Is it Really a Penicillin Allergy?

Evaluation and Diagnosis of Penicillin Allergy for Healthcare Professionals

Did You Know? 5 Facts About Penicillin Allergy (Type 1, Immunoglobulin E (IgE)-mediated)

- 1. Approximately 10% of all U.S. patients report having an allergic reaction to a penicillin class antibiotic in their past.
- 2. However, many patients who report penicillin allergies do not have true IgE-mediated reactions. When evaluated, fewer than 1% of the population are truly allergic to penicillins.¹
- 3. Approximately 80% of patients with IgE-mediated penicillin allergy lose their sensitivity after 10 years.¹
- 4. Broad-spectrum antibiotics are often used as an alternative to penicillins. The use of broad-spectrum antibiotics in patients labeled "penicillin-allergic" is associated with higher healthcare costs, increased risk for antibiotic resistance, and suboptimal antibiotic therapy.¹
- 5. Correctly identifying those who are not actually penicillin-allergic can decrease unnecessary use of broad-spectrum antibiotics.¹

10% of the population reports a penicillin allergy but <1% of the whole population is truly allergic.





Before prescribing broad-spectrum antibiotics to a patient thought to be penicillin-allergic, evaluate the patient for true penicillin allergy (IgE-mediated) by conducting a history and physical, and, when appropriate, a skin test and challenge dose.

History and Physical Examination

The history and physical examination are important components when evaluating a patient's drug reactions.¹

- Questions to ask during the examination:
 - What medication were you taking when the reaction occurred?
 - What kind of reaction occurred?
 - How long ago did the reaction occur?
 - How was the reaction managed?
 - What was the outcome?²
- Characteristics of an IgE-mediated (Type 1) reaction:
 - Reactions that occur immediately or usually within one hour¹
 - Hives: Multiple pink/red raised areas of skin that are intensely itchy³
 - Angioedema: Localized edema without hives affecting the abdomen, face, extremities, genitalia, oropharynx, or larynx⁴
 - Wheezing and shortness of breath
 - Anaphylaxis¹ requires signs or symptoms in at least two of the following systems:
 - Skin: Hives, flushing, itching, and/or angioedema (continued on next page)

- Broad-spectrum antibiotics are often used as an alternative to narrow-spectrum penicillins.
- Using broad-spectrum antibiotics can increase healthcare costs and antibiotic resistance, and may mean your patient receives less than the best care.
- Correctly identifying if your patient is actually penicillin-allergic can decrease these risks by reducing unnecessary use of broadspectrum antibiotics.



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- Respiratory: Cough, nasal congestion, shortness of breath, chest tightness, wheeze, sensation of throat closure or choking, and/or change in voice-quality (laryngeal edema)
- Cardiovascular: Hypotension, faintness, tachycardia or less commonly bradycardia, tunnel vision, chest pain, sense of impending doom, and/or loss of consciousness
- Gastrointestinal: Nausea, vomiting, abdominal cramping, and diarrhea⁵

Penicillin Skin Tests and Challenge Doses

Based on the patient history and physical exam, additional tests may be needed to confirm a penicillin allergy. Penicillin skin testing is a reliable and useful method for evaluating IgE-mediated penicillin allergy.⁵

A positive result means the patient is likely to have a penicillin allergy. If negative, the skin test is usually followed by an oral penicillin class challenge (e.g., with amoxicillin) to safely rule out an IgE-mediated penicillin allergy.^{1,7}

- Skin tests currently include penicilloylpolylysine, the major antigenic determinant that indicates hypersensitivity to penicillin.
- However, it is important to note that the patient can also be allergic to other reactive breakdown products, called minor determinants, which include penicillin G (benzylpenicillin), penicilloate, and penilloate—many of which are not commercially available. Of these, only penicillin G is available from pharmacies.
- To rule out penicillin allergy, an oral challenge dose can be done after skin testing. The negative predictive value of skin testing with the major and minor determinants is more than 95%, but approaches 100% when followed by a challenge dose.²

Special Considerations

Patients with severe hypersensitivity syndromes

Patients with other severe hypersensitivity syndromes—like Stevens-Johnson syndrome, toxic epidermal necrolysis, serum sickness, acute interstitial nephritis, hemolytic anemia, and drug rash with eosinophilia and systemic symptoms (DRESS)—should not use the offending drug in the future. The skin test and challenge described here are not appropriate for patients with these severe hypersensitivity syndromes.^{1,2,6}

Cephalosporin use in penicillin-allergic patients

Many cephalosporins, especially in the later generations, can be safely tolerated despite a penicillin allergy.^{6,8} Patients with anaphylaxis or other severe reactions to penicillin may require further evaluation prior to the use of cephalosporins.

Pediatric patients

Children who are receiving amoxicillin or ampicillin and have Epstein-Barr virus infection can develop a non-allergic, non-pruritic rash that can appear similar to an IgE-mediated reaction.^{1,9}

For more information about appropriate antibiotic use, visit www.cdc.gov/getsmart.

References

- 1. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010 Oct;105(4):259-273.
- 2. Gonzalez-Estrada A, Radojicic C. Penicillin allergy: a practical guide for clinicians. Cleve Clin J Med. 2015 May;82(5):295-300.
- 3. Herrier RN, Apgar DA, Boyce RW, Foster SL. Patient assessment in pharmacy. New York: McGraw-Hill; 2015 [cited 2015 Aug 14]. Available from: http://accesspharmacy.mhmedical.com/content.aspx?bookid=1074&Sectionid=62364288.
- 4. Bernstein JA. Update on angioedema: evaluation, diagnosis, and treatment. Allergy Asthma Proc 2011; 32(6):408-412.
- 5. Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A et al. Second symposium on the definition and management of anaphylaxis: summary report–second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Ann Emerg Med. 2006; 47:373-380.
- 6. Blumenthal KG, Shenoy ES, Hurwitz S, Varughese CA, Hooper DC, Banerji A. Effect of a drug allergy educational program and antibiotic prescribing guideline on inpatient clinical providers' antibiotic prescribing knowledge. J Allergy Clin Immunol. 2014;2(4):407-412.
- 7. Macy E, Ngor E. Recommendations for the management of beta-lactam intolerance. Clinical Rev Allerg Immunol. 2014; 47:46-55.
- 8. Pichichero, ME. A review of evidence supporting the American Academy of Pediatrics recommendation for prescribing cephalosporin antibiotics for penicillin-allergic patients. Pediatrics. 2005 Apr; 115(4):1048-1057.
- 9. Centers for Disease Control and Prevention [Internet]. About Epstein-Barr Virus (EBV) [cited 2015 Aug 17]. Available from: http://www.cdc.gov/epstein-barr/about-ebv.html.

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