

Friday 2 January 2026

Penicillin Allergy

Introduction

Penicillin allergy affects 10% of the population; however, 95% of patients with a history of penicillin allergy can actually tolerate this antibiotic. A label of penicillin allergy is not benign as patients may receive less effective, more toxic, more expensive antibiotics leading to increased antibiotic associated infections, longer hospital stays and possibly increased mortality. **Penicillin skin testing (prick and intradermal) is a validated and safe method for evaluating IgE mediated penicillin allergy and is superior to penicillin IgE blood tests. Pragmatically, evaluation of IgE mediated penicillin is indicated in cases where alternatives to penicillin-based antibiotics are inferior to alternative anti-microbial agents.** Infectious Diseases/Microbiology Consultant or other physician with a specialist interest in management of infectious disease will advise on the need for penicillin based therapy.

Clinical History

The **PENFAST protocol** can be used to determine whether patient with a history of penicillin allergy can be challenged with oral drugs or needs allergy evaluation with standard of care skin testing followed by oral drug challenge.

Does the patient report a history of penicillin allergy YES/NO: if yes proceed with assessment

F	Allergy reaction reported within last Five years ^a	2 points
A	Angioedema or Anaphylaxis	2 points
OR		
S	Severe cutaneous reaction ^b	2 points
T	Treatment required for reaction ^a	1 point

(a) Includes unknown

(b) Severe cutaneous adverse reactions include potential Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis. Patients with a severe delayed rash with mucosal involvement should also be categorized as a severe cutaneous adverse reaction. Acute interstitial nephritis, drug-induced liver injury, serum sickness and isolated drug fever were excluded

PENFAST SCORE

- 0 Very low risk of penicillin allergy less than 1%
- 1-2 Low risk of penicillin allergy less than 5.0%
- 3 Moderate risk of penicillin allergy 20%
- 4-5 High risk penicillin allergy 50%

A recent randomised clinical trial showed that the rate of immune mediated penicillin reaction following direct oral penicillin challenge in patient with low/no risk PENFAST scores was non inferior to combination of penicillin skin prick and intradermal test followed by oral challenge.

Specialist referral for assessment of penicillin allergy

Recent history of anaphylaxis and/or angioedema

Recent history of severe cutaneous drug reaction (oral challenges contra-indicated)

Direct oral penicillin challenge

Testing in patients with a history inconsistent with penicillin allergy (such as headache or family history of penicillin allergy), is not recommended, but an amoxicillin challenge may be offered to patients who are anxious or request additional reassurance to accept the removal of a penicillin allergy label.

Penicillin skin testing is not recommended before direct amoxicillin challenge in paediatric patients with a history of benign cutaneous reaction (urticaria or morbilliform drug rash).

Direct amoxicillin challenge should be considered in adults with a history of distant and benign cutaneous reactions (such as MDE and urticaria).

References

Khan DA, et al Drug allergy: A 2022 practice parameter update. J Allergy Clin Immunol. 2022; 150:1333-1393.

Banerji A, et al. -Drug Allergy Practice Parameter Updates to Incorporate Into Your Clinical Practice. J Allergy Clin Immunol Pract. 2023; 11:356-368.e5

Copaescu AM et al. [Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy: The PALACE Randomized Clinical Trial.](#) JAMA Intern Med. 2023; 183:944-952.