farm exposures and the presence of asthma or wheezing, including flower growing, working with horses, pigs, poultry and growing oats, rice and alfalfa hay. Studies of three very diverse farm populations in North America give conflicting information regarding the prevalence of asthma and wheezing in farmers compared with the general population. A large study in Europe indicated that the prevalence of asthma is similar to the population overall.

In contrast, there is evidence that New Zealand farmers have a lower prevalence of asthma than does the general population of that country. In general, the prevalence of hay fever does not appear to be higher in farming populations, although there is evidence of the presence of allergies in farmers to certain farm animals and crops. The fact that mortality from asthma is higher in farmers than in many other worker populations in Sweden suggests that workplace exposures may be causing asthma or asthma exacerbations. However, reduced access to healthcare at the time of an acute asthma attack was not ruled out as a factor. Data from the Finnish Registry of Occupational Diseases suggests that there is a high rate of occupational asthma in farmers compared with other occupations. It is possible that the detailed medical assessments routinely performed for compensation purposes concerning the occupational aetiology of asthma in Finland cause more asthmatic farmers to be classified as having occupational asthma than in countries where the healthcare system does not encourage such investigations to be performed.

Does growing up on a farm protect against allergy and asthma?

It has recently been observed in several different studies of children raised on farms in Europe and Canada that there is a lower prevalence of asthma and allergies in farm children than in children raised in nearby towns. A Swiss study of 1620 children in three age groups (6–7, 9–11 and 13–15 years of age) [19••] showed that farming as a parental occupation was associated with lower rates of hay fever and atopic sensitization after adjustment for a number of factors previously shown to influence the prevalence of allergic symptoms, including a family history of asthma and allergies, parental education, pet ownership, maternal smoking, number of siblings, indoor humidity and heating fuels. A study of Finnish university students [20••] also examined the role of growing up on a farm when compared with having grown up in a rural non-farm or urban setting. It was determined that the childhood farm environment had a protective effect against allergic rhinoconjunctivitis but not asthma.

Two other studies [21••,22••] showed a lower prevalence of asthma in farm children, in addition to showing similar effects in the prevalence of allergic rhinoconjunctivitis. A cross-sectional study of 2283 Austrian rural children aged 8–10 years [21••] revealed that the prevalence of hay fever, asthma and positive skin prick test reactivity to at least one of the common local allergens was significantly lower in children living on a farm. Interestingly, regular contact with livestock and poultry was associated with a reduced risk of atopic sensitization. Von Ehrenstein and colleagues [22••] made similar observations in a group of 10 163 children aged 5–7 years. They also noted that

increased exposure to livestock was associated with a lower prevalence of atopic disease.

A Canadian study of 1199 rural school children [23••], of whom half lived on farms, showed that current wheeze, airway hyperresponsiveness as determined by methacholine bronchoprovocation test, and skin test positivity to inhaled allergens were all significantly less common in adolescents raised on a farm. The prevalence of asthma in the farm children was 5.8%, compared with 8.3% in the non-farm children. No excess of allergic disease was found in the group that had lived on a farm in the past, making it unlikely that families had left the farm because of a child affected by asthma or allergies. Farm families in general tend to have more children, and this observation is associated with a reduction in the prevalence of allergic disease. Larger family size did not account for the differences in the prevalence of allergic disease in the study, which was also true in the European studies.

Interestingly, according to a Swedish study [24•], only 8.4 and 7.4% of farmers were sensitized to cat and dog antigens, respectively, despite the fact that these animals are present on more than 90% of farms, and that high allergen levels were found in the homes. It is possible that relatively intense exposure to a variety of antigens in farm children, including those from livestock and poultry as well as cats and dogs, leads to a lower prevalence of sensitization.

Do certain farm exposures cause asthma and allergy symptoms?

It is clear that farmers can develop IgE antibodies to antigens from farm animals, insects, plants and fungi. Allergy to grain storage mites has been implicated in asthma in farmers for some time [25]. Recently, sensitization to a mite that is often present on plants grown in greenhouses, *Tetranychus urticae*, was found to be more common in atopic greenhouse workers than in non-farm atopic and non-atopic subjects [26]. It was shown that 19% of the sensitized workers had allergic rhinitis symptoms and 7% had asthma symptoms. Work inside greenhouses was also found to be a marginal risk factor for asthma in a study of respiratory symptoms of obstructive lung disease in farmers from four European countries [4••].

In a recent Swedish study of asthma and rhinoconjunctivitis in farmers [27], sensitization to storage mites and house dust mites as well as pollens from birch, timothy grass and mugwort was a significant risk factor for both asthma and rhinoconjunctivitis. Spider mite allergy also appears to be a problem in farmers who raise apples, according to a recently published study from Korea [28•]. Of 725 apple growers, 8.6% had positive skin tests to two

common species of spider mites. Of 119 farmers with work-related asthma symptoms, the positive skin test response rates were 40.4 and 27.0%, respectively, to the two species of mite.

Fungi are ubiquitous in farm environments and can be present in very high levels. Their role in causing lung disorders in humans is not yet completely understood. It has been suspected that allergy to fungi contributes to asthma in farmers and other populations. However, a recent Scandinavian study of IgG antibodies to *Fusarium* spp. and *Wallemia sebi* [29] revealed that the titres were elevated in farmers with hypersensitivity pneumonitis but not in asthmatic farmers.

Exposure to grain dust has been found to be associated with asthma in grain workers [30]. Soy bean dust has been found to be associated with outbreaks of asthma occurring after the unloading of soy beans from ships [31]. Patients with asthma whose symptoms were exacerbated during these outbreaks had specific serum IgE antibodies that reacted strongly with glycoproteins from soybean extracts. Soybeans are a common crop in a number of countries, including the United States. Interestingly, little is known about soybean allergy or grain dust allergy in farmers. A recent cross-sectional study of 297 Midwestern grain farmers [32] did not show an association between handling soybeans and experiencing chest tightness or cough. However, such an association was found in the farmers who handled grain sorghum, which causes a more pronounced non-specific inflammatory response *in vitro* than dust from corn or soybeans [33]. It is not yet known if these symptoms occurred secondary to an allergic response.

Hog farmers are known to develop obstructive airway disease from their work [2]. Swine confinement workers commonly develop symptoms that include chest tightness, wheezing and cough. These symptoms can be associated with hyperresponsiveness to methacholine, a cross-shift decline in FEV₁ and accelerated lung function decline [34,35]. Recent studies lent support to the concept that endotoxin in the hog dust is the major determinant of the annual decline in FEV₁ in these workers [36]. Many of the workers do not have airway obstruction that is apparent on pulmonary function testing, and are felt to have the asthma-like syndrome, a non-IgE mediated process. However, there is evidence that some swine confinement workers with occupational asthma have pig-specific IgE antibodies, as determined by the measurement of basophil-bound IgE and serum IgE in a small number of subjects [14]. The presence of IgE antibodies to pig proteins can rarely be detected using the radioallergosorbent test method [37]. There was only one previous report of IgE-mediated occupational asthma secondary to pig exposure [38].

Conclusion

New evidence has been obtained from cross-sectional studies conducted in a number of different countries with diverse farming practices to suggest that the prevalence of asthma and allergy is no higher in most groups of farmers than in the general population. Also, it appears that being raised on a farm can protect children from allergic rhinoconjunctivitis and asthma. In particular, exposure to livestock in childhood may protect against allergic respiratory disorders. However, some farmers who do become asthmatic or who suffer from allergic rhinoconjunctivitis are sensitized to a variety of substances in their environment, including various species of mites and pig antigens. Further investigation must be conducted to determine whether exposure to these antigens is the cause of allergic respiratory disorders. It is also not known if heavy occupational exposure to antigens from soy bean dust or other types of grain dust, which are known to cause asthma in other settings, can cause occupational asthma and allergies in farmers.

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