The natural history of exposure to the imported fire ant *(Solenopsis invicta)*

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Background: *Imported fire ants (IFA) are a common cause of insect venom hypersensitivity in the southeastern United States. The purpose of this study was to determine the sting attack rate and development of specific IgE in an unsensitized population.*
Methods: *Study participants consisted of 137 medical students with limited exposure to IFA-endemic areas who were temporarily training in San Antonio, Tex. Subjects were surveyed for prior IFA exposure with a questionnaire, and IFA-specific IgE was evaluated with RAST and intradermal skin testing. Evaluations were performed on arrival and reported at departure from the endemic area 3 weeks later.*
Results: *One hundred seven subjects completed the study. Field stings were reported in 55 subjects, resulting in a sting attack rate of 51%. In these 55 subjects 53 (96%) reported a pustule or a small local reaction at the sting site, one (2%) reported an isolated large local reaction, and none reported a systemic reaction. At the 3-week follow-up skin test and RAST conversions occurred in seven subjects (13%) and in one subject (1.8%), respectively.*
Conclusions: *Even brief exposures to IFA-endemic areas result in significant sting rates and concurrent rapid development of IFA-specific IgE in 16% of stung subjects. (J ALLERGY CLIN IMMUNOL 1995;95:824-8.)*

Key words: *Imported fire ant, whole body extract, Hymenoptera, hypersensitivity*

In the southeastern United States stings from the imported fire ant (IFA) are a common cause of Hymenoptera insect venom hypersensitivity. As the name *imported* implies, IFA are not native to the United States but were probably imported from South America on agricultural products through the port of Mobile, Ala., during the early twentieth century.[1]

Fire ants are members of the insect family Formicidae. Together with the families Apidae and Vespidae, they constitute the medically important members of the order Hymenoptera. The IFA genus, *Solenopsis,* contains two relevant species of fire ants that inhabit the United States, *Solenopsis invicta* and *Solenopsis richteri.* Together these two species inhabit more than 250 million acres in at least 13 southeastern states.[2] The IFA is a particularly tenacious predator and eliminates other ant species from its habitat. The more aggressive *S. invicta* has prevailed over *S. richteri* and has colonized the majority of the inhabited territories and limited *S. richteri* to a small range in northern Mississippi and Alabama.[1, 3] The range of *S. invicta* is limited by cold climates to the north and desert to the west.[3]

The IFA is an aggressive and exceptionally

Abbreviations used
IFA: Imported fire ant
WBE: Whole body extract

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The opinions and assertions contained herein are the private views of the authors and are not to be considered as official or as reflecting the views of the Department of Defense or other departments of the U.S. Government.
Supported entirely by the U.S. Air Force. Except for Dr Hoffman, who contributed only technical support and reviewed the manuscript for accuracy, the authors have no other corporate or institutional affiliations.
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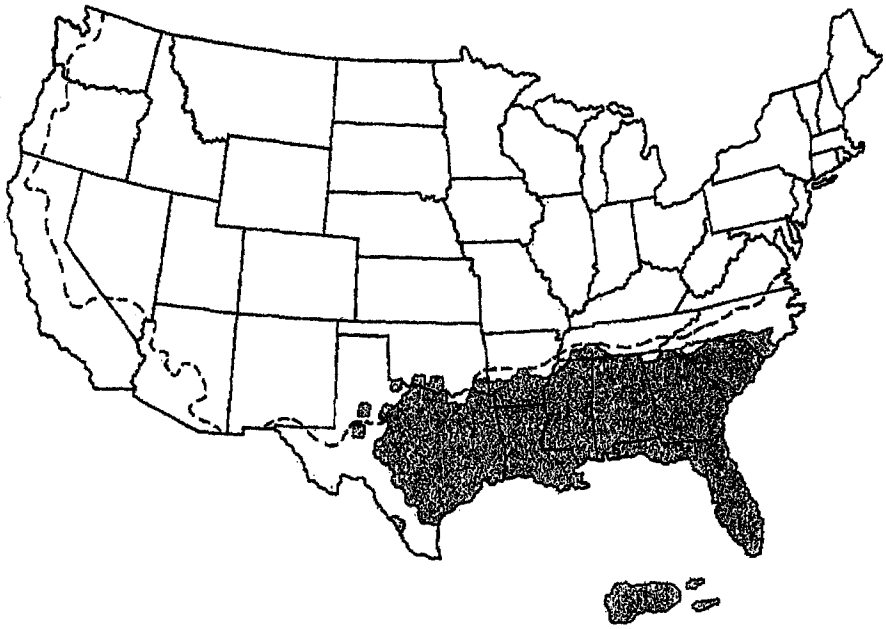

FIG. 1. Current area of fire ant infestation (*shaded area*). *Dotted line,* ten-degree isobar.

resourceful arthropod, using several biologic strategies to ensure survival of the species.[4, 5] Current evidence indicates that through interbreeding with local ant species, their range is expanding as new hybrids display drought and cold resistance.[4] Fig. 1 illustrates present fire ant infestation in the United States. The solid line shown is the 10-degree isobar, below which IFA can thrive and persist because the average lowest annual temperature is greater than 10° F. As the IFA's range continues to expand, its medical importance can also be expected to increase.

The IFA is a source of considerable morbidity and mortality for persons residing in endemic areas.[6-10] A survey done by Stafford et al.[11] in cooperation with the American Academy of Allergy and Immunology Fire Ant Subcommittee in 1989 reported that approximately 20,755 patients are treated annually for significant reactions to fire ant stings in the southeastern United States. Of these 20,755 patients, an estimated 63% were treated for local reactions only. An additional 2% of patients required medical intervention for life-threatening anaphylaxis.

In addition to their importance as a source of hypersensitivity sting reactions in human beings, IFA have become a considerable agricultural pest. Widespread infestation causes losses in crop yield and livestock, and costs millions of dollars each year.[12]

IFA's geographic restriction provides a unique opportunity to assess the chronologic development of Hymenoptera sensitivity. This study was designed to examine prospectively an unsensitized population exposed to the San Antonio, Tex., IFA-endemic area and to provide insights into the attack rate and the development of IFA-specific IgE hypersensitivity in this population after exposure to IFA.

METHODS

Subjects

The participants were enrolled from a group of military medical students ranging in age from 21 to 30 years and undergoing a 3-week educational program in San Antonio, Tex., during May through August, in 1991 and 1992. The program consisted primarily of classroom didactic instruction with structured outdoor activity limited to jogging and light calisthenics. There were no overnight outdoor activities or prolonged exposure to ground-dwelling insects.

Before enrollment subjects were surveyed regarding geographic residence, travel history, previous Hymenoptera stings, atopic history, medical history, and medications. Each enrolled subject signed a consent form approved by our institutional review board. A lecture on recognizing IFA, their stings, and the type of reactions that might be seen (including the development of a pustule) was delivered to each subject. On completion of their program 3 weeks later, enrolled subjects were again surveyed to assess for interim IFA and other Hymenop-

TABLE I. Summary of results

	Enrollment yr		
	1991	1992	Total
No. of subjects enrolled	48	89	137
No. of subjects disqualified	16	14	30
No. of subjects completing	32	75	107
No. (%) reporting IFA sting	13 (41)	42 (56)	55 (51)
No. (%) with positive skin test result	2 (15)	5 (12)	7 (13)
No. (%) with positive RAST result	0 (0)	1 (2.3)	1 (1.8)

tera stings, and the description of any resultant reactions. Ten subjects had an additional follow-up 6 weeks after initial enrollment. These 10 subjects had a total of 6 weeks' exposure because of additional training.

To be enrolled subjects were required to reside outside an IFA-endemic area and to have never visited endemic areas longer than 7 days. Endemic areas included states thought or known to contain areas of IFA infestation, and South and Central America. Additionally, all subjects enrolled were required to have negative initial skin test reactions to IFA. Patients were excluded if they were pregnant or had used systemic steroids, β-blockers, or antihistamines within 72 hours of enrollment.

Skin testing and RAST determination

At enrollment and at the 3-week follow-up visit, subjects underwent intradermal skin testing with Hollister-Stier IFA whole body extract (WBE) (1:1000 wt/vol extract dilution) and with standard histamine and negative controls. Skin test reactions were considered positive if the intradermal skin test wheal measured greater than 3 × 3 mm and demonstrated surrounding erythema.

Serum was obtained immediately before skin testing at enrollment and at the 3-week follow-up. All specimens were stored at −20° C until assayed, to preclude interassay variability. IFA venom RAST was performed with techniques previously described.[13, 14]

A simple attack rate was determined as the ratio of persons stung to the total number at risk.

RESULTS

Table I summarizes the results of 499 subjects examined on their arrival in San Antonio; 137 met initial geographic and exposure eligibility criteria. Of the 137 recruited subjects, a total of 30 were disqualified. A positive IFA skin test result during the initial evaluation was cause for disqualification in 23 subjects; 18 had a potential exposure history and five had no history of IFA exposure. In addition, seven participants were disqualified for failure to return or complete follow-up evaluations. A total of 107 persons completed the study.

Of the 107 subjects completing the study, 55 reported a suspected IFA sting, resulting in a self-reported sting attack rate of 51%. Among these 55 subjects, 53 (96%) reported a pustule or a small local reaction. Of the remaining two subjects (4%), one reported an isolated large local reaction of greater than 8 cm without a pustule and one reported a sting without identifiable skin findings. No immediate systemic or generalized reactions were reported.

Skin test conversion was observed in seven of these 55 stung subjects, whereas RAST conversion was noted in only one of the seven subjects with positive reactions. Thus skin test and RAST conversion rates were 13% and 1.8%, respectively, in stung subjects at the 3-week follow-up visit. Among the 52 subjects reporting no IFA sting during the 3 weeks, two additional subjects demonstrated skin test but not RAST conversion.

Finally, in the group of 11 subjects who had an additional follow-up after a total of 6 weeks' exposure, seven were stung in the second 3-week period. One additional subject became positive to skin testing between the 3- and 6-week follow-ups. Also, in one of these subjects who had a positive reaction to skin testing but who was RAST negative at 3 weeks, a borderline RAST result developed at 6 weeks.

DISCUSSION

The annual attack rate for fire ant stings has been reported to range from 23% to 58%, on the basis of surveys of populations living in areas endemic for the IFA.[6, 8-10, 15, 16] Using a retrospective random population survey in New Orleans, deShazo et al.[15] reported a sting attack rate of 58% during a 1-year recall period. Adams and Lofgren,[16] in Georgia in the 1970s and 1980s, reported that in a 1-year period 30% of the population was stung. They reported that children younger than 15 years were most likely to be stung,

having a rate of 32% to 53%, and stings most often occurred in the spring and summer. In Louisiana Clemmer and Serfling[6] reported similar results, which demonstrated a sting attack rate of 55% in persons less than 10 years of age and an overall 29% sting rate between June and August. In a 1989 review of IFA allergy, Stafford et al.[9] reported that an average attack rate of 30% is a conservative estimate when differences in IFA survey methodology are taken into account. Comparison of these data with our results is constrained by the retrospective nature of these previous studies.

Unlike previously reported studies, this study is unique in that it is prospective and in that the participants were previously unsensitized. Our prospective 51% sting rate for a population exposed for 3 weeks is greater than that reported in many retrospective studies. These differences may be accounted for by several factors, including increased exposures related to the youth of our subjects, their outdoor activity, and the occurrence of the study in the summer months. The study group was also motivated, well educated, and taught to recognize IFA stings.

This prospective study is the first of which we are aware to address the chronologic development of IFA-specific IgE, as measured by skin test and RAST. Previous cross-sectional studies have used skin testing to assess the prevalence of IFA-specific IgE in susceptible populations living in endemic regions. In a cross-sectional study of 99 patients living in the southeastern United States and being examined for inhalant allergy, Stafford et al.[9] reported that 28% had positive skin test reactions to IFA. Hoffman et al.[17] in Georgia reported that 24% of a study control population with no history of insect sting allergy had positive skin test reactions to IFA venom and IFA WBE and IFA venom RAST. In Texas 25% of nonallergic control subjects demonstrated skin test reactivity to IFA WBE.[18] In contrast, the prospective incidence of IFA-specific IgE development in this study of a previously unsensitized population during 3 weeks of IFA exposure was reported as a 13% skin test conversion rate and a 1.8% RAST conversion rate from negative to positive results. Although not directly comparable, these incidence rates are consistent with the prevalence rates from the cross-sectional studies.

The use of both IFA skin test and RAST in this study provide a limited opportunity to compare the sensitivity of IFA WBE skin testing with IFA venom RAST. In this study venom RAST appears to be less sensitive when compared with skin testing with IFA WBE (1.8% vs 13% conversion rate). Compared with IFA WBE skin testing as a standard, the venom RAST sensitivity rate was only 13.8%. Stafford et al.[19] in 1989 compared in vivo and in vitro tests in the diagnosis of IFA allergy. They observed equivalent sensitivities and specificities between IFA WBE skin testing, IFA venom skin testing, and IFA venom RAST. Only IFA WBE RAST was diagnostically less sensitive. In more recent work Stafford et al.[20] examined the sensitivity of WBE versus venom skin testing and WBE versus venom RAST. The study was not designed to compare directly WBE skin testing with venom RAST, and there was no direct statistical comparison between WBE skin testing and venom RAST. However, the data suggested that WBE skin testing was more sensitive, with a greater positive predictive value than venom RAST. These findings are consistent with our observations of greater sensitivity of IFA WBE skin testing compared with IFA venom RAST at the 3-week follow-up interval.

The observance of two subjects who converted to a positive skin test result without a self-reported IFA sting is intriguing. There are several possible explanations for this observation. First, the skin test at enrollment may have induced sensitization. Second, in their sting history both subjects reported previous winged Hymenoptera stings. Cross-reactivity between IFA and winged Hymenoptera has been reported,[17, 21] and the skin test may have resensitized these subjects. Finally, we believe that it is most likely that these subjects were actually stung but failed to recognize the sting and/or pustule.

Finally, the additional 6-week follow-up data on 10 subjects suggests that development of detectable IFA-specific IgE may occur beyond 3 weeks from exposure. Alternatively, because of our study design it is possible that some subjects tested at 3 weeks may have been stung shortly before testing and that converters may have been missed with a single follow-up visit. In addition, the fact that IFA WBE skin test conversion may be observed before IFA venom RAST conversion supports the conclusion that IFA WBE skin testing is more sensitive than IFA venom RAST.

A high attack rate of IFA stings (51%) was observed during 3 weeks of summertime exposure to an endemic area. Evidence of rapid development of IFA-specific IgE was also observed in our study population, with IFA WBE skin testing (13% conversion rate) being more sensitive than IFA-venom specific RAST (1.8% conversion rate) at 3

weeks. These prospective observations describe a natural history of IFA stings in unsensitized persons in which development of specific IgE is common and rapid. Because all study participants have military scholarships, many will be available for follow-up skin and RAST testing in the future. This should lend insight into the development and maintenance of IFA sensitivity.

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