
Management of imported fire ant allergy: results of a survey

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Background: Fire ant allergy is a significant health problem in the southern United States. Management of fire ant allergy is less clearly defined than management of allergy to the winged Hymenoptera.

Objective: To determine how fire ant allergy is managed by practicing allergists.

Methods: A survey form was developed and distributed to American College of Allergy, Asthma & Immunology members practicing in fire ant endemic states. Completed forms were returned to the American College of Allergy, Asthma & Immunology central office and forwarded to the authors for analysis.

Results: Three hundred twenty-nine of 879 (37.4%) surveys were returned; 81% of respondents have evaluated patients with imported fire ant allergy. Immunotherapy is used by 96.7% of respondents to treat fire ant allergy. A wide range of maintenance dosages are prescribed. Skin testing is the most common diagnostic method. Systemic reactions to stings while on maintenance immunotherapy were reported by 19%. Allergists utilize different criteria in consideration for stopping immunotherapy; 19% continue it indefinitely.

Conclusions: There are many areas of general uniformity and other areas of divergence in how allergists manage imported fire ant allergy. These findings suggest continued need for further investigation regarding the efficacy, dosage, and duration of immunotherapy, as well as further elucidation of the natural history of fire ant allergy.

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INTRODUCTION

Imported fire ant allergy is principally a concern for physicians and patients in the Southern region of the United States. It may, however, impact on allergy practice elsewhere, when fire ant-allergic patients move beyond endemic areas. Since imported fire ants entered the United States in the early part of the 20th century, their range has spread throughout the South. Figure 1 depicts their range in August of 1996.

With the increase in range of the imported fire ant, greater incidence of imported fire ant allergy has been seen since the 1940s. Treatment of imported fire ant allergy has varied over time. Immunotherapy with imported fire ant whole body extract was first reported

by Triplett in 1973.¹ Since then, other reports have supported its use in the treatment of fire ant allergy with the study by Freeman, et al, providing the strongest evidence for its efficacy.^{2,3} None of these studies has been a prospective, placebo-controlled study. Many questions about fire ant allergy and the indications, utilization, and efficacy of immunotherapy in the management of this problem remain unanswered. Imported fire ant whole body extract (unlike whole body extract of the winged Hymenoptera) has been shown to contain significant quantities of relevant venom allergens.⁴⁻⁶ No studies of immunotherapy with imported fire ant venom have been conducted.

To determine the current practice patterns of imported fire ant allergy management in imported fire ant endemic states, the American College of Allergy, Asthma & Immunology Insect Hypersensitivity Committee de-

veloped a research project to survey American College of Allergy, Asthma & Immunology members in spring 1995. Other surveys have documented the scope of the problem of fire ant allergy but have not examined details of its management.⁷⁻⁹ This paper describes the findings of the survey research project.

METHODOLOGY

Members of the American College of Allergy, Asthma & Immunology Insect Hypersensitivity Committee wished to determine how allergists manage fire ant allergy. As such, a survey of American College of Allergy, Asthma & Immunology members practicing in the imported fire ant endemic or border states and territories of Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, New Mexico, North Carolina, Puerto Rico, South Carolina, Tennessee, and Texas was conducted. Oklahoma was not surveyed as the authors were not aware of the presence of fire ants in Oklahoma at the time of the survey. The survey form (Table 1) was distributed by American College of Allergy, Asthma & Immunology staff members through a mass mailing from the Executive Office in Arlington Heights, Illinois.

Staff members used the American College of Allergy, Asthma & Immunology mailing list to identify all members practicing in areas listed above. Survey forms were then mailed to the office address of the American College of Allergy, Asthma & Immunology member with a request to return the survey within 3 weeks of receipt. A total of 879 surveys were sent. There was no follow-up with members who failed to return their surveys.

Surveys were compiled by the authors and analyzed using the statistical software at the University of Missis-

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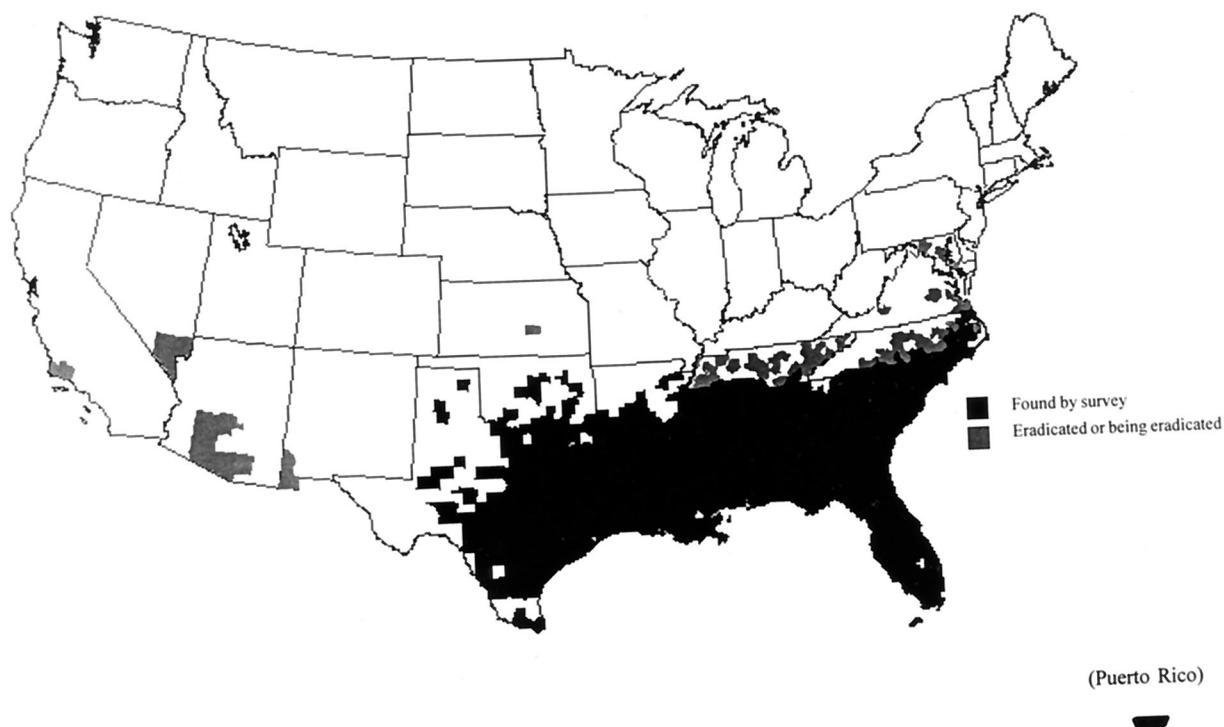


Figure 1. Reported August 1996 distribution of *Solenopsis invicta*, *richteri*, and *Saevissima richteri*. Map adapted from information made available by the Cooperative Agricultural Pest Survey/National Agricultural Pest Information System (<http://www.ceris.purdue.edu:80/napis/>).

issippi Medical Center. Results from the survey are reported below.

RESULTS

Of 879 members surveyed, 329 (37.4%) returned completed surveys. Survey responses indicate that 268 of 329 respondents (81.5%) have evaluated patients with imported fire ant allergy. The use of immunotherapy is almost universal (261 of 268 or 96.7%) among physicians who treat imported fire ant allergic patients. Of the physicians who use immunotherapy, over 98% recommend immunotherapy for adults and children with cardiorespiratory reactions; 77.6% recommend immunotherapy for adults and 28.9% for children with reactions limited to the skin (Fig 2).

A wide range of maintenance dosages was reported. The most commonly used maintenance vial concentration was 1:100 wt/vol followed by 1:10 w/v (Fig 3).

In order to analyze the data for maintenance dosages, values were converted to micrograms of Sol i III protein as indicated from prior studies conducted by Hoffman. Sol i III is one of the relevant allergens of the imported fire ant, *Solenopsis invicta*. In 1991, Hoffman determined that 0.5 mL of 1:10 wt/vol extract contained 15–22 μg of Sol i III protein.⁴ Calculations of dosage in this report are based on the midpoint (18.5 μg) of this range. The distribution of dosages is depicted in Figure 4. The most commonly reported (mode) and median maintenance dose was 1.85 μg Sol i III which corresponds to 0.5 mL of 1:100 wt/vol extract. The mean of the maintenance doses was 5.7 μg . Approximately 5.5% of respondents express dosage in protein nitrogen units (PNU). Of these the median dosage was 5000 PNU/mL; the mode was 5000 PNU/mL, and the mean dosage was 5941 PNU/mL. These values could not be expressed in

terms of venom protein content because no studies have quantified venom protein in relationship to PNU concentration.

The survey form included a space for respondents to list numbers of patients suffering cutaneous or more severe reactions after achieving their maintenance dosage. Two hundred forty-four respondents answered this question. Forty-seven (19%) of the 244 who answered this question reported at least one such reaction. Analysis of these data was difficult as many respondents included a range of patients and others indicated they had noted reactions, but did not supply a number. No fatal sting reactions were reported in patients on maintenance immunotherapy.

Skin testing is the most commonly used diagnostic procedure, used by 94.5% of responding physicians. RAST is the method of choice of only 2.5%. Approximately 19% continue

Table 1. Survey Form

Much has been learned about fire ant allergy over the last two decades. However, many questions remain unanswered about fire ant allergy. In order to determine how allergists manage patients with allergy to imported fire ants, the Insect Hypersensitivity Committee is conducting the following survey of members of the ACAAI who practice in our near fire ant endemic areas. Please answer the following questions in this brief survey. Please return the survey in the enclosed envelope. Thank you for your participation.

1. Do you see patients with imported Fire Ant Allergy? Yes No
(If no stop here and return survey; If yes continue with question #2) (Circle One)

2. If so, do you treat them with immunotherapy? Yes No
(If no stop here and return survey; If yes continue with questions #3 and complete the survey) (Circle One)

3. Given the following scenarios would you recommend fire ant immunotherapy for the patient described?
(Please circle your response)

Yes No A. Adult with systemic reaction including cardiorespiratory symptoms.

Yes No B. Adult with systemic reaction limited to the skin.

Yes No C. Child with systemic reaction including cardiorespiratory symptoms.

Yes No D. Child with systemic reaction limited to the skin.

4A and 4B involve questions about maintenance dose immunotherapy. If it is your practice not to prescribe a "maintenance dose" at the outset; but instead increase to a maximum tolerated dose, please answer 4A and 4B based on the dose which your patients usually achieve.

4. A. Please indicate the concentration of the maintenance vial you usually prescribe:

_____wt/vol or _____PNU/mL

B. What is the usual maximum volume from the maintenance vial (ie the maintenance dose) that you hope to achieve:

(Circle your response or fill in the blank if other)

0.05 mL 0.45 mL

0.10 mL 0.50 mL

0.15 mL 0.60 mL

0.20 mL 0.70 mL

0.25 mL 0.80 mL

0.30 mL 0.90 mL

0.35 mL 1.0 mL

0.4 mL _____other

5. Have any of your patients had systemic reactions to imported fire ant stings after achieving maintenance dose indicated in question 4?

Yes No

If yes: How many patients have had fatal reactions? _____

How many patients have had non-fatal cardiorespiratory reactions? _____

How many patients have had cutaneous only reactions _____

6. What method do you most commonly use to test for fire ant allergy?

1. Skin test

2. RAST

7. When do you recommend that fire ant immunotherapy be discontinued?
(Please circle the answer and fill in the blank if appropriate)

A. Continue indefinitely

B. After _____years.

C. After _____years and negative skin tests.

D. After _____years and negative RAST.

immunotherapy indefinitely and 81% discontinue immunotherapy based on certain criteria. Responses to the survey suggest that 36% recommend discontinuation after a specified period of time without retesting (mean 4.55 yr); 40% stop immunotherapy after a specified period (mean 4.38 yr) and negative skin tests; and 5% recommend discontinuation after a specified period (mean 4.29 yr) and negative RAST (Fig 5).

DISCUSSION

The results of this survey indicate that there are several areas of general uniformity and other areas of divergence in how allergists manage imported fire ant allergy. The vast majority utilize immunotherapy in the management of fire ant allergy. As the survey had only a 37.9% response rate, there may be some bias towards immunotherapy since individuals using immunotherapy are more likely respondents. Although there are no controlled studies on use of immunotherapy for imported fire ant allergy, there are a number of reports that have indicated that immunotherapy using whole body extracts of imported fire ant allergen is efficacious.¹⁻³ The most complete follow-up study demonstrating this was published by Freeman, in which only one of 47 patients who opted to receive immunotherapy and achieved the maintenance dose (0.5 mL of 1:100 wt/vol) suffered a sting reaction after a subsequent sting, while all six who chose not to receive immunotherapy and who subsequently suffered stings experienced systemic reactions.³

Allergists are fairly uniform in their recommendation of immunotherapy for either adults or children who suffer systemic reactions involving cardiorespiratory systems. There is significant divergence on the recommendations for immunotherapy for patients with fire ant allergy whose systemic reactions were confined to the skin. Approximately 77.6% of allergists surveyed recommended immunotherapy for adults who suffered systemic reactions confined to the skin, and 28.9% recommend immu-

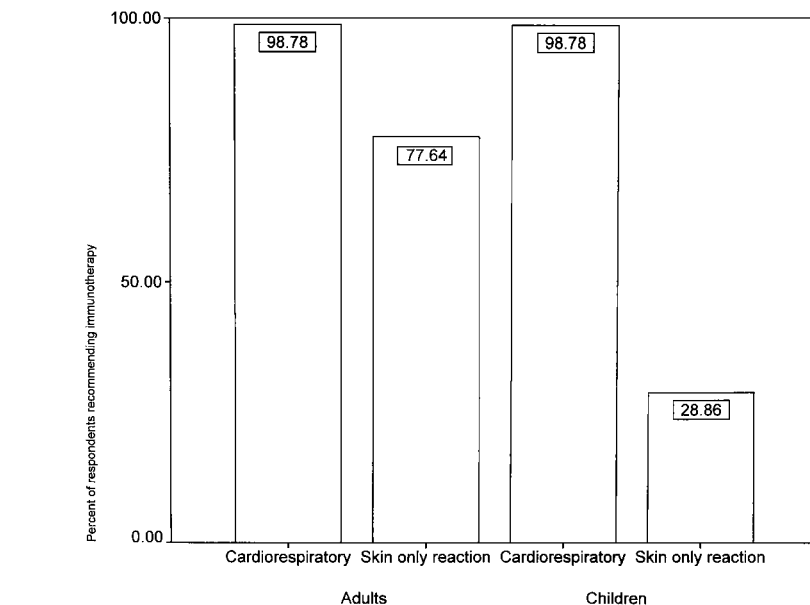


Figure 2. Allergists recommending immunotherapy by reaction severity and age group.

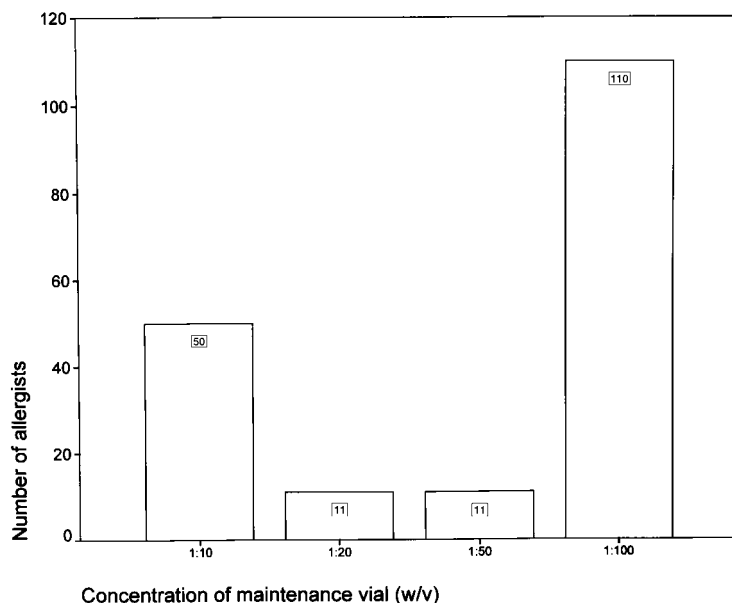


Figure 3. Distribution of responses for maintenance vial concentrations. All other concentrations combined account for fewer than 50 responses, including 18 expressed as PNU/mL. Data were missing for 102 allergists.

notherapy in children whose systemic reactions are confined to the skin. There have to date been no studies specifically investigating patients with systemic reactions to fire ant stings confined to the cutaneous system and therefore it is not known whether the natural history is

similar to that of patients suffering such reactions to stings of the winged Hymenoptera.¹⁰ This fact and the fairly high likelihood of suffering subsequent fire ant stings in endemic areas¹¹⁻¹⁴ probably explains the fact that approximately 28% of allergists recommend immunotherapy

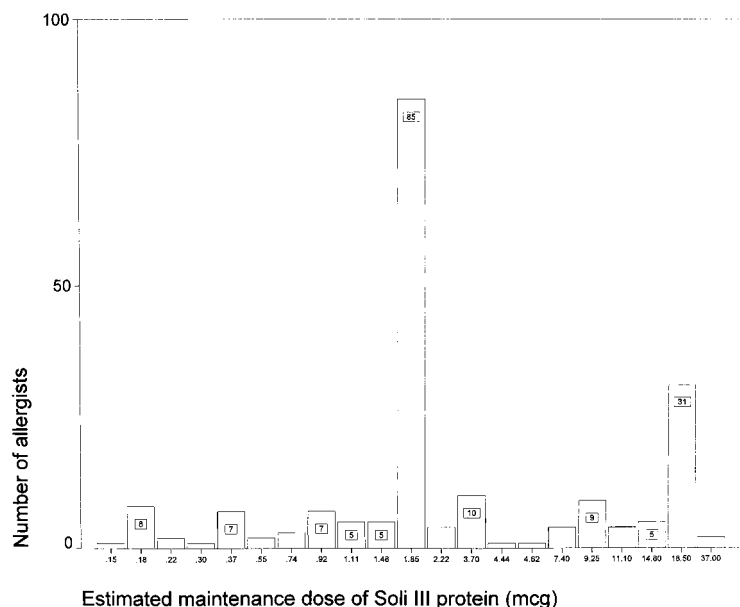


Figure 4. Distribution of responses for estimated maintenance dose. Data were missing for 114 allergists. There were 18 allergists who expressed immunotherapy maintenance concentration as PNU/mL.

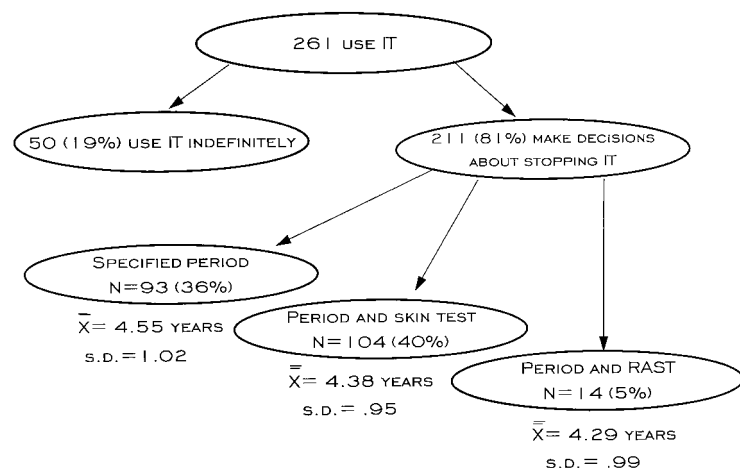


Figure 5. The number of physicians using immunotherapy and their criteria for discontinuation.

for children who have suffered these relatively mild systemic reactions.

There is significant range in maintenance dosage prescribed. Most authors have recommended a dosage of 0.5 mL of 1:100 wt/vol, although some recommend a higher dosage.^{1,2,3,15,16} The dosage of 0.5 mL of 1:100 wt/vol extract is estimated to be 1.85 μ g Sol i III protein, and this represents the median and mode dosage in this survey. Ap-

proximately 79.2% of respondents prescribe this dosage or higher. In a previous survey the mean maintenance dose was found to be 5.9 μ g which is similar to the mean maintenance dose of 5.7 μ g reported in this survey.⁹ Because of the statistical influence of higher doses on mean calculations, the median value is a more accurate description of current practice. These dosage calculations are made by ex-

trapolating measurements of venom protein in specific lots of imported fire ant whole body extract by Hoffman in 1991.³ There are inherent inaccuracies in making this extrapolation to multiple lots of extract made by different manufacturers used in clinical practice by survey respondents.

There is very little information in the literature about duration of immunotherapy for fire ant allergy. One study published in abstract form demonstrated lasting protection in patients who had completed courses of immunotherapy ranging from 15 months to 240 months.¹⁷ It is not surprising, therefore, that various allergists use different criteria when they consider discontinuing immunotherapy. Approximately 19% recommend indefinite continuation of immunotherapy. Eighty-one percent recommend its discontinuation based on certain criteria. Of those who recommend discontinuation of immunotherapy, they are almost evenly divided between those who recommend stopping it after completion of a specified period of time only and those who require completion of a specified period and demonstration of loss of IgE sensitivity either by negative skin test or negative RAST. Allergists who consider stopping immunotherapy tend to consider it after 4 to 5 years of immunotherapy. Nineteen percent of allergists reported having seen at least one patient suffering a systemic sting reaction after having reached maintenance dose of immunotherapy. Many physicians reported an estimate with a range of patients and others left the number blank but indicated that they noted systemic reactions. The authors did not feel that more detailed reliable data could be determined from this particular portion of the survey. The survey did not identify the total number of patients on immunotherapy. No allergist reported a fatal sting reaction in a patient who had achieved maintenance immunotherapy. Imported fire ant whole body extract treatment failures have been reported previously.^{18,19}

The survey also indicated that skin testing is the diagnostic method of

choice by the vast majority of allergists, as 94.5% of responding physicians use this method primarily and RAST is a method of choice of only 2.5% of the responding physicians.

CONCLUSIONS

There are many areas of general uniformity and other areas of divergence in how allergists manage imported fire ant allergy. These findings suggest continued need for further investigation regarding the efficacy, dosage, and duration of immunotherapy, as well as further elucidation of the natural history of fire ant allergy.

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