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Mosquito saliva–specific IgE and IgG antibodies in 1059 blood donors

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To the Editor:

There are few epidemiologic data on the prevalence of mosquito allergy, though reactions to mosquito bites are common. 1>3 Local cutaneous reactions vary from small papules to large, extremely pruritic swellings, including the recently described Skeeter syndrome. Systemic reactions include generalized urticaria, angioedema, and anaphylactic shock.^{2,3} These reactions are caused by proteins in the mosquito saliva and involve IgE, IgG1, and IgG4 responses and lymphocyte proliferation.^{1,4}

We have developed sensitive and specific ELISAs by which to measure mosquito saliva –specific IgE and IgG antibodies.⁵ We have previously reported that elevated mosquito saliva –specific IgE and IgG levels are associated with the development of mosquito allergy⁶ and correlate with mosquito bite reactions.⁴ Here, by measuring these antibodies, we investigated the prevalence of sensitization to mosquito saliva and its relationship with a history of allergic diseases.

This study was approved by the University of Manitoba Research Ethics Board and carried out in Winnipeg and Brandon, Manitoba, Canada, in 1999. Sera were obtained from 1059 random blood bank donors, either before (n = 595) or after (n = 484) the summer “mosquito season.” Each of the participants, who had a mean age of 39 years (range, 17-70 years), completed an anonymized questionnaire about his or her (a) personal history of asthma, allergic rhinitis, atopic dermatitis, food allergy, and stinging or biting insect allergy in the preceding 2 years, (b) family history of allergy, and (c) extent of exposure to mosquitoes. The control group consisted of 31 previously reported individuals with negative mosquito bite test results.⁴

Mosquito-specific IgE and IgG in human sera were measured through use of indirect ELISAs.⁵ Mosquito saliva extract from *Aedes vexans*, the indigenous species, was used as the capture antigen in the ELISAs.⁷ Briefly, microplates were coated with the saliva extract, incubated with test

samples or a reference serum (1:20 for IgE and 1:200 for IgG), and then incubated with goat antihuman IgE or goat antihuman IgG followed by incubation with a rabbit antigoat IgG conjugate.

The data were analyzed through use of SAS software. Associations among the different variables were examined by means of χ^2 and t tests. Variables were included in a multiple logistic regression model if they were found to be statistically significant in the univariate analysis. Odds ratios with 95% CIs were reported. The significance level was set at $\alpha = 0.05$.

In the 1059 blood donors studied, the positivity rate was 18 % for IgE and 9% for IgG using the mean of the 31 negative controls plus 1 SD as a cutoff level. The IgE and IgG levels were significantly correlated ($r = 0.304$; $P < .0001$), suggesting that IgG antibodies might also be involved in the pathogenesis of mosquito allergy, as found in our previous studies.^{1,4,6} The sera obtained after the “mosquito season” were strongly associated with positive IgE (odds ratio = 4.03; $P < .05$) and IgG (odds ratio = 6.50; $P < .01$) levels.

A family history of allergy, atopic dermatitis, self-reported allergy to mosquito bites, and residence in a high-exposure-to-mosquitoes area were significantly associated with positive IgE levels, whereas positive IgG levels were significantly associated with male sex, post-“mosquito season ” blood donation, and residence in the high-exposure area, but inversely associated with self-reported asthma (Table I).

Table 1. Correlation of serum mosquito saliva-specific IgE and IgG antibodies with various parameters (univariate)

Parameter/status	IgE					IgG				
	Positive (%)	Negative (%)	P value	Odds ratio	95% CI	Positive (%)	Negative (%)	P value	Odds ratio	95% CI
Location										
Brandon	13.5	86.5	.008*†	1.62	0.43-0.88	6.2	93.8	.020*	1.82	0.34-0.92
Winnipeg	20.0	80.0				11.0	89.0			
Sex										
Female	18.6	81.4	.62	0.92	0.66-1.29	6.7	93.3	.022*	1.72	1.08-2.76
Male	17.3	82.7				11.0	89.0			
Self-reported allergy to mosquito bites										
No	7.4	92.6	.020**	2.51	1.13-5.57	8.9	91.1	.53	0.69	0.21-2.25
Yes	17.0	83.0				6.2	93.8			
"Mosquito season"										
Pre	19.8	80.2	.099	0.76	0.56-1.06	5.0	95.0	.0001**	3.08	1.96-4.84
Post	15.9	84.1				14.0	86.0			
Allergy to stinging insects										
No	18.2	81.8	.74	1.12	0.57-2.22	9.3	90.7	.20	1.43	0.63-3.25
Yes	20.0	80.0				12.7	87.3			
Asthma										
No	18.3	81.7	.29	0.68	0.33-1.40	9.7	90.3	.023*	0.14	0.019-1.01
Yes	13.2	86.8				1.5	98.5			
Rhinitis										
No	18.3	81.7	.75	0.92	0.58-1.48	9.3	90.7	.99	1.0	0.54-1.84
Yes	17.1	82.9				9.3	90.7			
Atopic dermatitis										
No	17.3	82.7	.03*	2.02	1.06-3.86	9.4	90.6	.23	0.43	0.10-1.80
Yes	29.8	70.2				4.3	95.7			
Food allergy										
No	18.3	81.7	.67	0.86	0.42-1.73	9.4	90.6	.72	0.84	0.33-2.15
Yes	16.1	83.9				8.1	91.9			
Family history of allergy										
No	16.0	84.0	.031*	1.43	1.03-1.97	9.0	91.0	.86	1.04	0.67-1.61
Yes	21.0	79.0				9.4	90.6			

For location, reference is Brandon; for sex, reference is female.

*Variable is statistically significant with univariate analysis. Cutoff level = mean + 1 SD.

†Variable is statistically significant with multivariate regression analysis.

**Variable is statistically significant with univariate analysis. Cutoff level = mean + 2 SD.

There was no significant correlation of IgE or IgG with age.

The prevalence of mosquito allergy that we report here cannot be compared with the prevalence rates reported in other populations because there has been no previous similar epidemiologic study. One investigator measured mosquito salivary gland-specific IgE and IgG levels in 300 hospital outpatients; however, inasmuch as there were no negative controls and no information about exposure to mosquitoes or other allergic disorders was obtained, the results are difficult to interpret.⁸ Using a different approach—the mosquito bite test—in a small group of selected volunteers, other investigators demonstrated that 147 (91%) of 162 participants developed a positive skin reaction (wheal diameter > 5 mm).⁹ We previously reported that 29 (71%) of 41

volunteers developed a positive immediate skin reaction to A vexans (wheal area > 0.3 cm²).⁴ In the study we report here, the prevalence of mosquito allergy is considerably lower in the present study than in the mosquito bite studies, probably because the individuals investigated were healthy blood donors without any specific history of or interest in mosquito allergy. In addition, given that serum IgE and IgG measurements are less sensitive than mosquito bite tests, only those individuals with strong mosquito bite reactions have elevated saliva-specific IgE and IgG levels.

In the present study, mosquito saliva-specific IgG antibody levels were significantly different between the pre- and post –“mosquito season” groups but the specific IgE levels were not. Because the preseason and postseason groups consisted of different individuals and probably included many people without allergic reactions to mosquito bites, the typical postseason increase in specific IgE reported previously in patients highly allergic to mosquito bites with seasonal exposure^{1,10} was not observed. The IgE and IgG antibody levels were consistently higher in the Winnipeg participants than in the Brandon group, a finding that we attribute to the fact that mosquito counts were higher in Winnipeg than in Brandon throughout the summer of 1999 according to provincial government data. The finding that a positive history of allergy in 1 or more immediate family members was associated with mosquito saliva-specific IgE is in agreement with a previous publication.⁵ Male sex was positively associated with positive mosquito saliva-specific IgG levels; this is in agreement with one previous report that males developed larger mosquito bite wheals than females,⁹ but it does not agree with another report.⁵

In summary, 18% of midwestern North American blood donors had mosquito saliva-specific IgE levels greater than 1 SD above the mean for mosquito bite test-negative subjects.

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