



Letters

Successful completion of an imported fire ant cluster immunotherapy protocol



Since their introduction into Mobile, Alabama, in the 1920s, imported fire ants (IFAs) have slowly spread across the Southern United States.^{1,2} The leading cause of hypersensitivity in IFA endemic areas among all Hymenoptera, these venomous ants can cause clinical reactions, ranging from localized sterile pustules to systemic IgE-mediated reactions, including death.^{3,4} Immunotherapy with IFA whole body extract (WBE) is an effective and safe treatment for IFA hypersensitivity.^{5–8} Both conventional and rush immunotherapy schedules have been previously reported for IFA hypersensitivity, but there are no reports of an IFA cluster schedule. Conventional IFA WBE immunotherapy schedules can take as long as 6 to 12 months to reach a protective maintenance dose. To achieve protection sooner, 1- and 2-day rush immunotherapy schedules have been published.^{6–8} Using a rush schedule, a protective maintenance dose can be achieved in 1 to 2 days. Although rush protocols may be a more convenient option for some individuals, other patients may be unable to commit to an intensive 2-day regimen. Already used by allergists for venom and inhalant immunotherapy, a cluster schedule aims to achieve a maintenance dose in a shorter period than a conventional schedule with 2 to 3 injections administered at each visit. Cluster schedules provide decreased risk and shorter visits compared with a rush schedule and increased convenience compared with a conventional schedule. We describe the first report, to our knowledge, of a cluster IFA schedule.

A 66-year-old man residing in Northwest Mississippi presented with an initial history of dyspnea and a sense of impending doom after an IFA sting 6 years before his visit and no subsequent stings. Because of the severity of his reaction and the expected need for immunotherapy, skin testing was performed. The results of a skin prick test with IFA WBE (*Solenopsis invecta/Solenopsis richtera*) 1:2,000 wt/vol were negative with appropriate positive and negative controls. The results of the first intradermal test with 2,000,000 wt/vol were positive, with a wheal of 5 mm and surrounding erythema of 7 mm.

The patient was offered a 2-day IFA rush immunotherapy protocol but declined because of logistical issues of committing to 2 full days of therapy. Because he was interested in a more rapid schedule to achieve protection, a cluster protocol was created (Table 1). Written informed consent was obtained before initiation of immunotherapy. Six weekly cluster visits with 3 injections per visit were conducted in the clinic during a 6-week period with each injection separated by 30 minutes. The patient premedicated with 10 mg of oral cetirizine the morning of each cluster visit. After the 6 weeks of cluster injections, once-weekly injections were given

during the next 6 weeks until a maintenance dose of 0.5 mL (1:1 vol/vol) was achieved and then spaced to once-monthly maintenance injections. He had no systemic or bothersome local reactions. The maintenance vial of 1:1 vol/vol consisted of 0.5 mL of 1:20 wt/vol IFA WBE (*S. invecta/S. richtera*) with 4.5 mL of diluent. Since completion of his cluster schedule, he has had no other field stings.

The 2017 stinging insect hypersensitivity practice parameter recommends venom immunotherapy for patients who have experienced an anaphylactic reaction to an IFA sting and also demonstrate IFA specific IgE on skin or serologic testing. The goals of immunotherapy are “to prevent life-threatening reactions and to alleviate anxiety related to insect stings.”⁹ Allergists are encouraged to choose a dosing schedule that optimizes safety and convenience. Modified rush (8 weeks), rush (2–3 days), and ultra-rush (4–8 hours) regimens are discussed and recommended as safe and efficacious treatment options in the current parameter. Of interest, the 2017 practice parameter has only one brief mention of a cluster schedule within a table and no further discussion of this build-up regimen. In our case report, a 6-week/6-visit cluster build-up schedule to the 1:1 vol/vol maintenance vial was well tolerated. Oral cetirizine was taken the morning of each visit. An additional 6-week/6-visit conventional schedule was used to build-up

Table 1
Imported Fire Ant Immunotherapy Cluster Schedule^a

Week	Concentration, vol/vol ^b	Amount, mL
1	1:1000	0.05 0.15 0.25
2	1:1000	0.3 0.4 0.5
3	1:100	0.05 0.15 0.2
4	1:100	0.3 0.4 0.5
5	1:10	0.05 0.1 0.2
6	1:10	0.3 0.4 0.5
7	1:1	0.5
8		0.1
9		0.2
10		0.3
11		0.4
12		0.5

^aEach cluster injection was separated by 30 minutes.

^b1:1 vol/vol = 1:200 wt/vol.

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through the 1:1 vol/vol maintenance vial. This 12-week visit schedule is an alternative to a 1- to 2-day rush schedule or a standard 26- to 40-visit conventional schedule. Similar to previous rush schedules for IFA hypersensitivity, the safety and efficacy of this IFA cluster schedule should be further evaluated in a larger group of patients.

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Penicillin allergy testing

A strategic approach to increasing referrals from primary care physicians



Penicillin allergy is the most common β -lactam drug allergy and is estimated to affect approximately 10% of the population.¹ Large-scale efforts are under way to test and verify documented penicillin allergy to promote antibiotic stewardship and improve public health.² Multiple studies support this campaign because evidence clearly demonstrates increased rates of infection with drug-resistant organisms, more surgical site infections, and prolonged hospitalizations for patients with penicillin allergies.^{3,4} In addition, multiple guidelines, including those issued by the Choosing Wisely Campaign and the Infectious Diseases Society of America, recommend testing for penicillin allergy in certain patient populations.^{5,6}

Thus far, the emphasis of penicillin testing has been on hospitalized patients, targeting a population with a high probability of antibiotic exposure.^{2–4} However, most patients with a penicillin allergy presumably interact with outpatient primary care physicians for much of their care. Therefore, to maximize the effect of penicillin allergy testing, primary care physicians should be aware of the potential patient and health care system advantages and be motivated to refer patients for testing.

A recent study found that penicillin skin testing initiatives can be successful in outpatient allergy clinics.¹ However, primary care physicians and allergists may have different perspectives on the diagnosis and management of penicillin allergy.⁷ Other studies suggest that many primary care physicians are not aware of penicillin testing or lack the time to discuss the issue with patients.^{8,9} Therefore, primary care physicians should be encouraged to promote penicillin skin testing for their patients. The purposes of this study are to further examine the current perceptions of penicillin allergy, determine perceived barriers to allergy clinic referral, and describe a novel intervention to encourage more outpatient referrals for penicillin testing.

This study was approved by the University of California San Diego Institutional Review Board. Surveys were distributed via e-mail (Survey Monkey platform) to primary care physicians to assess their knowledge of penicillin allergy and determine barriers to allergy clinic referrals. Eligible participants included both attending and

resident physicians within the Department of Internal Medicine and the Department of Family Medicine at the University of California San Diego. Results were collected using Survey Monkey and exported into Microsoft Excel for analysis. On the basis of these results, an in-person, interactive session was designed to address issues identified in the survey. The intervention was completed with resident physicians in the Department of Family Medicine. Specifically, the authors reviewed the epidemiology of penicillin allergy, the public health benefits of testing, and the patient groups appropriate for referral. Emphasis was placed on the potential preventive health benefits of penicillin testing. Participants completed an anonymous hard-copy survey after the lecture to assess the effect of the intervention. The survey also gathered resident opinions on potential strategies for promoting awareness and discussions with patients. The number of referrals to allergy clinic for penicillin testing were then compared for the 3 months before and after intervention.

A total of 204 participants were invited to participate in the pre-intervention survey. Eighty-five participants (42%), including 26 attending and 59 resident physicians, completed the survey. Physicians identified the following as the most significant barriers to allergy clinic referral: “Patients have multiple other medical problems which take priority in time-limited encounters” (41%), “I did not realize that this service was available for my patients” (26%), “I am concerned that the allergy history is inaccurate or unclear” (12%), “I don’t think my patients will follow through with the referral” (5%), and “Other” (16%) (Fig. 1).

Nineteen primary care physicians in training participated in the educational intervention. All attendees completed the postlecture anonymous survey, and 100% of participants reported the educational outreach session as “useful for [their] practice.” Seventeen residents (89%) responded that they were more likely to refer patients with documented penicillin allergy for testing after attending the session. When surveyed about potential strategies to increase referral rates, 12 residents (63%) reported that an alert exclusively visible to patients on an electronic medical record portal prompting patients to discuss penicillin allergy with their physicians (when applicable) would not be “an onerous burden on [their] practice.” In addition, 11 residents (58%) responded that they would be interested in a smartphone application reviewing the best practice for