



EDUCATION: Penicillin Allergy

Consequences of an Unconfirmed Penicillin Allergy with Public Health Implications 1-8

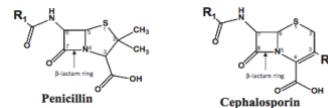
- Unconfirmed penicillin allergies and the use of alternative (second-line) and/or broader-spectrum antimicrobial agents such as [fluoroquinolones](#), clindamycin, vancomycin, and aztreonam have been associated with:
 - More treatment failure
 - Serious adverse effects
 - Higher incidences of *Clostridium difficile*, vancomycin-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA)
 - Longer hospital stays
 - Rising antimicrobial-related healthcare costs
- The [CDC](#), [NQF](#), [ABIM](#), alongside the IDSA and AAAAI, have recognized unconfirmed penicillin allergies as a public health concern.

Prevalence and Mislabeling of Penicillin Allergies 9-16,23

- Approximately 10-20% of hospitalized patients self-report a penicillin allergy with 15-24% requiring antimicrobial therapy.
- Less than 10% of these individuals when tested have a positive penicillin skin test and over 90% have been shown to tolerate penicillins without an immediate IgE-mediated hypersensitivity reaction.
- Reported allergies to penicillins are often mistaken for non-IgE-mediated adverse reactions: maculopapular/morbilloform rash due to underlying viral or bacterial infections, gastrointestinal intolerance, dizziness, and headache.
- IgE antibodies associated with a positive penicillin skin test wanes over time, with 80% of patients becoming tolerant after 10 years.
 - 50% of sensitivity lost by 5 years and 80% by 10 years.

β -Lactam Cross-Reactivity Due to Antibody

- The cross-reactivity between β -lactams with IgE-mediated hypersensitivity may be predicted by similarities of R-side chains. [\$\beta\$ -lactam Allergy Side Chain Chart](#)
- The rate of cross-reactivity between a penicillin and cephalosporin due to antibody recognition:
 - <2% in those who are skin test positive; <1% in patients not skin tested.
- Non-IgE-mediated hypersensitivity reactions (maculopapular rash, acute interstitial nephritis, immune-mediated hepatitis) have been reported with anti-staphylococcal penicillins (e.g. nafcillin).
 - Cefazolin is an option as it has a dissimilar R1 side chain to penicillins and cephalosporins.¹⁹
- Cross-reactivity with carbapenems is very unlikely (<1%).
- Cross-reactivity with aztreonam is absent, except for ceftazidime.



Recognition 9,17-20

β -Lactam Allergy Side Chain Chart

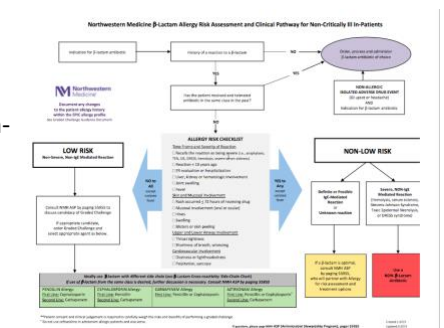
The chart is a grid with columns for Penicillins (R1), Cephalosporins (R2), Carbapenems, and Aztreonam. Rows list specific drugs like Penicillin G, Penicillin V, Nafcillin, Oxacillin, Cloxacillin, Amoxicillin, Ampicillin, Cefazolin, Cefuroxime, Cefepime, Meropenem, and Aztreonam. Symbols (triangles and crosses) indicate the level of cross-reactivity between different classes and side chains.

Allergy Assessment Methods and Northwestern β -Lactam Allergy Clinical Pathway

Conducting a risk assessment with allergy history leads to fewer treatment failures and deaths compared to giving an alternative antibiotic.²³

- Penicillin Skin Testing (PST) 9,13,16,23
 - Required to evaluate a penicillin allergy in patients with a **moderate to high-risk for IgE-mediated hypersensitivity reaction**: urticaria, angioedema, bronchospasm, anaphylaxis. [\$\beta\$ -Lactam Allergy Guideline: Clinical Pathway](#)
 - Contact Allergy and Immunology for PST
 - Has a negative predictive value (NPV) of 95% and approaches 100% when followed with an oral amoxicillin challenge.
 - A positive skin test, however, does not necessarily predict challenge reactions for benign skin rashes.
 - PST is not reliable to predict low-risk, non-IgE-mediated reactions.
- Direct Graded Challenges (GC) 9,16,21-22,23
 - Recommended to verify penicillin tolerance in patients with a **low-risk (or unlikely) IgE-mediated reaction** using a β -lactam with a dis-similar R1 side chain. [\$\beta\$ -Lactam Allergy Guideline: Clinical Pathway](#)
 - Contact Antimicrobial Stewardship for GC instructions & order set (pager 55955)
 - Direct GC (without prior skin testing) has been shown to be safe in patients with a non-life threatening, low-risk history for an IgE-mediated reaction.
 - Tolerance verifies that a patient will not experience an immediate adverse reaction from the challenged agent with no increased risk for future reactions compared with the general population.
 - Allergy profiles should be updated to reflect tolerance to the challenged agent.

β -Lactam Allergy Guideline: Clinical Pathway



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