

β-lactam Allergy

BOTTOM LINE:

- 10% of patients report a penicillin allergy but less than 1% are truly allergic.¹
- Patients with true penicillin allergy (other than severe non-IgE mediated reactions such as SJS) can be given cephalosporins after ensuring that the side chains of the penicillin and cephalosporin are not similar (cefazolin OK).

Background

β-lactams (penicillins, cephalosporins, carbapenems) are the most commonly prescribed antibiotics in both inpatient and outpatient settings and remain one of the safest antibiotic classes available.

Prevalence of IgE-mediated reaction:

- **0.01-0.05%** for penicillin^{4,10}
- **0.0001-0.1%** for cephalosporins^{5,6,10,11}

Penicillin allergy reports are often unfounded:

- Important to obtain detailed history as adverse events or intolerances should not be classified as an allergy

Patient harms associated with inaccurate allergy record

Unnecessary use of alternative antibiotics in a patient without true allergy is harmful as they:

- may be more broad-spectrum, more toxic, and less effective and more likely to lead to colonization or infection with multidrug-resistant organisms such as VRE and MRSA⁷
- could result in increased hospital length of stay, increased re-admission and *C. difficile* rates.^{7,8}

Assessment of β-lactam allergy - Document:

- Specific β-lactam received and route of administration
- Date of reaction(s) – 80% of penicillin allergic patients lose sensitivity to penicillin after 10 years
- Timing of reaction onset post β-lactam administration - IgE-mediated reactions usually occur immediately or within one hour
- Description of reaction (e.g. throat swelling, trouble breathing, drug fever, SJS, vs. GI upset, rash (distinguish from hives)) and management (e.g. need for hospitalization)
- Concurrent medications at the time of reaction
- Exposure to any β-lactams since reaction

Cross reactivity

Cross reactivity between penicillins & cephalosporins:

- ~ **1%** when penicillin allergy is reported²
 - 0.00002% anaphylaxis to cephalosporin¹³ (similar to background rates with no reported penicillin allergy)
- **2.55%** when penicillin allergy is confirmed²

Cross reactivity between penicillins and carbapenems:

- **4.3%** for any type of hypersensitivity reaction³
- **2.4%** for IgE-mediated reactions³

Among cephalosporins, and between cephalosporins and carbapenems, cross reactivity is very low, and similar to background allergy rates, based on experience (few studies).

Cross reactivity between β-lactams is related to the similarity in side-chain structures rather than the structure of their β-lactam core. See Table 1.

Management

1. Avoid unnecessary antimicrobial use, especially in the setting of viral infections.
2. Complete a thorough allergy assessment.
3. If patient has a true IgE reaction to a penicillin with 1 or more of respiratory difficulty, hypotension, or hives (Table 2):
 - avoid that penicillin and other penicillins.
 - avoid cephalosporins with similar side chains (Table 1).^{10,11}
 - before administering a β-lactam, counsel the patient on the risk versus benefit of the proposed β-lactam, including discussion of the risks of administration (which are much lower than usually assumed) and the benefits (e.g., use of first line antibiotic that is less likely to cause other adverse effects).
4. **Avoid all β-lactams in patients with a documented severe non-IgE-mediated reaction to penicillin:** interstitial nephritis, hepatitis, hemolytic anemia, serum sickness, severe cutaneous reactions [e.g. Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug rash with eosinophilia & systemic symptoms (DRESS)], including their use for graded challenge, desensitization, or skin testing.
5. Update the patient's allergy history in the medical record and with the patient after doing the allergy assessment, including documentation of what was successfully administered.

Table 1. Groups of β -lactams with similar side chains^{2,10}

Group 1	Group 2	Group 3
Penicillin	Amoxicillin	Cefotaxime
Cefoxitin	Ampicillin	Ceftriaxone
Group 4	Cefadroxil	Cefepime
Cefuroxime	Cephalexin	Group 5
Cefoxitin	Cefprozil	Aztreonam
		Ceftazidime

Each group in Table 1 consists of β -lactams with similar side chains. If the patient has had an allergic reaction to one β -lactam, avoid using other β -lactams in that group.
NB: Cefazolin does not have a similar side chain as any other β -lactam.

Table 2. Classification of β -lactam allergic reactions

Type of Reaction	Clinical Manifestations	Usual Onset
I. Immediate (IgE-mediated) Occurs upon repeat exposure Includes: ▪ Anaphylaxis ▪ Isolated urticaria or angioedema ▪ Allergic rhinitis	Anaphylaxis – hypotension with exposure, or two of : ▪ urticaria (hives) or angioedema/ laryngeal edema ▪ bronchospasm or respiratory compromise ▪ vomiting or cramping abdominal pain	Less than 1 hour (anaphylaxis) - up to 72 hours
II. Cytotoxic (IgG or IgM mediated)	Hemolytic anemia, agranulocytosis, leukopenia, thrombocytopenia	Greater than 72 hours
III. Immune Complex	Serum sickness, drug-induced fever, allergic vasculitis, interstitial nephritis	7-14 days
IV. T-cell mediated Delayed	Contact dermatitis, exfoliative dermatitis, maculopapular or morbilliform drug eruptions	Greater than 72 hours

See [Bugs & Drugs](#) for more information, including penicillin skin testing, graded challenge, and desensitization.

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