

Imported fire ant field reaction and immunotherapy safety characteristics: The IFACS study

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Background: Imported fire ants (IFAs) are endemic in the southeastern United States, including Texas; can sting multiple times; and are a well-known cause of anaphylaxis. There are few data available on how many stings typically lead to systemic reactions (SRs). Likewise, there are no reports currently in the literature that characterize the safety of IFA subcutaneous immunotherapy (SCIT).

Objective: We sought to analyze a case-cohort sample of patients for IFA SCIT risk factors and to characterize the index field reactions of these patients.

Methods: A case-cohort study based on a 3-year retrospective chart review (2005-2008) at a single institution was performed for patients receiving IFA SCIT. Field reactions leading to initiation of IFA SCIT were also reviewed.

Results: Seventy-seven patients (40 female patients; mean age, 34 years) received 1,887 injections, and 7 patients experienced 8 SRs, for a rate of 0.4% per injection and 9.1% per patient. SRs were mild. Having an SR to skin testing was associated with increased odds of having an SR to IFA SCIT (odds ratio, 4.75; 95% CI, 1.13-20.0), as were large local reactions (odds ratio, 34.5; 95% CI, 6.52-182). No other risk factors were identified. Of the index field reactions leading to IFA SCIT, 59% were the result of 1 sting, and 87% of subjects experienced only 1 SR before initiation of IFA SCIT. Two of 4 patients who experienced loss of consciousness during the index field reaction required an increased maintenance dose for optimal response.

Conclusions: IFA SCIT is safe; however, having an SR to skin testing or the presence of large local reactions increases the odds of having an SR to IFA SCIT. The majority of SRs to IFA field stings resulted from 1 sting. (*J Allergy Clin Immunol* 2010;■■■:■■■-■■■.)

Key words: Ant, insect, sting, immunotherapy, safety, risk factors, systemic reactions, anaphylaxis, skin test

Abbreviations used

AIT:	Aeroallergen immunotherapy
ACE:	Angiotensin-converting enzyme
BAM:	Build-up after maintenance
EMR:	Electronic medical record
IFA:	Imported fire ant
IDST:	Intradermal skin test
LLR:	Large local reaction
LOC:	Loss of consciousness
MWS:	Mean wheal size
OR:	Odds ratio
ST:	Skin test
SPT:	Skin prick test
SCIT:	Subcutaneous immunotherapy
SR:	Systemic reaction
VIT:	Venom immunotherapy
WBE:	Whole-body extract

Since their introduction from South America in the 1920s, imported fire ants (IFAs) have spread to become endemic in the southeastern United States, including Texas. Potential range modeling notes this expansion might eventually include areas as far north as Delaware in the east and northern California in the west.¹ This could be further exacerbated by global climate change, as suggested with other insects.² Likewise, it appears that IFAs have become endemic in parts of mainland China, Hong Kong, and parts of Australia,^{3,4} and anaphylaxis has been reported in Europe.⁵ Thus the effect of these venomous aggressive ants is being felt worldwide.

Stings from both red IFAs (*Solenopsis invicta*) and black IFAs (*Solenopsis richteri*) typically result in a wheal-and-flare response accompanied by a burning sensation, followed within 24 hours by sterile pustule formation. This pustule is the result of transpiperidine alkaloids that cause local tissue necrosis; it can last for several days and is considered pathognomonic for IFA stings.^{6,7} Large local reactions (LLRs) can also occur and can occasionally be debilitating. Systemic reactions (SRs) to IFA stings are well described, and more than 85 fatalities have been documented.⁸⁻¹¹

Despite this, there are few data on the number of IFA stings that result in anaphylaxis. This is significant given the nature of an IFA attack. IFAs anchor themselves to their victim by their mandibles, then arch their abdomen to inflict the sting and can sting multiple times if left undisturbed.^{12,13} Likewise, IFAs are aggressive when disturbed and tend to be in groups. These characteristics have led to an assumption that IFA attacks leading to anaphylaxis often are the result of multiple stings.¹⁴ Yet the only published data on the number of stings that induce anaphylaxis is a report of fatal SRs, which observed that most deaths were caused by less than 5

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stings.⁹ However, these were survey data and did not address non-fatal SRs, and 76% was obtained by nonmedical sources, such as news media reports. In addition, a recent study of patients receiving subcutaneous immunotherapy (SCIT) evaluated sting events but did not record the actual number of stings per event.¹⁵

An effective means to prevent SRs that occur as a result of IFA stings is SCIT with IFA whole-body extract (WBE).¹⁶⁻¹⁸ This efficacy is thought to be due to the fact that IFA WBE (in contrast to that of flying hymenoptera) contains adequate amounts of venom.¹⁹ Yet after more than 25 years of use,²⁰ there are few published safety data regarding IFA SCIT. A single study reports an SR rate but examined only rush injections and did not address conventional build-up or maintenance injection, nor did it examine risk factors for SR.²¹ This paucity of IFA data contrasts with more than 20 studies cited in the stinging insect and allergen immunotherapy (AIT) practice parameters describing safety characteristics for flying Hymenoptera venom immunotherapy (VIT) or AIT.^{17,22}

In the present study we sought to identify IFA SCIT safety characteristics and to characterize the index field reactions in patients being treated with IFA SCIT, including the number of stings leading to these reactions.

METHODS

Study design

In a retrospective case-cohort study, data on all patients treated with IFA SCIT at a single institution for 3 years were entered into a database (Microsoft Excel). Demographic data, index field sting SR data, and results of skin tests (STs) were recorded before initiation of IFA SCIT.

Data were collected from 3 sources: injection data were obtained from an SCIT electronic medical record (EMR; Rosch Immunotherapy; Rosch Visionary Systems, Inc, Altoona, Pa); SR information was obtained from the SCIT EMR, as well as dedicated SR records completed at the time of the SR; and index field sting and ST data were obtained from the patient medical records. The study was approved by the Wilford Hall Medical Center Institutional Review Board.

Patients

Data were collected for each patient treated with IFA SCIT at this institution between August 2005 and August 2008.

Skin Testing

IFA STs were performed in concordance with practice parameter recommendations¹⁷ and commenced with a skin prick test (SPT) using a 1:1,000 wt/vol WBE with the Quintip device (Hollister-Stier, Spokane, Wash; manufactured in England). Histamine base (1 mg/mL; histamine phosphate, 2.75 mg/mL; ALK-Abelló, Port Washington, NY) and 50% glycerin diluent were used as the positive and negative SPT controls, respectively. If the SPT response was negative, intradermal skin tests (IDSTs) were performed with a 1:1,000,000 wt/vol dilution IFA WBE and progressed in 10-fold increments until positive or to a maximum concentration of 1:1,000 wt/vol. A 0.1 mg/mL histamine base (histamine phosphate, 0.275 mg/mL, ALK-Abelló) in 0.4% phenol was the positive IDST control, and saline solution was the negative IDST control. A positive SPT response was a wheal of 3 mm or larger and a positive IDST was a wheal of 5 mm or larger than that elicited by the diluent control with associated flare. IFA SCIT and STs were performed with IFA WBE (Hollister-Stier, Spokane, Wash) that consisted of an *S invicta*/S *richieri* mix from a 50-mL 1:10 wt/vol stock bottle in 0.4% phenol.

Mean wheal sizes (MWSs) were calculated retrospectively as the arithmetic mean of the largest diameter and its perpendicular diameter. IFA serum-specific IgE was measured with the ImmunoCAP 250 machine (Phadia, Inc, Portage, Mich) in accordance with the manufacturer's instruction, with 0.35 kU/mL or greater being classified as positive.

TABLE I. Grading scale for SRs

Grade 1	Mild SR involving generalized urticaria, upper respiratory tract symptoms (eg, itching of the palate and throat and sneezing), or both
Grade 2	Moderate SR with asthma (eg, PEFR decreases 20% to 40%), abdominal symptoms (eg, nausea and cramping), or both with or without generalized urticaria or upper respiratory tract symptoms
Grade 3	Severe life-threatening anaphylaxis involving severe airway compromise caused by severe bronchospasm (eg, PEFR decreases >40%) or upper airway obstruction with stridor, hypotension, or both*

PEFR, Peak expiratory flow rate.

*Any manifestation of hypotension (eg, dizziness or LOC) was considered a grade 3 reaction.

TABLE II. Clinical demographics

	SR to IFA SCIT (n = 7)	No SR to IFA SCIT (n = 70)	P value
Age (y), $\pm$ SD	23.7 $\pm$ 15.9	35.3 $\pm$ 19.2	.13
Age <18 y	2 (29%)	13 (19%)	.61
Age >50 y	0 (0%)	15 (21%)	.33
Female sex	5 (71%)	35 (50%)	.43
Asthma	2 (29%)	15 (21%)	.64
MWS* (mm), $\pm$ SD	7.8 $\pm$ 4.3†	6.9 $\pm$ 1.5	.44

SD, Standard deviation.

*MWS for positive ST response at 1:1,000,000 or 1:10,000,000 (n = 29).

†All patients with an SR to IFA SCIT where positive at the 1:1,000,000 intradermal concentration.

IFA SCIT

IFA SCIT was administered in concordance with practice parameter recommendations.¹⁷ A 1:1 vol/vol maintenance vial consisted of 1 mL of IFA WBE and 9 mL of human serum albumin diluent mixed in a 10-mL vial. The initial build-up phase began with 0.05 mL of the 1:1,000 vol/vol vial and progressed over 3 to 6 months (1-2 injections per week) to a maintenance dose of 0.5 mL 1:1 vol/vol (ie, 1:100 wt/vol). Maintenance doses were subsequently spaced to once every 4 weeks. The resultant allergen dose at this maintenance dose has been estimated as 15 to 20 μ g of Sol i III.²³ Patients remained in the clinic for 30 minutes after each injection. LLRs and SRs were documented in the SCIT EMR. SRs were also recorded in separate dedicated paper records. Dose adjustments were made when starting a new maintenance vial, when more than 2 weeks late for an injection, or for a SR to the prior injection. Dose adjustments were not made for LLRs, which were defined as local reactions larger than the patient's palm (average adult, 8-10 cm).

Systemic Reactions

Index field reactions were defined as the SR leading to allergy referral and were characterized during the patient's initial clinic visit before initiation of IFA SCIT. Field reactions were deemed SRs as defined by the stinging insect hypersensitivity practice parameter.¹⁷ A SR to IFA SCIT was defined as any reaction other than a local reaction deemed by the attending allergist to be related to the IFA SCIT injection. SRs to both IFA SCIT and the index field reaction were graded retrospectively by using a 3-point scale (Table I). Epinephrine was the preferred treatment for SRs resulting from IFA SCIT.

Risk factors

Two groups were used for comparison to estimate the odds of an SR for putative risk factors: those who experienced an SR and those who did not experience an SR. The risk factors studied were sex, age, phase of SCIT, asthma, angiotensin-converting enzyme (ACE) inhibitor use, LLRs, severity

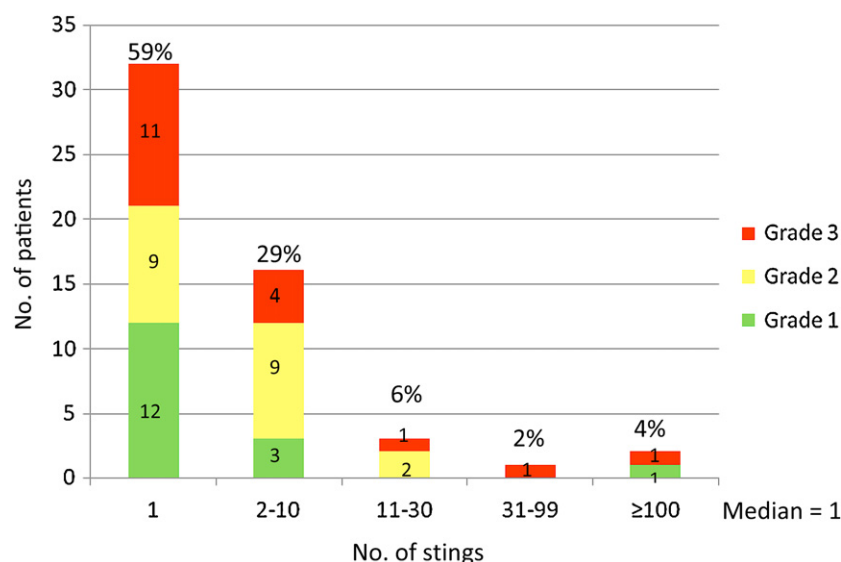


FIG 1. Number of stings leading to the index field reaction (the SR leading to allergy referral and initiation of IFA SCIT) along with severity of the reaction.

of the index field reaction, concentration and MWS of the positive ST response, and occurrence of a prior SR to an IFA ST. Phases of SCIT examined included build-up, maintenance, and build-up after maintenance (BAM). BAM refers to injections given after the patient achieves maintenance but then build back up after dose reduction because of any factor.

Statistical analysis

Odds ratios (ORs) were calculated between groups by patient and injection; 95% CIs were generated. In the case of zero events, a zero-cell correction factor of 0.5 was used. *P* values were calculated by using the Fisher exact test for categorical data and the unpaired 2-tailed *t* test for continuous data. *P* values of less than .05 were considered statistically significant. GraphPad statistical software (GraphPad Software, Inc, La Jolla, Calif) was used for statistical analysis.

RESULTS

Patients' characteristics

A total of 77 patients (40 female patients) received 1,887 injections over the 3-year period. The mean age was 34 years (range, 3-76 years). Clinical demographics are described in Table II.

Index field sting SR characteristics

Of the 77 patients receiving IFA SCIT, 67 (87%) had experienced only 1 SR (the index field reaction) before initiating IFA SCIT. Nine patients had experienced 2 SRs, and 1 experienced more than 2 SRs. The average time interval from the index field reaction to initiation of IFA SCIT was 1.7 months. Index field reaction data were available on 66 of the patients. There were 19 grade 1 reactions, 25 grade 2 reactions, and 22 grade 3 reactions. Four of the grade 3 reactions included loss of consciousness (LOC). The patient's estimate of the number of stings leading to the index field reaction was available for 54 patients (Fig 1). In terms of the number of lifetime sting events experienced by a patient before initiation of IFA SCIT, an average of 2.88 sting events were reported by 36 patients for which these specific data were available, 2 of whom experienced 2 SRs and the remaining 34

of whom experienced only 1 SR (the index field reaction). Eight patients were noted to have had "many" prior sting events, and data were not available for the remaining 33 patients. Data regarding the actual number of stings per event were not available for most sting events other than that leading to the index field reaction.

ST characteristics

ST data were available for 61 patients. Seventy-two percent had positive results at either the prick (*n* = 17) or the 1:1,000,000 (*n* = 27) intradermal concentrations. The remaining patients had positive results at the 1:100,000 (*n* = 7) and 1:10,000 (*n* = 10) intradermal concentrations. None required testing at the 1:1,000 concentration. Seven patients (or 9.5% of the 74 who underwent skin testing) had an SR to an IFA ST (5 at 1:1,000,000, 1 at 1:10,000, and 1 at prick). Data were not adequate to grade these SRs; however, none were severe. None of these 7 patients were receiving another form of SCIT. Serologic specific IgE testing was performed in place of STs in 3 patients, and the concentration of the positive ST response was unavailable for 11 patients.

IFA SCIT injection and reaction characteristics

The numbers of injections given in the maintenance, build-up, and BAM phases are noted in Fig 2. The SR rate was 9.1% (7/77) per patient and 0.42% (8/1887) per injection. 75% (6/8) of IFA SCIT-induced SRs were grade 1, and there were no grade 3 reactions (Fig 3). In the patients with grade 2 reactions, both occurred within 30 minutes. One patient had nausea and diarrhea, and the other was a patient with asthma who had chest tightness in addition to upper respiratory tract symptoms. Of the 8 SRs, 5 were treated with epinephrine. The remaining 37.5% of SRs (3/8) were not treated with epinephrine because they were delayed (symptom onset after a 30-minute wait period) and resolved without medical intervention or they were brought to the physician's attention either after symptoms had resolved or at the time of the patient's next scheduled injection. Two patients who had

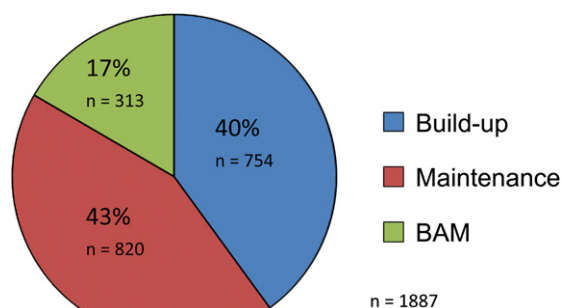


FIG 2. Total injections by phase.

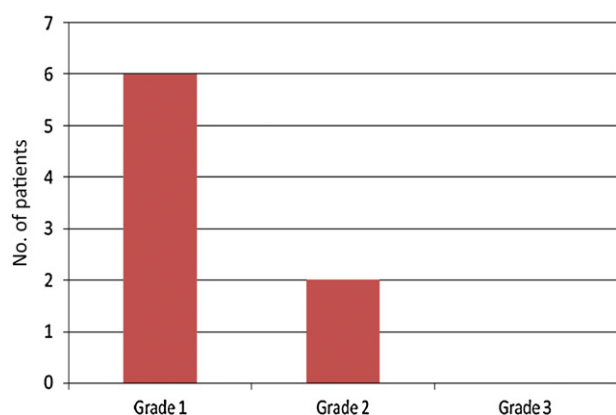


FIG 3. Severity of SRs to IFA SCIT. Seven of 77 patients experienced SRs to IFA SCIT. There were no emergency department visits, hospitalizations, or fatalities. One patient experienced more than 1 SR, and she had a total of 2 SRs, each grade 1. In 2 different patients 2 SRs were delayed (one presented at 35 minutes and the other at 60 minutes).

SRs to IFA SCIT had also received an AIT injection on the same day (of 12 patients receiving IFA SCIT and AIT).

Nine percent (7/77) of patients underwent the majority of their build-up phase in a 1-day rush as part of a separate research protocol. All injections and any SRs that occurred during the rush phase in these patients were not counted for the purposes of this study, and none experienced an SR during their maintenance or BAM injections. Sixteen patients experienced 20 LLRs, for a rate of 1.1% per injection and 20.7% per patient. No patient had a serum sickness–like reaction or other non–IgE-mediated reaction.

Risk factors for SRs to IFA SCIT

ORs for having an SR to IFA SCIT per injection are presented in Table III. Having a SR to a ST or a LLR resulted in a statistically significant increase in the odds of having a SR to IFA SCIT. ORs were also calculated per patient and were similar; however, no statistically significant associations were observed (data not shown).

IFA SCIT efficacy

Two patients had their maintenance doses increased to 1.0 mL monthly because they each had 1 breakthrough SR (grade 1 and grade 2, respectively) to field stings, despite receiving maintenance IFA SCIT of 0.5 mL. The index field reactions for both patients were grade 3 and involved LOC. Both patients subsequently

reported IFA stings with no SRs after reaching the higher maintenance dose. Because this was not an efficacy study, we did not collect data on how many patients experienced field stings during the maintenance period. However, no other patients reported SRs to field stings once they achieved the usual maintenance dose ($n = 55$).

DISCUSSION

This investigation represents the largest study to date reporting nonfatal IFA field sting reactions and IFA SCIT safety characteristics.

Index field reactions

We made the unexpected observation that 59% of index field reactions were reported to be the result of 1 sting. Although the number of stings is subject to recall bias, the immediate burning sensation and subsequent pustule allow for accurate assessments. Additionally, the immediate burning is a powerful motivation to remove the IFA before additional stings. Unfortunately, we do not know how many patients were stung but experienced no SRs and thus cannot determine an actual SR rate per sting.

The remaining 41% of index field reactions resulted from 2 or more stings. One could suppose that with multiple stings a non–IgE-mediated mechanism could explain a patient's systemic symptoms. However, although toxic reactions have been reported with multiple flying Hymenoptera stings, no fatal non–IgE-mediated reactions caused by IFA stings have been reported, and subjects have sustained even thousands of stings with no complications other than the pustules.^{13,24}

SRs to IFA SCIT and STs

A SR rate for IFA SCIT of 0.42% per injection and 9.1% per patient was observed. The SRs that did occur were predominantly grade 1, and all responded readily to treatment and resulted in no mortality or significant morbidity. In comparison, investigations presenting data on safety characteristics for VIT observed 12% SR rates for patients undergoing routine build-up protocols.^{25,26}

Regarding SRs to STs, we observed a rate of 9.5%. This is higher than that seen with flying Hymenoptera (2.0%)²⁷ and with aeroallergen, food, and Hymenoptera combined (3.6%).²⁸ The latter study used a similar definition of an SR (ie, only 1 systemic symptom is required to diagnose and treat anaphylaxis). Although a single study, it is interesting that the SR rate for IFA STs appears higher than that for other allergens. One explanation could be differing centers' practices regarding diagnosis or treatment of an SR. One could also speculate that STs with IFA closely mimic the route of natural exposure to the antigen, namely the ant's sting, which is presumably more superficial than that of a flying Hymenoptera sting, and thus IFA ST might result in a higher rate of SRs.

SCIT phase

Evaluation of the phases of IFA SCIT demonstrated the majority of injections (60%) were build-up injections. Of note, the SR rates for build-up (2/70 [2.9%]) and maintenance (3/77 [3.9%]) were similar. This is in contrast to what is typically reported in the literature, in which build-up reactions are considered a risk factor for SRs.¹⁷ This difference might reflect unusual

TABLE III. Risk factors for SRs to IFA SCIT per injection

	SR to IFA SCIT	No SR to IFA SCIT		OR	95% CI
LLR	2 (25%)	18 (1.0%)		34.4*	6.51-182
Asthma	2 (25.0%)	523 (27.8%)		0.87	0.18-4.32
Sex (female)	6 (75%)	1,071 (57.0%)		2.29	0.46-11.4
Age (>50 y)	0 (0%)	666 (35.4%)		0.11	0.01-1.98
ACE inhibitor	0 (0%)	173 (9.21%)		0.62	0.04-10.8
Field reaction†	3 (37.5%)	608 (36.4%)		1.04	0.25-4.39
Maintenance‡	3 (37.5%)	817 (43%)		0.78	0.19-3.27
Build-up and BAM‡	5 (62.5%)	1,062 (59.7%)		1.28	0.31-5.38
Build-up‡	2 (25.0%)	752 (42%)		0.5	0.10-2.48
BAM‡	3 (37.5%)	310 (18%)		3.04	0.72-12.8
SR to ST	3 (37.5%)	175 (11.1%)		4.75*	1.13-20.0
Concentration of ST§	8 (100%)	0 (0%)		4.33	0.25-75.7

*Statistically significant value.

†Grade 3 versus grades 1 and 2.

‡Phase compared with injections from remaining phases(s).

§Prick through 1:1,000,000 versus 1:100,000 through 1:1,000 (insufficient data to separately analyze by concentration).

characteristics of IFA SCIT or the use of WBE versus standardized venom extract, or it might be due to the small sample size in this study or other unknown variables. It is also noteworthy that results are conflicting with other forms of immunotherapy in which VIT studies demonstrate increased SRs during build-up^{25,26} and AIT studies demonstrating conflicting results.²⁹⁻³² Additional investigations, ideally prospective, are necessary to better understand these differences. There are no prior studies that specifically evaluate BAM injections. In the present study, separating these phases demonstrated that build-up injections given before any maintenance doses trended toward reduced odds of a SR (OR, 0.5), whereas BAM injections trended towards increased odds of a SR (OR, 3.04). Importantly, neither value reached statistical significance; however, it suggests that further investigation regarding BAM injections as a risk factor for SRs to SCIT is warranted. Specifically, because dose adjustments leading to BAM injections can occur due to a number of factors (eg, prior SR, late for an injection, and new vials), future research should delineate these factors.

Patients' responses to allergen

Having an SR to an IFA ST increased the odds of having an SR to IFA SCIT 4.74-fold. To our knowledge, these are the first such data to be reported for any form of SCIT.

Although the immunotherapy practice parameter states "heightened sensitivity" is a risk factor for an SR to SCIT,²² the investigations supporting this observation are limited, primarily being survey data and reporting heightened sensitivity only in terms of ST grade and not wheal size.³²⁻³⁴ Additionally, published data address only fatal or near-fatal reactions and do not present data on how many patients with "heightened sensitivity" received SCIT and did not have an SR. Furthermore, definitions of "heightened sensitivity" vary. One report notes "skin sensitivity or RAST score was reported to be high in 71%" of fatal reactions.³⁴ What defines "high" is not noted. Another observes "nine of 24 fatalities after IT had been reported to be extremely sensitive by ST" defined as "3+ or 4+,"³³ and a third study evaluating nonfatal SRs noted most patients who had an SR to SCIT "showed large

reactions (3+) to prick tests."³² The wheal-and-flare sizes that correspond to 3+ or 4+ reactions were not defined.

Conversely, other studies have not observed an increased risk of SRs in patients with increased allergen sensitivity as defined by ST wheal size.^{29,35} One recently observed that an ST response with a wheal size of greater than 10 mm versus a 3- to 5-mm wheal to aeroallergen SPT did not increase the odds of an SR to conventional SCIT.³⁵

In terms of other proxies for allergen reactivity, the present study observed that LLRs are associated with increased odds of having an SR to IFA SCIT, whereas a severe index field reaction, as well as the concentration and MWS of positive ST responses, were not associated with increased odds of having an SR to IFA SCIT.

Taken together, these data suggest that SR risk to SCIT is related to "biological reactivity" (SRs to STs and LLRs) rather than "heightened sensitivity" (MWS and concentration of positive ST response).

ACE inhibitors

ACE inhibitor use did not increase the odds of having an SR to IFA SCIT. This supports 2 investigations that found no association between ACE inhibitor use and increased frequency of SRs to IFA and VIT³⁶ or AIT.²⁹ However, there are case reports of severe allergic reactions in patients taking ACE inhibitors subsequent to being stung or receiving VIT,³⁷ and the stinging insect practice parameter, as well as package inserts, mention a possible increased risk of SRs to VIT when patients are concomitantly taking an ACE inhibitor. Likewise, decreased ACE levels have recently been associated with more severe anaphylaxis to nuts.³⁸ Thus more study is needed.

Efficacy

Although this study was not designed to evaluate efficacy and, significantly, data are lacking regarding the natural history of IFA sting anaphylaxis, one finding is worth mention. Four of 66 patient experienced LOC with their index field reaction. Two of

these 4 patients experienced relatively mild breakthrough SRs to field stings, necessitating increased maintenance doses. Thus LOC might represent a risk factor for treatment failure at usual maintenance doses, and increasing the maintenance dose to 1 mL might improve efficacy, but this requires further examination.

An important limitation of this investigation is the small study population, and thus the lack of statistical significance observed for some risk factors might not exclude a true correlation. Unfortunately, it might be difficult to study larger populations of the patients evaluated in this study. Despite an estimated prevalence of IFA-induced anaphylaxis of 2.1% in endemic areas, only 0.6% of new referrals to allergists in an endemic area were for IFA-related events.³⁹ This reflects a lack of awareness in the general medical and lay communities of the availability of an effective and safe treatment. An additional limitation is that this is a retrospective study, making it subject to recall bias. The strengths of this study include careful recording of all IFA SCIT injections and reactions through an SCIT EMR, a unique study population, and the availability of detailed ST and index field reaction data.

In summary, we have demonstrated that IFA SCIT is safe and that SRs that do occur tend to be mild. Having LLRs to IFA SCIT injections or a SR to a IFA ST increase the odds of having a SR to IFA SCIT. Similarly, BAM injections might represent a new risk factor and require further investigation. Finally, we observed that the majority of field reactions leading to IFA SCIT occurred after just 1 sting.

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Clinical implications: Fifty-nine percent of SRs to IFA field reactions result from 1 sting. IFA SCIT is safe; however, having LLRs or a SR to skin testing increases the odds of having a SR to IFA SCIT.

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