



Guest Editorials

A novel approach to improving antibiotic selection in patients reporting penicillin allergy



Penicillin allergy remains the most commonly reported medication allergy. Approximately 10% of patients are diagnosed as being penicillin allergic, but when they undergo formal allergy evaluation with penicillin skin testing and challenge (if test results are negative), 90% or more are found to not be allergic and are able to tolerate penicillins. This discrepancy between reported and confirmed penicillin allergy is partly because penicillin allergy is known to wane in most (but not all) individuals. In addition, some index reactions likely did not represent a true allergy but rather were predictable adverse effects (such as diarrhea) or a manifestation of the underlying illness (such as viral-induced urticaria), which may be indistinguishable from a true allergy.

The diagnosis of penicillin allergy is not benign and has public health implications. There are 2 primary reasons for this. First and most important, patients diagnosed as being penicillin allergic are more likely to be treated with antibiotics, such as quinolones, vancomycin, and clindamycin, compared with patients without a history of penicillin allergy.^{1,2} Broad-spectrum antibiotics, such as quinolones, are a strong risk factor for the development of drug-resistant infections, such as vancomycin-resistant *Enterococcus* (VRE) and *Clostridium difficile*. Therefore, it was not surprising when Macy et al reported that hospitalized patients considered to be penicillin allergic were more likely than matched controls to be diagnosed as having VRE, *C difficile*, and methicillin-resistant *Staphylococcus aureus*.²

A second reason penicillin allergy has public health repercussions is increased medical costs. Antibiotic costs (in both outpatient and inpatient settings) have been reported to be higher in patients with a history of penicillin allergy compared with patients without a history of penicillin allergy.^{3,4} In the aforementioned study by Macy et al, inpatients considered to be penicillin allergic were hospitalized 0.59 days longer than matched controls, which translated to an additional cost of \$64.6 million.² Penicillin allergy evaluation, which usually results in negative penicillin skin test results, decreases antibiotic costs.⁵

Given the unfavorable clinical outcomes of patients with a history of penicillin allergy, a number of centers in the United States have initiated penicillin skin testing campaigns in an effort to reduce use of broad-spectrum antibiotics (by virtue of ruling out penicillin allergy in most individuals). Most prominently, at the Mayo Clinic, all elective surgery patients with a history of penicillin allergy, as part of their preoperative evaluation, are offered an allergy consultation with penicillin skin testing. This effort has resulted in large reductions in the use of perioperative vancomycin in favor of antibiotics, such as cefazolin.^{6,7} Similar beneficial outcomes of penicillin skin testing (ie, decrease in use of quinolones and vancomycin) have been reported by others.^{8,9}

In this issue of the *Annals*, Blumenthal et al¹⁰ report on their study of a novel approach to decreasing broad-spectrum antibiotic use in hospitalized patients with a history of penicillin or cephalosporin allergy. The investigators targeted nonallergist inpatient practitioners and developed a clinical guideline that relied on drug allergy history taking to determine which β -lactam antibiotic could be administered to patients with a history of penicillin or cephalosporin allergy. After educational intervention of general inpatient practitioners, the authors compared outcomes before and after implementation of the clinical guidelines. In patients with a mild penicillin reaction history (defined as mild nonurticarial rash or maculopapular rash), the pathway recommended use of penicillins and first- and second-generation cephalosporins via test dosing (also known as the graded challenge) and third- and fourth-generation cephalosporins via a single full dose. In patients with a reaction history consistent with a possible IgE-mediated reaction or unknown reaction, the pathway allowed for administration of third- and fourth-generation cephalosporins via graded challenge, but an allergy and immunology consultation was required for treatment with penicillins and first- and second-generation cephalosporins. Similarly, for patients with a history of cephalosporin allergy, the treatment algorithm recommended different approaches to treatment with penicillins and cephalosporins, depending on the reaction history (mild reactions vs IgE-mediated or vague reactions).

In the preguideline period, there were a median of 2 β -lactam test doses per month compared with a median of 14.5 in the postguideline period ($P < .001$). Test doses were performed sooner during patients' hospitalizations in the postguideline period compared with the preguideline period (median of 2 vs 4 days; $P = .002$). In the preguideline period, all challenged patients underwent an allergy and immunology consultation, as was required by the preguideline policy, compared with 14% of patients in the postguideline period ($P < .001$). Likewise, the percentage of challenged patients who underwent an infectious disease consultation decreased significantly (91% to 49%; $P < .001$). Overall, hospital allergy and immunology and infectious disease consultations did not change during the 2 periods. In the preguideline to postguideline periods, the proportion of penicillin test doses decreased significantly, whereas the proportion of cephalosporin test doses increased significantly. Notably, there was no significant difference in the adverse drug reaction rate during the 2 periods. Most important, among the challenged patients during the postguideline period, the clinical guideline resulted in significant decrease in use of vancomycin (68% to 37%; $P < .001$), quinolones (15% to 3%; $P < .001$), and aztreonam (12% to 0.6%; $P < .001$) in favor of penicillins and cephalosporins.

The study by Blumenthal et al indicates that a drug allergy educational campaign of hospital nonallergists can successfully lead to increased use of β -lactams instead of broad-spectrum

Disclosures: Dr Solensky is employed by The Corvallis Clinic, has received research support from Astra Zeneca, and has provided expert testimony.

antibiotics in patients with a history of penicillin or cephalosporin allergy. Although this novel strategy does not require specialty consultation services or training to perform skin testing, it is entirely dependent on a comprehensive, recurring educational campaign. It remains to be seen whether implementation of similar guidelines is feasible in other inpatient settings.

Although the findings of Blumenthal et al are important, they should not deemphasize the importance of penicillin skin testing, which remains the ultimate tool in evaluating patients with history of penicillin allergy. The approach taken at Massachusetts General Hospital can supplement penicillin skin testing efforts because no facility currently possesses the resources to skin test 10% of all inpatients with a history of penicillin allergy. Moreover, third- and fourth-generation cephalosporins, which many patients were switched to because of the guideline algorithm, are still problematic and more strongly associated with development of VRE and *C difficile* compared with penicillin/ β -lactamase inhibitors.¹¹ The advantage of a negative penicillin skin test result is that the penicillin allergy diagnosis can be permanently removed, whereas performing a challenge with cephalosporins (without penicillin skin testing) does not negate the penicillin allergy or the need to perform challenges with other cephalosporins in the future.

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Acupuncture for seasonal allergic rhinitis: is it ready for prime time?



Allergic rhinitis refers to an IgE-mediated process in which exposure to allergenic proteins triggers an inflammatory cascade resulting in nasal and ocular itching, sneezing, nasal congestion, and rhinorrhea. Symptoms can have a profound effect on quality of life (QoL) and are a significant health care burden. Allergic triggers can be perennial allergens, such as pet dander, cockroach, and house dust mites, or seasonal allergens, such as pollens from grasses, trees, and weeds. Conventional pharmacologic treatment of allergic rhinitis symptoms consists of the use of antihistamines, leukotriene modifiers, nasal glucocorticoids, decongestants, and in some cases allergen immunotherapy and supportive therapies, such as saline irrigation and allergen avoidance. The use of complementary and alternative medicine (CAM) as an adjunct or alternative to conventional Western medicine has increased in recent years, with approximately 26% of allergy sufferers endorsing trying CAM.¹ Reasons cited include lack of adequate response to conventional medicine (66.3%), belief in fewer side effects (78.3%), and a desire to pursue all treatment options (71.7%).¹ Approximately 17% of patients using CAM therapies for their allergies endorse the use of acupuncture.¹

In their study published in this month's *Annals*, Xue et al² examined the effectiveness of acupuncture on relief of seasonal allergic rhinitis (SAR) symptoms in 175 subjects from Melbourne, Australia using a parallel, randomized, single-blinded, sham-controlled study design. Subjects were randomly selected to receive real acupuncture (RA; n = 88) or sham acupuncture (SA; n = 87) 3 times per week over a 4-week period during peak rye grass season with an additional 4-week follow-up period.

Participants were allowed to use standardized relief medications, including an oral antihistamine or nasal decongestant spray, for refractory symptoms. In addition to assessing the primary outcome of nasal and non-nasal symptoms, 2 separate screening questionnaires were used to assess QoL and an overall global assessment of change was measured. Similar to their 2002 study, Xue et al³ found that the RA group had statistically decreased sneezing and itching of the ears and palate at the end of the treatment compared with the SA group and improvement in several QoL scores at the end of the treatment and during follow-up. Despite showing an improvement in isolated nasal and non-nasal symptom scores, Xue et al² found no significant differences among the other 6 symptom scores in their primary outcome or in the assessment of “global change” between the RA and SA groups at the end of the treatment and follow-up phases. As with previous acupuncture studies, the treatment was safe, with no significant adverse events.²

In recently updated clinical practice guidelines for allergic rhinitis published by the American Academy of Otolaryngology–Head and Neck Surgery, acupuncture is listed as a treatment option for clinicians based on “a preponderance of benefit over harm,” although they cited a low level of confidence in the evidence.⁴ A systematic review performed in 2009 by Lee et al⁵ examined 5 trials assessing the use of acupuncture in the management of SAR and found that the results “fail to show specific effects of acupuncture” compared with SA. The results of this current study are similar to the results of Williamson et al⁶ and the 2002 study by Xue et al.³ A more recent randomized, single-blinded, crossover study by Brinkhaus et al⁷ in 2013 examined QoL and RM scores in 422 patients with SAR who received RA, SA, or RM alone and found a statistically significant improvement in QoL and antihistamine use in RA. However, owing to study limitations, the investigators admitted that such findings

Disclosures: Authors have nothing to disclose.

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