



EDUCATION: Penicillin Allergy

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

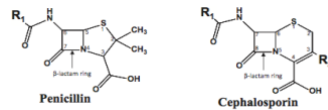
- Unconfirmed penicillin allergies and the use of alternative (second-line), broader-spectrum, antimicrobial agents such as [fluoroquinolones](#), clindamycin, vancomycin, and aztreonam have been associated with:
 - More treatment failure
 - Serious adverse effects
 - Higher incidences of *Clostridium 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}

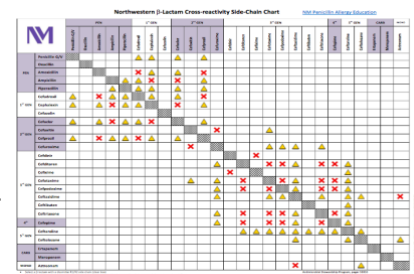
- Approximately 10-20% of hospitalized patients self-report a penicillin allergy with 15-24% requiring antimicrobial therapy.
- Under 10% of these individuals result in a positive skin test and over 90% have been shown to tolerate penicillins without an immediate IgE-mediated hypersensitivity reaction.
- 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 Recognition ^{9,17-20}

- 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.



β -Lactam Allergy Side Chain Chart



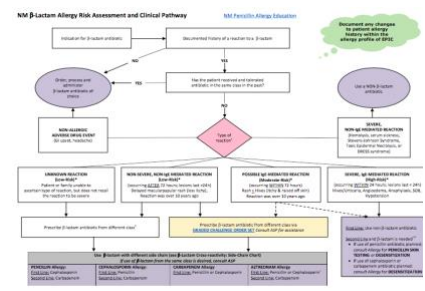
Allergy Assessment Methods and Northwestern β -Lactam Allergy Clinical Pathway

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 and usually not indicated for patients with 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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Created 1.2019

Updated 1.2019