

Penicillin Allergy Testing Should Be Performed Routinely in Patients with Self-Reported Penicillin Allergy

Penicillin Allergy in Antibiotic Resistance Workgroup

AAAAI Position Statements, Work Group Reports, and Systematic Reviews are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. The statement below is not to be construed as dictating an exclusive course of action nor is it intended to replace the medical judgment of healthcare professionals. The unique circumstances of individual patients and environments are to be taken into account in any diagnosis and treatment plan. The statement reflects clinical and scientific advances as of the date of publication and is subject to change.

For reference only.

Adverse reactions to medications are frequently observed. Among the drugs associated with IgE-mediated allergic reactions, penicillins are most commonly implicated.¹ Penicillin allergy is estimated to affect 7% to 10% of community populations and up to 20% of hospitalized patients.^{1,2} However, when penicillin allergy testing is performed in individuals who report a history of penicillin allergy, the overwhelming majority do not exhibit positive reactions. The rate of positive skin test results to penicillin in recent studies is only 1% to 8%.³⁻⁵ The reasons for the low rate of confirmed penicillin allergy include mislabeling of a side effect (eg, gastrointestinal upset) or a coincidental event (eg, headache or cutaneous eruption due to underlying infection) as an allergic reaction, reduced rates of exposure to parenteral penicillins, and loss of IgE-mediated allergy with avoidance of penicillins over time.²

Skin testing was introduced as a diagnostic intervention for the evaluation and management of patients with a history of penicillin allergy in the late 1950s and early 1960s, independently by Charles Parker and Bernard Levine.⁶ This procedure is commonly performed, and with minimal risk. Penicillin skin testing can be done safely in properly selected patients with suspected penicillin allergy, even in pregnant women with group B Streptococcal infections⁷ and in patients who require organ transplantation.⁸ Systemic reactions have been reported, although rarely; for this reason, penicillin allergy testing should be performed in a health care setting only by clinicians with the knowledge, training, and experience to select appropriate patients for this procedure, interpret test results, and manage a systemic allergic reaction should it occur.^{1,2} Patients with negative skin testing to penicillin reagents, followed by an oral challenge that is well tolerated, are able to receive penicillins without increased risk of IgE-mediated allergic reaction. The negative predictive value of penicillin allergy testing exceeds 99%.⁹

Reporting a history of penicillin allergy is associated with a morbidity that has not been widely appreciated until recently. Unverified penicillin allergy in hospitalized patients is associated with longer hospital stays and increased rates of serious drug-resistant infections.¹⁰ For this reason, the Choosing Wisely program of the American Board of Internal Medicine Foundation recommended in 2014 that clinicians not overuse non-beta-lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation.¹¹ The National Quality Partners' Antibiotic Stewardship Action Team recommends penicillin allergy skin testing as a component of a comprehensive antibiotic stewardship program.¹²

In the absence of appropriate evaluation for penicillin allergy, patients providing a history of penicillin allergy must continue to avoid penicillins. For example, when such patients undergo a surgical procedure, preoperative antibiotics are commonly administered prophylactically to safeguard against postoperative infection. Hospitalized patients frequently report allergy to penicillin. Providing this history leads to receiving an alternative antibiotic (eg, vancomycin, a quinolone, or a carbapenem). These alternative therapies can be associated with higher cost and/or greater risk for untoward effects. More frequent use of alternative non—beta-lactam antibiotics also may lead to greater

Approved by the AAAAI Board of Directors, July 2016.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

For more information, contact the AAAAI at info@aaaai.org. 2213-2198

^{© 2016} American Academy of Allergy, Asthma & Immunology http://dx.doi.org/10.1016/j.jaip.2016.12.010

nosocomial rates of resistant gram-positive (eg, enterococci and staphylococcus) and gram-negative (eg, klebsiella) strains, which are associated with increased costs, poorer patient outcomes, and other burdens.

In 2015, President Obama released an Executive Order for a National Action Plan for combating antibiotic-resistant bacteria.¹³ This plan focuses on reducing the emergence and spread of resistant bacteria and infections, and promotes antibiotic stewardship in hospital and ambulatory settings. The National Quality Forum (NQF) has committed its support and resources to this initiative. Antibiotic stewardship was selected by attendees at the March 2015 annual NQF meeting as 1 of its 2 priority issues for this year. The AAAAI, which has been a member of the NQF since 2011, has joined as an active participant in this praiseworthy effort.

Penicillin allergy testing is associated with an unrealized potential: this procedure can accurately identify the approximately 9 of 10 patients who despite reporting a history of penicillin allergy can receive penicillins safely, that is, without elevated risk for an IgE-mediated allergic reaction compared with the general population. In the context of the recently launched national antibiotic stewardship initiative, the AAAAI encourages more widespread and routine performance of penicillin skin testing for patients with a history of allergy to penicillin or another beta lactam (eg, ampicillin or amoxicillin). More frequent performance of penicillin allergy testing can be expected to lead to a greater proportion of patients safely receiving penicillins, including patients undergoing surgical procedures, hospitalized patients with serious infections, and patients who require antibiotics in the ambulatory setting. On the basis of current evidence, we are confident that more frequent and routine performance of penicillin allergy testing will be associated with reduced costs of care, enhanced patient safety, and improved outcomes of care.

Acknowledgment

The American Academy of Allergy, Asthma & Immunology Board of Directors acknowledges the contributions of David M. Lang, MD, FAAAAI (Cleveland Clinic), chair of the Penicillin Allergy in Antibiotic Resistance (PAAR) workgroup, and work group members Mariana C. Castells, MD, PhD, FAAAAI (Brigham and Women's Hospital and Harvard Medical School); David A. Khan, MD, FAAAAI (University of Texas Southwestern Medical Center); Eric M. Macy, MD, FAAAAI (SCPMG-Kaiser Permanente San Diego); and Andrew W. Murphy, MD, FAAAAI (Asthma, Allergy and Sinus Center).

REFERENCES

- Lieberman P, Nicklas RA, Oppenheimer J, Kemp SF, Lang DM, Bernstein DI, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 update. J Allergy Clin Immunol 2010;126:477-522.
- Solensky R, Khan DA, Bernstein IL, Bloomberg GR, Castells MC, Mendelson LM, et al. Drug allergy: an updated parameter. Ann Allergy Asthma Immunol 2010;105:259-73.
- Macy E, Schatz M, Lin C, Poon KY. The falling rate of positive penicillin skin tests from 1995 to 2007. Permanente J 2009;13:12-8.
- Gadde J, Spence M, Wheeler B, Adkinson NF Jr. Clinical experience with penicillin skin testing in a large inner-city STD clinic. JAMA 1993;270: 2456-63.
- Macy E, Ngor E. Safely diagnosing clinically significant penicillin allergy using only penicilloyl-poly-lysine, penicillin, and oral amoxicillin. J Allergy Clin Immunol Pract 2013;1:258-63.
- Sullivan TJ. Advances in the diagnosis and management of penicillin allergy. N Engl Reg Allergy Proc 1985;6(2):160.
- Philipson E, Lang D, Gordon S, Burlingame J, Emery S, Arroliga M. Management of group B Streptococcus in pregnant women with penicillin allergy. J Reprod Med 2007;52:480-4.
- Gutta R, Radojicic C. Safety and effectiveness of penicillin allergy evaluation in the pre-lung transplant patient population. J Allergy Clin Immunol 2012;129: A102.
- del Real GA, Rose ME, Ramirez-Atamoros MT, Hammel J, Gordon SM, Arroliga AC, et al. Penicillin skin testing in patients with a history of betalactam allergy. Ann Allergy Asthma Immunol 2007;98:355-9.
- Macy E, Contreras R. Healthcare utilization and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. J Allergy Clin Immunol 2014;133:790-6.
- Choosing Wisely. American Academy of Allergy, Asthma & Immunology: Ten Things Physicians and Patients Should Question. Available from: http://www. choosingwisely.org/doctor-patient-lists/american-academy-of-allergy-asthmaimmunology/. Accessed August 3, 2015.
- National Quality Forum. National Quality Partners Playbook: Antibiotic Stewardship in Acute Care. Available from: http://www.qualityforum.org/ Publications/2016/05/National_Quality_Partners_Playbook__Antibiotic_ Stewardship_in_Acute_Care.aspx?utm_source=internal&utm_medium= link&utm_term=ABX&utm_content=Playbook&utm_campaign=ABX. Accessed February 1, 2017.
- The White House Office of the Press Secretary. National Action Plan for Combating Antibiotic-resistant Bacteria. https://obamawhitehouse.archives. gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-res istant_bacteria.pdf. Accessed February 1, 2017.