



Letter

Evaluation of the risk of infection associated with subcutaneous allergen immunotherapy

American Academy of Allergy, Asthma, and Immunology and American College of Allergy, Asthma, and Immunology National Surveillance Study on Allergen Immunotherapy, 2014–2015

Questions have recently been raised by regulatory bodies in the United States regarding a potential risk of infections related to subcutaneous allergen immunotherapy (SCIT) injections. In response to a fungal meningitis outbreak from contaminated, compounded injectable medications, the US Food and Drug Administration endorsed the US Pharmacopeia's Pharmaceutical Compounding—Sterility Preparations guidelines as the standard for pharmaceutical compounding in 2013.¹ An exemption was granted to allergen extracts as long as they addressed specific procedures that were feasible in an office setting. In more recent years, it has been proposed that the exemption for allergen extracts be removed, making possible the application of more rigid guidelines for allergen extract preparation and storage that cannot be performed in an office setting. In addition, the US Food and Drug Administration subsequently issued a proposed guidance that would require routine environmental monitoring, including nonviable airborne particulate sampling, viable airborne particulate sampling, and personnel and surface sampling.² Practices that are not compliant with new regulations would be required to immediately halt SCIT preparation. Concerns about current preparation methods are based on theoretical risks of injection-related infections associated with possible contamination of allergen vials prepared by mixing single allergen commercial extracts in allergists' outpatient facilities. Although clinical evidence documenting infections from SCIT infections has not been published, a few articles have confirmed the safety of SCIT as currently practiced related to infection risks.³ To monitor the annual incidence of fatal and nonfatal systemic allergic reactions to SCIT and allergy skin testing experienced by practicing allergists, a web-based surveillance program was initiated in North America in 2008 among physician members of the American Academy of Allergy, Asthma, and Immunology (AAAAI) and the American College of Allergy, Asthma, and Immunology (ACAAI). Starting in 2014, to identify sentinel postinjection infection events, participants were also queried regarding local skin or systemic infections that required antibiotics after SCIT.

Physician members of the AAAAI and ACAAI (3,459 SCIT prescribers) were surveyed using previously described methods to identify the number of prescribers and number of SCIT injections given.^{4–8} A single respondent was identified for multimember practices to report the experience of his or her practice, starting on July 1, 2014, and ending on July 31, 2015. The following questions were included for 2014–2015. First, "During the past year, have any patients in your practice (including those of your associates) receiving SCIT developed local cutaneous infections, including cellulitis or abscess, at or near the site of allergen injections from a mixed allergen vial prepared in your office? (if yes, how many?)" Second, "During the past year, have you identified any patients in your practice (including those of your associates) receiving SCIT who developed systemic infections or sepsis associated with administration from a mixed allergen vial prepared in your office? (if yes, how many?)" Participants responding positively to these questions were contacted by the study coordinator to confirm that reported events were diagnosed as infectious and required treatment with antibiotics. Multiple contacts were made to nonresponders by telephone, e-mail, and fax to enhance the participation rate.^{4,5}

Between 2014 and 2015, 1,046 SCIT prescribers (30% of potential respondents) from 494 practices across the United States and Canada responded, including data from 9,469,586 injection visits and 1,360,828 patients. No confirmed local or systemic infection events that required antibiotics were reported. On the basis of these data representing hundreds of US allergy practices, not a single infection was identified after SCIT injections administered from mixed vaccine vials prepared from single allergen commercial products in the outpatient setting. These findings of our study, along with those of another recent study,³ indicate that there is no scientific evidence that confirms a risk of infection from SCIT as currently practiced. From this survey examining the risk of infections in approximately 9.5 million SCIT injections, we find no evidence to justify changes in current regulations regarding preparation guidelines.

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