

Drug and Vaccine Allergy



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KEYWORDS

• Allergy • Beta-lactam • Penicillin • Egg allergy • Influenza vaccination

KEY POINTS

- Children labeled as allergic to penicillin should undergo penicillin skin testing and oral challenge to identify the vast majority who are not currently penicillin-allergic.
- Children with a distant history of a mild reaction to penicillin can safely be administered oral cephalosporins.
- Reactions to carbapenems among children with penicillin allergy are rare, and such medications can be administered cautiously under observation.
- Leaving egg-allergic patients unvaccinated against influenza leaves them at risk for morbidity and mortality from influenza.
- Studies involving thousands of egg-allergic subjects, including hundreds with histories of severe reactions to the ingestion of eggs, have shown a low rate of minor reactions that is not different from nonegg-allergic controls.
- Current guidelines from the American Academy of Pediatrics (AAP) and Centers for Disease Control and Prevention (CDC) recommend that egg-allergic patients receive annual influenza vaccine and be observed for 30 minutes afterward; however, given the safety data, even this precaution may be unnecessary.

INTRODUCTION

It is important to identify children who are allergic to drugs and vaccines, because administration of these substances to such children can lead to serious, even life-threatening systemic allergic reactions (anaphylaxis). Recent updates of practice parameters on adverse reactions to drugs¹ and vaccines² provide excellent resources on these topics.

However, it is also important not to overdiagnose such allergy (ie, label children as allergic when they are not), because this deprives them of the most appropriate treatment. This article specifically reviews allergic reactions to beta-lactam antibiotics and the administration of influenza vaccine to egg-allergic recipients. These are areas where recent evidence has allowed the administration of these treatments to children from whom they had previously been withheld.

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BETA-LACTAM ANTIBIOTICS

Penicillin and its derivatives are regarded as the most common cause of drug allergy,¹ due to propensity to cause such reactions, but also because of frequent use. However, the incidence of penicillin allergy appears to be falling over time, perhaps related to the less frequent use of penicillin by the potentially more sensitizing parenteral route in the outpatient setting.^{3,4} Approximately 6% of children are reported to be allergic to penicillin.⁵ However, only approximately 4% to 9% of such children have positive immediate type (immunoglobulin E [IgE]) skin tests to penicillin reagents.⁶⁻⁹ The remainder were either never allergic to penicillin or the allergy was lost with the passage of time.¹⁰ Those who were never allergic may have been mislabeled, because they suffered a nonimmunologic side effect from the medication such as emesis, or because they suffered an adverse event that was coincidental to, but not caused by the penicillin administration. Thus, most children labeled as penicillin-allergic are not, and are inappropriately denied treatment with this class of antibiotics. The use of alternative antibiotics may be associated with suboptimal treatment and higher costs and may promote antibiotic resistance.¹¹ Thus, a strong argument can be made for testing such patients in advance of need in order to identify the vast majority who are not currently allergic to penicillin.^{1,10}

It had previously been advocated that penicillin skin testing be performed in patients with suspected penicillin allergy only at the time of infection and only when there were no acceptable alternatives.¹² The rationale for this recommendation was based in part on a concern that skin testing and challenge with penicillin could resensitize previously allergic children who had lost sensitivity over time, placing them at risk for allergic reactions when administered penicillin in the future. However, such resensitization is rare with orally administered penicillins,^{6,9} although it may be somewhat higher after parenterally administered penicillin.¹³

Penicillin is a small molecule and must act as a hapten with a protein carrier to have a large enough size and high enough valency to elicit an IgE-mediated response. Penicillin is metabolized to so-called major and minor determinants. The majority of the drug is metabolized to the penicilloyl (major) determinant, while the remainder is metabolized to penilloate and penicilloate (minor) determinants. Unmetabolized benzylpenicillin, known as penicillin G, is also typically regarded as a minor determinant. Penicillin G has always been available as a skin test reagent simply as a dilution of the drug used for treatment. The penicilloyl (major) determinant is available commercially as benzylpenicilloyl polylysine, where multiple penicilloyl determinants (haptens) are linked to an amino acid polymer (carrier). Penilloate and penicilloate (minor) determinants have never been available commercially in the United States, although many allergists with access to laboratory facilities have generated these reagents from penicillin G through acid and alkaline hydrolysis, respectively.¹⁴ The rationale for including penilloate and penicilloate minor determinants for skin testing patients with suspected penicillin allergy is that some patients with such histories will have positive skin test results only to these reagents.^{6,15} Some centers perform penicillin skin testing with the readily available benzylpenicilloyl polylysine and penicillin G, and if negative perform an oral amoxicillin challenge under observation to identify those patients who are clinically allergic to penicillin despite negative skin test with these 2 reagents, some of whom would presumably have had positive skin tests to penilloate, penicilloate, or amoxicillin.¹⁶ However, when 496 patients with suspected penicillin allergy but negative benzylpenicilloyl polylysine and penicillin G skin tests underwent amoxicillin challenge, only 4 (0.8%) were positive, all developing only hives within 1 hour. The authors calculated that 3375 patients would have to be tested with a panel

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