

Farm Exposure and Atopy in Men and Women: The Saskatchewan Rural Health Study

Donna C. Rennie,^{1,2} Joshua A. Lawson,¹ Chandima P. Karunanayake,¹
Punam Pahwa,¹ Yue Chen,³ Luan Chu,¹ James A. Dosman,¹
and the Saskatchewan Rural Health Study Group

¹Canadian Centre for Health and Safety in Agriculture, University of Saskatchewan,
Saskatoon, Saskatchewan, Canada

²College of Nursing, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

³Department of Epidemiology and Community Medicine, Faculty of Medicine,
University of Ottawa, Ottawa, Ontario, Canada

ABSTRACT. Associations between farming exposures and atopy can vary by timing of exposure and sex. We examined associations between adult atopy, sex, and farm living in a rural Canadian population. In 2010, we conducted a baseline survey of 11,982 households located in four agricultural regions of Saskatchewan, Canada. Of the 7225 adults aged 18–75, 1658 underwent clinical assessments including skin testing. Of these, 1599 participants underwent skin prick testing to four common allergens. We defined atopy as >3 mm reaction to any of four allergens compared with saline control. Farming exposures were farm living in the first year of life and current farm living. All analyses were stratified by sex. The prevalence of atopy was 17.8% and was higher in men than women ($P < .001$). The most common allergy was to grasses (8.8%) followed by house dust mite (HDM) mixed (8.1%). Atopy was lower in those subjects with an early farm exposure ($P = .08$) and who were female ($P = .03$). After adjusting for education, age, and smoking status, both current and early farm exposures were associated with decreased sensitization to cat atopy in women that was stronger with current exposure ($P < .05$).

The Saskatchewan Rural Health Study Team consists of James Dosman, MD (Designated Principal Investigator, University of Saskatchewan, Saskatoon, SK, Canada); Punam Pahwa, PhD (Co-principal Investigator, University of Saskatchewan, Saskatoon, SK, Canada); John Gordon, PhD (Co-principal Investigator, University of Saskatchewan, Saskatoon, SK, Canada); Yue Chen, PhD (University of Ottawa, Ottawa, ON, Canada); Roland Dyck, MD (University of Saskatchewan, Saskatoon, SK, Canada); Louise Hagel (Project Manager, University of Saskatchewan Saskatoon, SK, Canada); Bonnie Janzen, PhD (University of Saskatchewan, Saskatoon, SK, Canada); Chandima Karunanayake, PhD (University of Saskatchewan, Saskatoon, SK, Canada); Shelley Kirychuk, PhD (University of Saskatchewan, Saskatoon SK Canada); Niels Koehncke, MD (University of Saskatchewan, Saskatoon, SK, Canada); Joshua Lawson, PhD, (University of Saskatchewan, Saskatoon, SK, Canada); William Pickett, PhD (Queen's University, Kingston, ON, Canada); Roger Pitbaldo, PhD (Professor Emeritus, Laurentian University, Sudbury, ON, Canada); Donna Rennie, RN, PhD (University of Saskatchewan, Saskatoon, SK, Canada); and Ambikaipakan Senthilselvan, PhD (University of Alberta, Edmonton, AB, Canada).

Address correspondence to: Dr. Donna C. Rennie, Canadian Centre for Health and Safety in Agriculture, University of Saskatchewan, 104 Clinic Place, Saskatoon, SK S7N 2Z4, Canada (E-mail: donna.rennie@usask.ca).

Color versions of one or more figures in this article are available online at www.tandfonline.com/wagr

Men had significantly decreased atopic sensitization to *Alternaria* with an early farm exposure and increased atopic sensitization to HDM with a current farm exposure. In this rural population, the protective effect of an early farm exposure for any atopy was weak overall. The impact of farming exposures on atopy was allergen dependent and varied by sex.

KEYWORDS. Adults, allergy, farming

INTRODUCTION

Nearly one quarter to one third of adults living in certain westernized countries are allergic to at least one aeroallergen.^{1–3} The immunological response appears to vary by age, with younger populations including young adults experiencing more allergies.^{3–6}

Living on a farm may protect from adult-onset allergy.⁵ The effect of the farming environment on the development of allergic disease has been the subject of epidemiological and occupational research and debate in past years.^{4–5,7–9} The nature of the farming environment with both livestock and crop production makes it a suitable environment for both increased and decreased susceptibility to allergy in farm dwellers.^{10,11} The protective effect of farming has been shown to vary by the timing^{2,10} with continuance^{6,12,13} and by type of farming exposure.^{5,13,14} The allergic response to farm environments by farm dwellers can vary by sex.^{15,16} In recent years, the association between decreased atopic sensitization and early farm exposure has been of an area of primary interest in adult farming populations.

The purpose of this investigation was to examine if adult atopy is negatively associated with timing of a farming exposure in adults and if such an association varies by sex and specific atopy.

METHODS

The analysis was based on data from an ongoing prospective cohort study of rural residents conducted in Saskatchewan, Canada. Phase 1 of this study is a baseline survey with a clinical component completed in 2010–2011 on a subpopulation of the Phase 1 survey respondents. Phase 2 is a follow-up study being conducted in 2014–2015. We report

here on findings from the clinical component of Phase 1.

The overall objective of the cohort study is to assess the social determinants of health and their relationship with respiratory health over time in farming and nonfarming rural populations. The detailed methodology for the study has been published by Pahwa et al.¹⁷ Briefly, we selected geographical regions of the southern half of the province (southeast, southwest, northeast, and northwest) that included rural municipalities (RMs) and towns located >60 km from an urban center as defined by Statistics Canada.¹⁸ Within regions RMs and towns were randomly selected as target areas for the study, and meetings were held with the preselected town councils and RMs. Ethics approval for this study was received from the Biomedical Ethics Review Board at the University of Saskatchewan, Saskatoon, Canada.

In Phase 1 a cross-sectional mail-out survey was sent to 11,982 target households located in the four geographical regions. A questionnaire was completed by a key respondent from each household. The questionnaire included a general household component and separate components assessing personal and environmental characteristics for each adult occupant 18 years of age or older. The questionnaire also asked for participation in a clinical assessment component of the study. Of the 11,004 eligible households identified, 4624 households with 8261 individuals, aged 18 years to 101 years, returned questionnaires (response rate = 42.0%). Of the 1675 participants who completed clinical assessments, there were 1615 who underwent allergy testing. The age cutoff for this analysis was set at 75 years, and as a result, 1599 participants were available for the current analysis.

Allergy testing was conducted by skin prick tests (SPTs) to four common allergens (local

grasses, standardized house dust mite [HDM] mixed, cat, and *Alternaria*) and positive (histamine) and negative (saline) controls (ALK; Abello Pharmaceuticals, Mississauga, Ontario, Canada). Atopy, as described by the World Allergy Association,¹⁹ was defined a priori as a positive skin prick test to common allergens. A positive SPT for this study was determined as a wheal size of >3 mm to any of the allergens compared with the negative control.

Two types of farming residency exposures were assessed and the questionnaire asked: having lived on a farm in the first year of life (yes/no) and current location of home (farm/nonfarm). Besides age and sex, other variables examined included years of education (12 years or less, more than 12 years) and smoking status (nonsmoker, ex-smoker, current smoker).

Chi-square test was used to assess the relationships between sex and sociodemographic, farming (current and early farm living) and atopy. To examine the relationships between atopy and farm residency (early farm living and current farm living), we conducted logistic regression analyses separately for overall atopy and specific allergens. All multivariable analyses assessing associations between atopy variables and type of farm residency were completed separately for men and women. The strength of associations were presented by using adjusted odds ratios (aORs) and their 95% confidence intervals (CIs).

RESULTS

There were 1559 participants between 18 and 75 years of age who completed allergy testing. As the distribution of age was skewed, we categorized age into two groups, with cutoffs at the median (56.0 years). More women (52.2%) than men (47.8%) participated in the clinical assessments.

Current smoking was uncommon in this population (8.4%). Approximately two thirds of the clinic participants lived on a farm in the first year of life, and a lower proportion (47.9%) are currently living on a farm (Table 1). The prevalence of atopy was 17.8%. The most frequent allergy was to grasses (8.8%), followed by

mixed HDM (8.1%). Atopy varied significantly by sex, as more men than women were atopic ($P < .001$).

Table 1 also presents the distribution of sociodemographic and personal characteristics of the study population stratified by sex. Men were more likely to have a Grade 12 or less level of education ($P < .001$), to have lived on a farm in the first year of life ($P < .05$), and to be currently living on a farm ($P < .001$). Women were less likely to be atopic ($P < .001$). Specific atopic sensitizations also differed by sex with men more likely to be atopic to grasses ($P < .01$) and house dust mite ($P < .05$) compared with women.

We examined the associations for atopy and living on a farm in the first year of life or currently living on a farm, overall and stratified by sex (see Figure 1). Overall, those who had early farm exposure tended to have a lower prevalence of any atopy ($P < .10$). Women who had lived on a farm in the first year of life were significantly less likely to be atopic compared with women who did not (12.3% versus 17.9%; $P < .05$). Although nonsignificant, the prevalence of atopy was also lower for men with an early farm exposure (20.4%) compared with men who did not have this early exposure (24.1%). There were no significant associations between atopy and current farm living overall or when stratified by sex.

After adjusting for potential covariates of interest, early farm living showed a similar pattern as seen in the univariate analyses of a protective association with atopy for women but this was no longer significant ($P = .11$) (Table 2). Both cat and grass atopy showed similar protective associations in women ($P = .09$ and $P = .12$). Men who had lived on a farm in the first year of life were less likely to have an allergy to *Alternaria* ($P = .03$) compared with those men who did not live on a farm in the first year of life; however, there was no significant association between early farm exposure and overall atopy in men.

There was no association between current farm living and overall atopy after adjusting for potential confounders for either men or women. Compared with their nonfarming counterparts, men currently living on a farm were more likely to have an increase in risk of an allergy to house

TABLE 1. Comparison by Sex of Personal Characteristics and Atopy Results for Clinical Assessment Participants

Variable	Men (<i>n</i> = 764) <i>n</i> (%)	Women (<i>n</i> = 835) <i>n</i> (%)	Total (<i>N</i> = 1599) <i>n</i> (%)	<i>P</i> value
Age groups				
18–55 years	346 (45.3)	446 (53.4)	792 (49.5)	.001
56–75 years	418 (54.7)	389 (46.6)	807 (50.5)	
Smoking status				
Current smoker	74 (9.7)	61 (7.3)	135 (8.4)	.064
Ex-smoker	304 (39.8)	309 (37.0)	613 (38.3)	
Never smoker	386 (50.5)	465 (55.7)	851 (53.2)	
Education				
≤Grade 12	470 (61.5)	366 (43.8)	836 (52.3)	<.0001
Grade 12	294 (38.5)	469 (56.2)	763 (47.7)	
First year of farm living				
Yes	573 (75.0)	495 (59.3)	1068 (66.8)	<.0001
No	191 (25.0)	340 (40.7)	531 (33.2)	
Current farm living				
Yes	387 (50.7)	379 (45.4)	766 (47.9)	.035
No	377 (49.3)	456 (54.6)	833 (52.1)	
Any atopy				
Yes	163 (21.3)	122 (14.6)	285 (17.8)	<.0001
No	601 (78.7)	713 (85.4)	1314 (82.2)	
Cat atopy				
Yes	61 (8.0)	61 (7.3)	122 (7.6)	.609
No	703 (92.0)	774 (92.7)	1477 (92.4)	
<i>Alternaria</i> atopy				
Yes	24 (3.1)	22 (2.6)	46 (2.9)	.545
No	740 (96.9)	813 (97.4)	1553 (97.1)	
Grass atopy				
Yes	85 (11.1)	55 (6.6)	140 (8.8)	.001
No	679 (88.9)	780 (93.4)	1459 (91.2)	
House dust mite (mixed)				
Yes	74 (9.7)	56 (6.7)	130 (8.1)	.029
No	690 (90.3)	779 (93.3)	1469 (91.9)	

dust mite ($P < .06$) and women currently living on a farm continued to have a decreased risk for an allergy to cat ($P < .03$).

DISCUSSION

In this study, we assessed the impact of early and current farming status on the prevalence of atopy in rural men and women. The prevalence of overall atopy in this study was higher in men than in women and there was a trend for lower atopy with participants who lived on a farm in the first year of life. Our findings indicate that timing of home location could influence the prevalence of specific allergic

sensitizations to aeroallergens for both male and female subpopulations. Although men as a group showed a protective effect to *Alternaria* allergy if they had lived on a farm in the first year of life, the protective effect was not apparent for men who currently lived on a farm. Instead, these men were more likely to have a borderline increased risk for HDM. For women, the borderline protective effect to cat allergen identified with early farm living was much stronger with a history of current farm living.

The prevalence of atopic sensitization (17.8%) reported in this study is lower than what has been previously reported in another Canadian study of a rural population.¹ In the study of a rural population in Humboldt,

FIGURE 1. The prevalence of atopic sensitization for overall and men and women groups for the exposures of living on a farm in the first year of life and currently living on a farm.

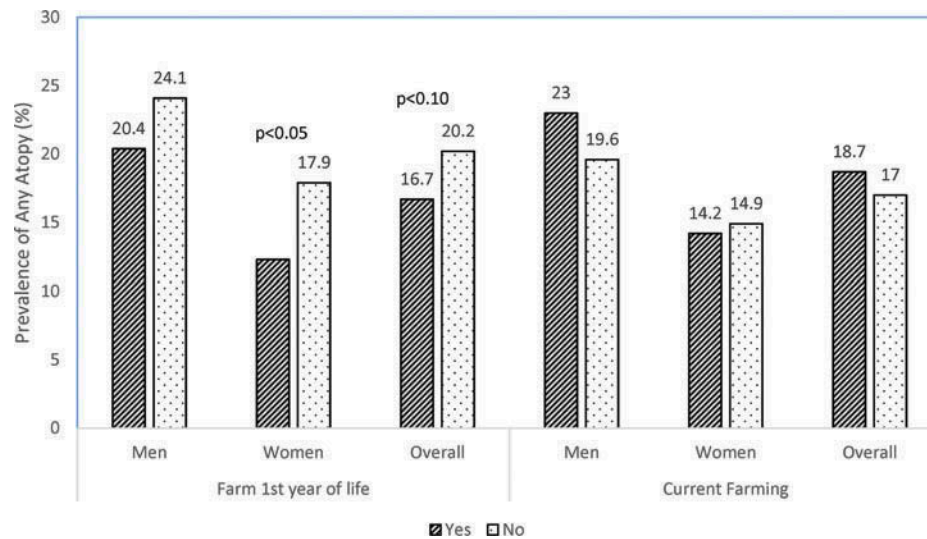


TABLE 2. Bivariable and Multivariable Logistic Regression Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for The Associations Between Atopy Variables and Living on a Farm in the First Year of Life or Current Farming for Men and Women Aged 18–75 Years ($N = 1599$)

Outcome	First year of life		Current farming	
	OR (95% CI)	Adjusted [#] OR (95% CI)	OR (95% CI)	Adjusted OR [#] (95% CI)
Men				
Any atopy	0.81 (0.55, 1.19)	0.83 (0.56, 1.24)	1.22 (0.86, 1.73)	1.24 (0.87, 1.78)
Cat	0.72 (0.41, 1.26)	0.73 (0.41, 1.29)	1.16 (0.69, 1.96)	1.16 (0.68, 1.99)
<i>Alternaria</i>	0.45 (0.20, 1.04) [†]	0.40 (0.17, 0.93)*	1.03 (0.46, 2.32)	0.83 (0.36, 1.90)
Grass	0.64 (0.40, 1.04)	0.71 (0.43, 1.16)	1.11 (0.71, 1.74)	1.18 (0.74, 1.88)
House dust mite	1.35 (0.75, 2.43)	1.35 (0.74, 2.45)	1.58 (0.97, 2.58) [†]	1.63 (0.99, 1.15) [†]
Women				
Any atopy	0.64 (0.44, 0.94)*	0.72 (0.48, 1.07)	0.95 (0.64, 1.40)	0.93 (0.63, 1.39)
Cat	0.60 (0.35, 1.01) [†]	0.63 (0.36, 1.08) [†]	0.56 (0.32, 0.98)*	0.54 (0.31, 0.94)*
<i>Alternaria</i>	0.82 (0.35, 1.92)	0.91 (0.38, 2.19)	1.47 (0.61, 3.54)	0.67 (0.28, 1.62)
Grass	0.51 (0.29, 0.88)*	0.63 (0.36, 1.12)	0.79 (0.45, 1.38)	0.81 (0.46, 1.42)
House dust mite	0.78 (0.45, 1.34)	0.88 (0.50, 1.55)	1.32 (0.76, 2.27)	1.32 (0.76, 2.28)

[#] Adjusted for age, education and smoking status.

* $P < .05$; [†] $P < .10$.

Saskatchewan, Chen et al.¹ reported atopic sensitization to similar allergens to be 29.8%. The differences in our reports of atopic sensitization could be a result of a slightly more stringent cutoff of >3 mm in our definition of atopy. Post hoc, using a less stringent definition of atopy (≥ 3 mm), the prevalence of atopy in

our study was 26.1%, closer to the prevalence reported by Chen et al.¹

The prevalence of atopy in our study did not differ between current farming and nonfarming adult populations. No difference in atopy between the farming and nonfarming population was found in one other study of rural

populations in Norway that included farmers⁴; in most other studies, however, current farm living has been shown to be associated with less atopy.^{1,5,12}

Our finding of a decrease in atopy with a history of living on a farm in the first year of life supports the findings from other studies examining the effects of early farm exposure for atopy in adulthood.^{2,5,12,20–23} Although we were unable to explore the specific farming exposures associated with a decrease in atopy, others have found that the decrease in atopic sensitivity associated with farming is strongly associated with an exposure to farm animals or animal husbandry during adulthood,^{5,12} with an early life farm exposure,^{5,12,20} and with prenatal exposure.^{2,22} Endotoxin exposure and other microbial agents, including gram-positive bacteria and molds found in high levels in the farming environment, appear to be important for providing protection against atopy in both child and adult populations.⁷ It is thought that the stimulation of Th1 helper cell development as a result of increased microbiological exposures in early life results in a down-regulation of Th2 helper cell immunity necessary for allergic responses to antigens.⁸ Exposure to endotoxin found in high levels on farms with livestock production is thought to be a major initiator of the Th1 immune response in young farm children, resulting in a subsequent reduction of an ability to mount an allergic response in children and adults to allergenic environmental agents.^{24,25} Particular farming environments (cattle, straw, and farm milk) have been shown to account for the majority of the protective effect for asthma reported in a study of farm children.²⁶ The particular risk factors for atopy, on the other hand, appear to not as clearly delineated,²⁶ suggesting that the agents involved in a protective effect with atopy within farming environments still require further identification.⁸

Sex differences in atopic sensitization for farming have been noted in one other study. Ernst and Cormier¹⁵ observed that Canadian adolescents living on a farm compared with those not living on a farm had lower occurrences of atopic sensitization to any of 21 aeroallergens ($P < .001$). Upon examination of the importance of atopy for farming exposures, the decrease in

sensitization found in the farming group was significant only for women ($P < .001$). This latter study supports our consistent findings for women. The consistent findings of a lowered atopic sensitization to cat with two different farming living exposures suggests that the farming environment may offer long-term protection against atopy for farm-exposed women. The specific exposures involved in lowered atopy with early life and current exposure in farming environments have not been delineated. Results from the Agricultural Health Study in the United States provide some evidence to support the importance of farming living characteristics for protection from atopic asthma.¹⁶ Hoppin et al.¹⁶ noted that farming women in the Agriculture Health Study who grew up on a farm and who did not apply pesticides had the lowest risk of atopic asthma compared with women who never grew up on a farm.

Although atopic sensitization in our study appeared to be generally protective for those who lived on a farm in the first year of life, this pattern of protection did not hold with current farming, with the exception of a continued decrease sensitization to cat allergen for women who had current farm exposure as well. For men, there was a trend for an increased risk of atopy to HDM for those who currently lived on a farm. Because of the cross-sectional nature of this study, we are not able to provide an evidence for the differences in association between atopy and farming by sex over time. We did find, however, upon reexamination of the data that only half of the current farming population had been exposed to farm environment in the first year of life.

The continuance of lowered atopic sensitization with long-term exposure to farming environments has been investigated by others. Prior et al.¹³ noted the increased protective effect in 4 years for atopy and specifically for grass atopy with young Tyrolean farmers. Recent studies show that working on a farm seems to have a protective effect against ongoing or newly developing sensitization to common allergens, independent of childhood farm exposure.¹² In a 14-year follow-up of 994 young farmers and 172 rural controls, current farming with a history of early farm exposure was negatively

associated with new onset atopic sensitization to cat allergen on SPT.¹² Reversal of atopy prevalence in a population previously exposed to a farming environment has also been recently found.⁶ Horak et al.¹⁴ noted as well that the protective effect of farm living for atopy was more likely to be lost in farming children compared with nonfarming children. This “plasticity” of atopy to vary over time requires further and more intense investigation of the nature of environmental conditions between investigative periods of atopic status in farming populations.²⁴

This study has several limitations. When considering the association with overall atopy, although we did find a statistical trend for an inverse associations for atopy with early farm exposure, the reduction in the prevalence of atopy (3.5%) may not be clinically important. As such, the results should be interpreted with caution. It is possible that the associations found between specific allergens and farm-living experiences could be spurious, given the number of statistical tests conducted. However, the odds ratios for each allergen are generally consistent for the reduced risk for allergy for both men and women with an early life farming exposure and for men, higher risk for atopy with a current farming exposure. The population understudy when compared with the overall study population did not differ in the report of early farm exposure or sex status. However, the clinic population appears to be younger, better educated, nonsmokers, and more likely to live on farms than the overall study population. A selection bias with the clinic population cannot be ruled out. There may have been some differential misclassification towards the null for atopic status in our sample, as our assessment of atopy by SPT was limited to four common aeroallergens. However, the allergens chosen were similar in nature and to the number that were evaluated in other studies.^{1,2,12,21,22} As a diagnostic tool, SPT has been shown to have better diagnostic efficiency compared with other measures of atopy-related asthma.²⁷ Due to sample size limitations, we were not able to examine the relationship between atopy, sex, and early or current farm living by types of farm production. As this analysis was conducted using information from

the baseline cross-sectional survey, we are not able to determine causality between farm living and decreased atopic sensitivity.

In conclusion, there are associations between atopic sensitization and farm living that appear to vary by sex. Specific allergens appear to be more important for an increase in or protection from allergy that is related to the timing of farming exposures.

FUNDING

This study was funded by a grant from the Canadian Institutes of Health Research “Saskatchewan Rural Health Study,” Canadian Institutes of Health Research MOP-187209-POP-CCAA-11829.

REFERENCES

1. Chen Y, Rennie D, Cormier Y, McDuffie H, Pahwa P, Dosman J. Reduced risk for atopic sensitization among farmers: the Humboldt study. *Int Arch Allergy Immunol*. 2007;144:338–342.
2. Lampi J, Canoy D, Jarvis D, et al. Farming environment and prevalence of atopy at age 31: prospective birth cohort study in Finland. *Clin Exp Allergy*. 2011;41:987–993.
3. Olivieri M, Verlato G, Corsico A, et al.; Italian European Community Respiratory Health Survey group. Prevalence and features of allergic rhinitis in Italy. *Allergy*. 2002;57:600–606.
4. Eduard W, Omenaas E, Bakke PS, Douwes J, Heederik D. Atopic and non-atopic asthma in a farming and a general population. *Am J Ind Med*. 2004;46:396–399.
5. Radon K, Schultze A, Nowak D. Inverse association between farm animal contact and respiratory allergies in adulthood: protection, underreporting or selection? *Allergy*. 2006;61:443–446.
6. Sozanka B, Blaszczyk M, Pearce N, Cullinan P. Atopy and allergic respiratory disease in rural Poland before and after accession to the European Union. *J Allergy Clin Immunol*. 2014;133:1347–1355.
7. Heederik D, von Mutius E. Does diversity of environmental microbial exposure matter for the occurrence of allergy and asthma. *J Allergy Clin Immunol*. 2012;130:40–50.
8. Wlasiuk G, Vercelli D. The farm effect, or: when, what and how a farming environment protects from asthma and allergic disease. *Curr Opin Allergy Clin Immunol*. 2012;12:461–466.

9. Braun-Fahrlander C. Editorial: the role of the farm environment and animal contact for the development of asthma and allergies. *Clin Exp Allergy*. 2001;31:1799–1803.
10. Ege MJ, Mayer M, Normand AC, et al.; GABRIELA Transregio 22 Study Group. Exposure to environmental microorganisms and childhood asthma. *N Engl J Med*. 2011;364:701–709.
11. Walusiak J, Krawczyk-Adamus P, Hanke W, Witczak T, Palczynski C. Small nonspecialized farming as a protective factor against immediate-type occupational respiratory allergy? *Allergy*. 2004;59:1294–1300.
12. Enholm G, Schlunssen V, Doekes G, et al. Become a farmer and avoid new allergic sensitization: adult farming exposures protect against new-onset atopic sensitization. *J Allergy Clin Immunol*. 2013;132:1239–1241.
13. Prior C, Falk M, Frank A. Longitudinal changes of sensitization of farming-related antigens among young farmers. *Respiration*. 2001;68:46–50.
14. Horak F, Studnicka M, Gartner C, et al. Parental farming protects children against atopy: longitudinal evidence involving skin prick testing. *Clin Exp Allergy*. 2002;12:1155–1159.
15. Ernst P, Cormier Y. Relative scarcity of asthma and atopy among rural adolescents raised on a farm. *Am J Respir Crit Care Med*. 2000;161:1563–1566.
16. Hoppin JA, Umbach DM, London S, et al. Pesticides and atopic and non-atopic asthma among farm women in the Agricultural Health Study. *Am J Respir Crit Care Med*. 2008;177:11–18.
17. Pahwa P, Karunanayake CP, Hagel L, et al. The Saskatchewan Rural Health Study: an application of a population health framework to understand respiratory health outcomes. *BMC Res Notes*. 2012;5:400.
18. du Plessis V, Beshari R, Bollman RD, Clemenson H. Definitions of “Rural.” Agriculture and Rural Working Group Paper Series, Working Paper No. 61. Catalogue no. 21-601-MIE-No. 061. Ottawa, Canada: Agricultural Division, Statistics Canada, 2002. Available at: <http://www5.statcan.gc.ca/olc-cel/olc.action?ObjId=21-601-M2002061&ObjType=46&lang=en&limit=0>. Accessed November 15, 2014.
19. Johansson SG, Bieber T, Dahl R, et al. Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol*. 2004;113:832–836.
20. Leynaert B, Neukirch C, Jarvis D, Chinn S, Burney P, Neukirch F. European Community Respiratory Health Survey. Does living on a farm during childhood protect against asthma, allergic rhinitis, and atopy in adulthood? *Am J Respir Crit Care Med*. 2001;164:1829–1834.
21. Portengen L, Sigsgaard T, Omland Ø, Hjort C, Heederik D, Doekes G. Low prevalence of atopy in young Danish farmers and farming students born and raised on a farm. *Clin Exp Allergy*. 2002;32:247–253.
22. Pekkanen J, Xu B, Jarvelin MR. Gestational age and the occurrence of atopy at age 31—a prospective birth cohort study in Finland. *Clin Exp Allergy*. 2001;31:95–101.
23. Kilpelainen M, Terho EO, Helenius H, Koskenvuo M. Farm environment in childhood prevents the development of allergies. *Clin Exp Allergy*. 2000;30:201–208.
24. Ege M, von Mutius E. Atopy: a mirror of environmental changes [editorial]. *J Allergy Clin Immunol*. 2014;133:1354–1355.
25. Smit LAM, Heederik D, Doekes G, Lammers JW, Wouters IM. Occupational endotoxin exposure reduces the risk of atopic sensitization but increases the risk of bronchial hyperresponsiveness. *Int Arch Allergy Immunol*. 2009;152:151–158.
26. Illi S, Depner M, Genuneit J, Horak E, et al.; GABRIELA Study Group. Protection from childhood asthma and allergy in alpine farm environments—the GABRIEL Advanced Studies. *J Allergy Clin Immunol*. 2012;129:1471–1477.
27. Tschoep JM, Sistek D, Schindler C, et al. Current allergic asthma and rhinitis: diagnostic efficiency of three commonly used atopic makers (IgE, skin prick tests, and Phadiatop®): results from 8329 randomized adults from the SAPALDIA study. Swiss Study on Air Pollution and Lung Diseases in Adults. *Allergy*. 1998;53:608–613.

Copyright of Journal of Agromedicine is the property of Taylor & Francis Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.