

Title: New avenues for antimicrobial stewardship: the case for penicillin skin testing by pharmacists

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Summary: Although penicillin skin testing to verify true allergies has been recommended for decades, problems with implementation have been encountered. We suggest wider adoption of a model wherein pharmacists play an active role in such testing.

Abstract:

It is well-appreciated that patients with documented penicillin allergies often receive broader-spectrum antibiotics. This practice has been associated with increased antimicrobial resistance and cost. In recent years, considerable efforts have been made to spread awareness on the implications of self-reported penicillin allergies. The use of penicillin skin testing to evaluate for true allergies has been strongly recommended by major organizations for decades. However, testing remains underutilized. Current literature has suggested various models incorporating penicillin allergy screening and testing by different health-care practitioners (i.e., physicians, allergists, nurses, pharmacists). We suggest broader adoption for the role of pharmacists in provision of penicillin skin testing. This would help expand the service and maximize the potential benefits of penicillin skin testing.

Keywords: penicillin skin testing, penicillin allergy, pharmacists scope of practice

With all the attention being paid in the lay and medical press regarding the epidemic of opioid and benzodiazepine overuse, an “endemic” persists that has significant consequences for patients’ well-being. We are referring to the “endemic” of patient reported penicillin allergy which greatly increases the use of broad-spectrum antibiotics and is considered a factor associated with increasing bacterial resistance. This is not to say that the problem of evaluating patients with penicillin allergy has been ignored and it has gained more attention of late.¹ However, processes to assess the likelihood of a patient having a penicillin allergy need to be made more available with a multidisciplinary approach.²

Penicillin allergy is one of the most frequently self-reported drug allergies in the United States population with an incidence ranging from 10 to 20 percent; with less than one percent being truly allergic.³⁻⁵ These reported allergies may represent predictable adverse reactions or be true immunoglobulin-E (IgE)-mediated allergies with anaphylactic symptoms.³⁻⁵ Furthermore, hypersensitivity reactions have been documented to wane over time; up to 80 percent over ten years.^{5,6} Treatment options for patients who report penicillin allergy are limited and patients are frequently prescribed broader-spectrum antibiotics that are often considerably more expensive, may compromise intravenous to oral de-escalation, induce broader resistance, and deviate from standard treatment regimens.^{5,7} In a recent study of hospitalized patients with hematologic malignancies, a reported beta-lactam allergy was associated with worse clinical outcomes and higher healthcare costs.⁸

Several models for penicillin allergy screening and testing have been developed. Screening generally requires an algorithm that categorizes patients as at high risk or not for serious allergic reactions. Those at low risk may be given cephalosporins and at times penicillins without desensitization or further testing. In some algorithms, patients with less well-documented allergies receive test doses of the antibiotic to be used to assess whether full doses can be prescribed. In 2013, Blumenthal et al. reported a significant impact on antimicrobial use post-implementation of a guideline to assist providers in assessing the risk for significant penicillin and cephalosporin allergy which employed test dosing.⁹ Implementation of this guideline resulted in significantly more patients treated with penicillins (19% vs 2%, $p<0.001$) and 1st (10% vs 0.6%, $p<0.001$), 3rd (30% vs 5%, $p<0.001$) or 4th (32% vs 7%, $p<0.001$) generation cephalosporins. Furthermore, fewer patients were treated with vancomycin (37% vs 68%, $p<0.001$), aminoglycosides (1% vs 6%, $p=0.004$), aztreonam (0.6% vs 12%, $p<0.001$), or fluoroquinolones (3% vs 15%, $p<0.001$).⁹

Even with such guideline-based algorithms, many providers will not feel comfortable using penicillins and opt to utilize broader-spectrum antibiotics that have low or no cross-reactivity with penicillins such as carbapenems, tigecycline, or aztreonam. Blumenthal et al. conducted a survey of 521-inpatient providers pre- and post- implementation of the clinical guideline previously mentioned. The survey results concluded that inpatient

providers' prior education, knowledge and comfort regarding drug and penicillin allergies are lacking.¹⁰

Standardized penicillin skin testing (PST) dates back to 1948 and has been recommended by the American Academy of Allergy, Asthma, and Immunology for all patients believed to be allergic to penicillin to verify the allergy.^{5,11} In addition, the Centers for Disease Control and Prevention recommends to evaluate patients for true penicillin allergy before prescribing broad-spectrum antibiotics.^{3,11} PST is an objective method to assess type I (IgE-mediated) reactions that has been shown to be safe and effective. The negative predictive value of PST ranges from 97 to 99 percent and systemic adverse reactions are extremely uncommon (<1%), so that the vast majority of patients testing negative can receive a penicillin.⁵

Many institutions have made an interdisciplinary effort to implement PST services in conjunction with screening algorithms. The most common model has been for pharmacists to screen and interview patients with documented penicillin allergies and to refer patients to allergists for PST when appropriate.^{7,12-14} An increase in utilization of beta-lactam antibiotics and decrease in non-beta-lactam antibiotics has been observed with this model.^{7,12-14} A meta-analysis evaluating clinical outcomes following inpatient PST services demonstrated an increase in the use of penicillins (range 9.9% to 49%) and cephalosporins (range 10.7% to 48%) and a decrease in vancomycin and fluoroquinolone use.¹⁵

Unfortunately, PST is not routinely offered in many healthcare settings. PST is only available in about 60 percent of institutions.¹⁵ Availability of local allergists and the potentially large number of patients needing testing has limited the use of such testing.^{4,7,11} We argue that a model wherein pharmacists play a more active role in providing PST would help expand the service. In 2004, Wall et al. described a model where pharmacists under the guidance of allergists conducted PST in patients with a history of penicillin allergy. The service allowed for all 26 patients enrolled to receive a penicillin or a beta-lactam antibiotic.¹⁶ In 2015, Gugkaeva et al. implemented a pharmacist-provided PST service and reported that after PST, 78% (40/51) of patients who tested negative were switched to a narrower-spectrum beta-lactam.¹¹ Other institutions have adopted pharmacist-led models and have shown similar results.⁴ However, this practice is limited. There are several challenges to this model such as lack of standardized training programs and limited experience with implementation of such services.^{4,11} However, the biggest obstacle is the fact that the scope of practice for pharmacists as defined in state board regulations more often than not does not include PST.

We queried the state board of pharmacies from 50 states and the District of Columbia (D.C.) via email and found that of the 38 that responded, only 12 (31.5%) states permitted this practice. Pharmacist-directed PST in all cases was allowed under only collaborative practice agreements (CPA). This is interesting because as of May 2016, 48 states permit

some type of pharmacist and prescriber CPA.¹⁷ Thus, there is the potential for more states to expand the role of pharmacist-directed PST through CPAs. The pharmacist's role on patient care teams has expanded greatly in recent years. For instance, it has become fairly common practice for pharmacists to administer immunizations. Today, pharmacists have authority to administer immunizations in all 50 states and D.C. and this has led to increased immunization rates.^{18,19} Advancing pharmacist's roles to provide PST would be a step in the same direction and we suspect an important contribution to patient care.

Potential conflicts:

The authors have no conflict of interest and have both contributed equally to this manuscript.

References

1. Zuger A. Penicillin allergies overblown. The New York Times website. <https://well.blogs.nytimes.com/2013/09/09/penicillin-allergies-overblown/>. September 9, 2013. Accessed March 1, 2018.
2. Sacco KA, Chirila R, Libertin C, et al. Utilization and timeliness of an inpatient penicillin allergy evaluation. *Allergy Asthma Proc.* 2018; 1; 39(3):245-251.
3. Centers for Disease Control and Prevention. Evaluation and diagnosis of penicillin allergy for healthcare professionals (October 31, 2017). <https://www.cdc.gov/antibiotic-use/community/for-hcp/Penicillin-Allergy.html>. (Accessed March 1, 2018).
4. Chen JR, Tarver SA, Alvarez KS, et al. A proactive approach to penicillin allergy testing in hospitalized patients. *J Allergy Clin Immunol Pract.* 2017; 5:686-693.
5. Unger NR, Gauthier TP, Cheung LW. Penicillin skin testing: potential implications for antimicrobial stewardship. *Pharmacotherapy.* 2013; 33:856-867.
6. Kuruvilla ME, Khan DA. Antibiotic allergy. In: Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and practice of infectious diseases.* 8th ed. Philadelphia, PA: Elsevier Inc.; 2015: 300-303.
7. Jones BM, Bland CM. Penicillin skin testing as an antimicrobial stewardship initiative. *Am J Health-Syst Pharm.* 2017; 74:232-237.
8. Huang KG, Cluzet V, Hamilton K, Fadugba, O. The impact of reported beta-lactam allergy in hospitalized patients with hematologic malignancies requiring antibiotics. *Clin Infect Dis.* 2018; 67(1):27-33.

9. Blumenthal KG, Shenoy ES, Varughese CA, et al. Impact of a clinical guideline for prescribing antibiotics to inpatients reported penicillin or cephalosporin allergy. *Ann Allergy Asthma Immunol.* 2015; 115:294-300.
10. Blumenthal KG, Shenoy ES, Hurwitz S et al. Survey of inpatient clinical providers' antibiotic prescribing knowledge. *J Allergy Clin Immunol Pract.* 2014; 2:407-413.
11. Gugkaeva Z, Crago JS, Yasnogorodsky M. Next step in antibiotic stewardship: pharmacist-provided penicillin allergy testing. *J Clin Pharm Ther.* 2017; 42:509-512.
12. Park MA, McClimon BJ, Ferguson B, et al. Collaboration between allergists and pharmacists increases beta-lactam antibiotic prescriptions in patients with a history of penicillin allergy. *Int Arch Allergy Immunol.* 2011; 154:57-62.
13. King EA, Challa S, Curtin P, Bielory, L. Penicillin skin testing in hospitalized patients with beta-lactam allergies: effect on antibiotic selection and cost. *Ann Allergy Asthma Immunol.* 2016; 117:67-71.
14. Ramsey A, Staicu ML. Use of a penicillin allergy screening algorithm and penicillin skin testing for transitioning hospitalized patients to first-line antibiotic therapy. *J Allergy Clin Immunol Pract.* 2017.
15. Sacco KA, Bates A, Brigham TJ, et al. Clinical outcomes following inpatient penicillin allergy testing: a systematic review and meta-analysis. *Allergy.* 2017; 72:1288-1296.
16. Wall GC, Peters L, Leaders CB, Wille, JA. Pharmacist-managed service providing penicillin allergy skin tests. *Am J Health-Syst Pharm.* 2004; 61:1271-1275.
17. Centers for Disease Control and Prevention. Advancing team-based care through collaborative practice agreements: a resource and implementation guide for adding

pharmacists to the care team (2017). <https://www.cdc.gov/dhds/pubs/docs/CPA-Team-Based-Care.pdf> (Accessed March 1, 2018).

18. American Pharmacists Association. Pharmacist-administered immunizations: what does your state allow? (October 1, 2015).

<https://www.pharmacist.com/pharmacist-administered-immunizations-what-does-your-state-allow> (Accessed March 1, 2018.)

19. Bonner L. With proper tools, pharmacists increase adult vaccination rates.

PharmacyToday. 2017; 23:33.