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Fungal and Atopic Sensitization are Low among Farmers in the Agricultural Health Study

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Clinical Summary

Prevalence of fungal sensitization and atopy was lower among farmers than the US population. Fungal sensitization was related to growing specific agricultural commodities.

Keywords

fungal sensitization; atopy; agriculture; farmers; specific and total IgE

To the Editor:

Farm work may result in exposure to microbial bioaerosols. In agriculture, average airborne concentrations of fungal conidia are several orders of magnitude higher than in nonagricultural, indoor environments without water damage. 1 We used data from Iowa (IA) and North Carolina (NC) farmers to explore associations between farming activities and fungal sensitization.

We analyzed serum samples from a neurobehavioral sub-study of 677 male private pesticide applicators in the Agricultural Health Study (AHS). 2 Blood was collected from male pesticide applicators in 2006-8 who had completed all AHS interviews. Blood samples were not available for the whole cohort. Individuals were excluded if they had never been a farmer or had neurologic diseases; women were excluded due to their low prevalence in the

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cohort (<3%). 2 Participants in the sub-study were similar to the cohort as a whole with regard to farm history (Hoppin et al submitted). The study was approved by Institutional Review Boards of the University of Iowa, the National Institutes of Health and its contractors.

Serum samples were analyzed for total immunoglobulin E (tIgE) and screened for fungal positivity to a fungal-mix (mx2) by fluoroenzymeimmunoassay using ImmunoCAP 100 (Phadia AB, Uppsala, Sweden). Sensitization to other allergens was not measured. If sera were fungal- mix positive, they were tested for sIgE to ten fungal species (*Aspergillus fumigatus*, *Penicillium chrysogenum*, *Alternaria alternata*, *Curvularia lunata*, *Epicoccum purpurascens*, *Phoma betae*, *Candida albicans*, *Botrytis cinerea*, *Fusarium proliferatum*, and *Cladosporium herbarum*). Fungal sensitization was defined sIgE ≥ 0.35 kU/L to at least one fungus; atopy was defined as tIgE ≥ 100 kU/L. 3

Pesticide applicators completed three questionnaires about their agricultural and medical history: one at enrollment and two five-year followup interviews. Farming practices included specific crops and animals raised, growing up on a farm, and years worked or lived on a farm. Data from all three questionnaires was used for the analysis. Exact logistic regression models were used to estimate associations with farming characteristics and fungal sensitization or atopy while controlling for state; other factors such as age and smoking did not confound the associations.

The prevalence of fungal sensitization was 4% and the prevalence of atopy was 21%. While the prevalence of atopy was greater for NC than IA farmers (Odds Ratio (OR) =1.5, 95% Confidence Interval (CI) 1.0-2.1), fungal sensitization did not differ. Twenty-five percent of fungal-sensitized participants were not classified as atopic (n=7; Table E1). Fungal-sensitized farmers (N=28) were slightly older than those who were not (63 years vs. 61 years), however, there was no difference in the average age of the two groups (p=0.27).

Specific commodities were related to fungal sensitization (Table 1). After adjusting for state, farmers who grew tobacco, orchard fruit, or raised animals, particularly cattle, were more likely to be fungal sensitized than farmers not performing these activities. Growing soybeans, field corn, or other grains were also positively associated with fungal sensitization, but were not statistically significant. We lacked the ability to assess multiple crops in the same model due to the low prevalence of fungal sensitization and the high degree of correlation among crops. Sensitization to any specific fungal antigen was low, ~2% for all farmers and between 4 to 8% when limited to those classified as atopic (Table 2). Sensitization to specific fungi showed 11 of the 28 individuals (39%) were monosensitized and 17 (61%) were multisensitized.

Fungal sensitization was less common among these farmers compared to white men, 40 years and older from the National Health and Nutrition Examination Survey (NHANES) in 2005-2006. 4 Among farmers, sensitization prevalence to both *Alternaria* and *Aspergillus* was 2% (95%CI=1-3%) lower than NHANES with 7% for *A. alternata* (95%CI=5-9%) and 6% for *A. fumigatus* (95% CI=4-7%). Atopy prevalence was also lower (21%, 95%CI=17-25) compared to NHANES participants (30%, 95%CI=27-33%).

Other studies of agricultural workers suggest greater fungal sensitization among farmers. 5-8 While no studies appear to have focused on fungal sensitization associated with specific field crops, 18% of greenhouse workers were sensitized to at least one of four fungal species as measured by skin prick test, much higher than we observed even though our panel included the same fungi in addition to six other species. 5

While our study is among the largest to characterize fungal sensitization among farmers, our analysis was limited due to the low prevalence of sensitization and high prevalence of certain types of crop production and high correlation among these crops. Our panel contained ten common fungal species; many, but not all, have been associated with commodity crops. If the panel included a greater diversity of species, the prevalence of sensitization may have been higher; however, given that most farmers were multisensitized to fungi, it is unlikely that the addition of other fungi would greatly alter our results. The participants were older farmers so a healthy worker effect is possible where sensitized farmers have been selected out of agriculture prior to sampling. Our population was not selected based on respiratory disease history, thus our lower estimates may reflect the fact that other studies may have been enriched for individuals with respiratory outcomes. The agricultural exposure history was well characterized by detailed questionnaires; however, no environmental exposure assessments were conducted. Due to the high degree of correlation between some crops, most notably corn and soybeans, and the high prevalence of growing these two crops, we lacked statistical power to fully evaluate whether one or both of these major crops contributed to fungal sensitization.

In conclusion, this study represents one of the largest and most heterogeneous studies of fungal sensitization with regard to agricultural activities. Both fungal sensitization and atopy were low in this sample of U.S. farmers compared to the U.S. population. Individuals working with tobacco, orchard fruit, or animals had a higher prevalence of fungal sensitization; however, the sample size limited our ability to evaluate the influence of specific crops. Because fungal exposures differ around the world and rates of allergen sensitization differ based on farming history, future studies will need to focus not only on commodities produced and specific fungal agents, but also on population characteristics that may impact sensitization.

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Abbreviations

AHS	Agricultural Health Study
CI	Confidence Interval
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
sIgE	Specific Immunoglobulin E
tIgE	Total Immunoglobulin E
SPT	Skin Prick Test

References

1. Eduard W. Fungal spores: a critical review of the toxicological and epidemiological evidence as a basis for occupational exposure limit setting. *Crit Rev Toxicol.* 2009; 39:799–864. [PubMed: 19863384]
2. Starks SE, Gerr F, Kamel F, Lynch CF, Jones MP, Alavanja MC, et al. Neurobehavioral function and organophosphate insecticide use among pesticide applicators in the Agricultural Health Study. *Neurotoxicol Teratol.* 34:168–76. [PubMed: 21907279]
3. Burney P, Malmberg E, Chinn S, Jarvis D, Luczynska C, Lai E. The distribution of total and specific serum IgE in the European Community Respiratory Health Survey. *J Allergy Clin Immunol.* 1997; 99:314–22. [PubMed: 9058686]
4. National Center for Health Statistics (NCHS) US Centers for Disease Control and Prevention (CDC). Department of Health and Human Services (CHHS). National Health and Nutrition Examination Survey (NHANES). 2005-2006. I2006. Available from http://www.cdc.gov/nchs/nhanes/nhanes2005-2006/nhanes05_06.htm
5. Monso E, Magarolas R, Badorrey I, Radon K, Nowak D, Morera J. Occupational asthma in greenhouse flower and ornamental plant growers. *Am J Respir Crit Care Med.* 2002; 165:954–60. [PubMed: 11934721]
6. Rimac D, Macan J, Varnai VM, Vucemilo M, Matkovic K, Prester L, et al. Exposure to poultry dust and health effects in poultry workers: impact of mould and mite allergens. *Int Arch Occup Environ Health.* 83:9–19. [PubMed: 19921239]
7. Terho EO, Vohlonen I, Husman K, Rautalahti M, Tukiainen H, Viander M. Sensitization to storage mites and other work-related and common allergens among Finnish dairy farmers. *Eur J Respir Dis Suppl.* 1987; 152:165–74. [PubMed: 3478215]
8. Zhang Y, Chen J, Chen Y, Dong J, Wei Q, Lou J. Environmental mycological study and allergic respiratory disease among tobacco processing workers. *J Occup Health.* 2005; 47:181–7. [PubMed: 15824484]

Table 1
Farming Characteristics and Fungal Sensitization and Atopy Among 677 Farmers in the Agricultural Health Study

Enrollment Variables	Fungal Sensitized				Atopic* (n=141)				Non-atopic (n=536)			
	Yes (n=28)	%	n	%	Yes (n=28)	%	n	%	Yes (n=28)	%	n	%
	n	%	n	%	n	%	n	%	n	%	n	%
Grew up on a farm												
No	3	11	68	11			15	11	56	11		
Yes	25	89	575	89	1.0	0.3	5.5	89	474	89	1.1	0.6
Years worked/lived on farm												
<30	4	15	151	24			24	17	131	25		
30	23	85	489	76	1.9	0.6	7.7	114	83	398	75	1.1
Currently farming												
Yes	22	79	519	80	0.9	0.3	3.0	106	76	435	81	0.8
No	6	21	127	20			34	24	99	19		1.3
Crops grown												
Field Corn	25	89	504	78	3.1	0.9	11	104	74	425	79	0.9
Soybeans	25	89	490	76	3.0	0.9	10	102	72	413	77	0.9
Hay and Alfalfa	15	54	314	48	1.5	0.6	3.6	68	48	261	49	1.3
Other grains	19	68	336	52	2.1	0.9	4.7	82	58	273	51	1.4
Tobacco	11	39	139	21	3.6	1.1	11	38	27	112	21	1.2
Cotton	5	18	65	10	2.0	0.6	5.9	11	8	59	11	0.5
Peanuts	5	18	64	10	2.0	0.7	6.1	14	10	55	10	0.8
Row crops	5	18	86	13	1.4	0.5	3.8	21	15	70	13	1.0
Orchard fruits	4	14	15	2	6.9	2.1	23	9	6	10	2	3.4
Silage	9	32	153	24	2.0	0.7	6.1	34	24	128	24	1.3
Animals raised												
Any animals	22	79	415	64	2.6	1.0	6.8	92	65	345	64	1.3
Cattle (dairy and beef)	19	68	308	47	2.8	1.2	6.7	72	51	255	48	1.4
Swine	8	29	216	33	0.8	0.3	2.2	38	27	186	35	0.8
Poultry	4	14	55	8	1.8	0.6	5.3	15	11	44	8	1.3

Row crops are blueberries, cabbage, grapes, cucumbers, peppers, snap beans, strawberries, tomatoes, melons, and pumpkins.

* Defined as total IgE 100 kU/L

^a Adjusted for state Orchard fruits are apple and peaches

Table 2

Prevalence of Fungal Sensitization to 10 Fungal Agents Among 677 Male Agricultural Health Study Farmers, 2006-8

	All Farmers (n = 677)		Atopic* Farmers (n = 141)	
	n	%	n	%
Any Fungal Sensitization**	28	4	21	15
Eurotiales				
<i>Aspergillus fumigatus</i>	14	2	11	8
<i>Penicillium chrysogenum</i>	14	2	11	8
Pleosporales				
<i>Alternaria alternata</i>	14	2	8	6
<i>Curvularia lunata</i>	7	1	7	5
<i>Epicoccum purpurascens</i>	14	2	11	8
<i>Phoma betae</i>	14	2	11	8
Saccharomycetales				
<i>Candida albicans</i>	14	2	10	7
Helotiales				
<i>Botrytis cinerea</i>	7	1	6	4
Hypocreales				
<i>Fusarium proliferatum</i>	7	1	6	4
Capnodiales				
<i>Cladosporium herbarum</i>	7	1	6	4

* Defined as total IgE ≥ 100 kU/L

** Sensitized (specific IgE ≥ 0.35kU/L) to any fungi

Demographic, Lifestyle, and Medical Characteristics of the 677 Agricultural Health Study Farmers by Fungal Sensitization and Atopic Status

Table E1

Characteristics	Fungal Sensitized				Atopic**				Non-atopic			
	Yes (n=28)		No (n=649)		Atopic (n=141)		Non-atopic (n=536)					
Age at blood draw (years)												
Mean (SD *)	63(14)		61(12)		63(12)		60(12)					
	n	%	n	%	n	%	n	%	n	%	n	%
Atopy**	21	75	120	18	141	100	0	0				
Body Mass Index(BMI), kg/m^2												
<25	6	21	122	19	26	19	102	19				
25-30	12	43	327	50	65	46	274	51				
>30	10	36	200	31	50	36	160	30				
Smoking history												
Ever smoked	11	39	277	43	61	44	227	42				
Never smoker	17	61	371	57	80	57	308	57				
Alcohol consumption												
Ever	16	57	406	63	87	62	335	63				
Never	12	43	243	37	54	38	201	38				
State												
Iowa	13	46	329	51	61	43	281	52				
North Carolina	15	54	320	49	80	57	255	48				
Respiratory symptoms and diseases:												
Hay fever	13	46	119	18	37	27	95	18				
Wheeze in the past 12 months	12	43	131	20	42	30	101	19				

* Standard deviation (SD)

** Defined as total IgE 100 kU/L