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 truly penicillin-allergic can decrease unnecessary use of broad-spectrum antibiotics.¹

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
  - Anaphylaxis

¹ Centers for Disease Control and Prevention. (2023). National Center for Emerging and Zoonotic Infectious Diseases. CS262696A-PO
Anaphylaxis requires signs or symptoms in at least two of the following systems:
- **Skin**: Hives, flushing, itching, and/or angioedema
- **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 diarrhea

**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 and challenge doses are reliable and useful methods for evaluating for IgE-mediated penicillin allergy.**

**Penicillin Skin Testing**

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.

- The current standard of care is to perform a skin test with the major determinant penicilloylpolylysine and commercially-available penicillin G.
- 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.

A direct oral challenge without prior skin testing may also be performed in selected patients and can rule out penicillin allergy. For more information, please consult an allergist.

**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.

**Cephalosporin use in penicillin-allergic patients**

Many cephalosporins, especially in the later generations, can be safely tolerated despite a penicillin allergy. 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 allergic reaction.

For more information about antibiotic use, visit [www.cdc.gov/antibiotic-use](http://www.cdc.gov/antibiotic-use).

**References**


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