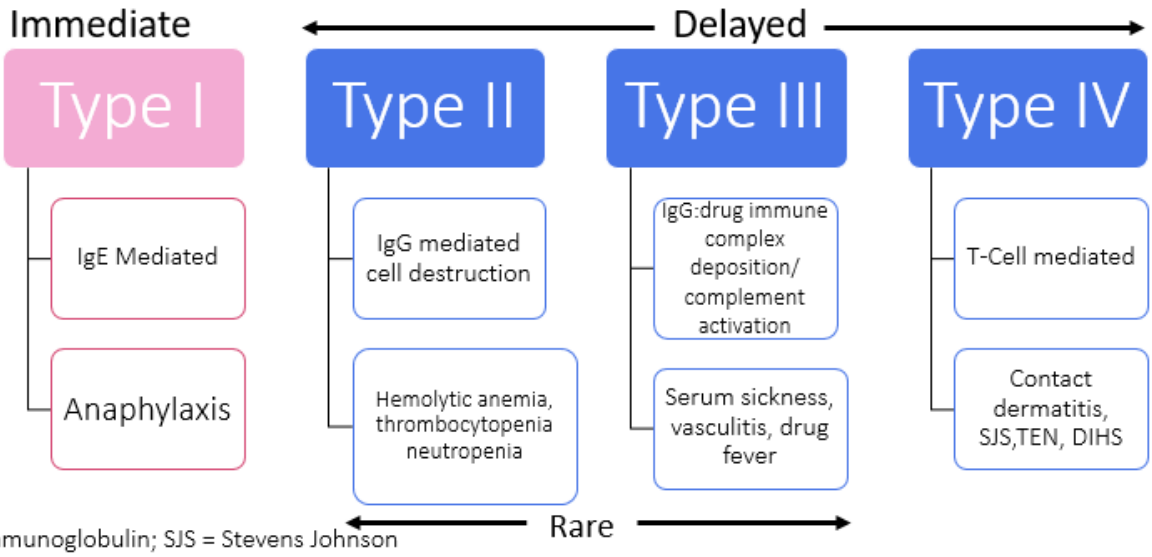
Beta-lactam Allergy Tip Sheet

Hypersensitivity Type, Mechanism, and Clinical Manifestations



Ig = immunoglobulin; SJS = Stevens Johnson Syndrome; TEN = Toxic Epidermal Necrolysis; DIHS = drug-induced hypersensitivity symptoms

Solensky, et al. Ann Allergy Asthma Immunol. 2010; 105:259-73.
Legendre, et al. Clin Infect Dis 2014;58(8):1140-8.

Beta-Lactam Cross Reactivity		PCNs					1st Gen CPNs			2nd Gen CPNs				3rd Gen CPNs					4th Gen CPN	Advanced CPNs			CARB		MONO
		Penicillin G/V	Oxacillin	Amoxicillin	Ampicillin	Piperacillin	Cefadroxil	Cephalexin	Cefazolin	Cefador	Cefoxitin	Cefprozil	Cefuroxime	Cefdinir	Cefotaxime	Cefpodoxime	Ceftazidime	Ceftriaxone	Cefepime	Ceftaroline	Ceftolazone	Cefiderocol	Ertapenem	Meropenem	Aztreonam
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	Ceftriaxone																								
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Advanced CPNs	Ceftaroline																								
	Ceftolazone																								
	Cefiderocol																								
CARB	Ertapenem																								
	Meropenem																								
MONO	Aztreonam																								

CAUTION	Cross reaction less likely, Similar R1 or R2 side chain
AVOID	Cross reaction likely, identical R1 or R2 side chain

PCNs = penicillins
CPNs = cephalosporins
CARB = carbapenems
MONO = monobactams

Penicillin allergy Facts

- Approximately 10% of all U.S. patients report having an allergic reaction to a penicillin class antibiotic in their past.
- However, many patients who report penicillin allergies do not have true IgE-mediated reactions. When evaluated, fewer than 1% of the population have IgE mediated hypersensitivities.
- Approximately 80% of patients with IgE-mediated penicillin allergy lose their sensitivity after 10 years.
- Broad-spectrum antibiotics are often used as an alternative to penicillins. The use of broad-spectrum antibiotics in patients labeled "penicillin-allergic" is associated with higher healthcare costs, increased risk for antibiotic resistance, and suboptimal antibiotic therapy.
- Correctly identifying those who are not truly penicillin-allergic can decrease unnecessary use of broad-spectrum antibiotics.

Reference: Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010;105(4):259-273.

Beta-lactam Allergy Documentation

- If a patient states they have a beta-lactam allergy, get a specific medication, reaction, and timing of reaction (immediate vs. delayed) DO NOT accept "penicillin" or "cephalosporin" as an allergy
- Update allergy label with specific medications, reactions, and tolerances (i.e. "tolerates ceftriaxone")

Beta-lactam Cross Reactivity

Cross-reactivity between penicillins and cephalosporins or carbapenems is not a class effect but an allergic reaction to antibiotics with similar side chains.

The table shows penicillins and cephalosporins with similar side chains. The exact risk of cross-reactivity between each pair is largely unknown and likely varies amongst pairs. Until more data is available avoiding beta-lactams with similar side chains is an appropriately cautious approach (e.g, for a patient with amoxicillin allergy, avoid cephalexin, but ok to use cefazolin).

Cross-reactivity with similar side chains: PCN-CEPH ≈ 20-40% and CEPH-CEPH ≈ 40%

Penicillins and Cephalosporins Clinical Studies

252 patients with immediate hypersensitive (IgE mediated) to a penicillin-based antibiotic underwent cephalosporin skin and ImmunoCAP testing. 99 (39%) also reacted to a cephalosporin. 95 (38%) reacted to cephalosporin with similar side to penicillin (cefaclor, cephalexin, cefadroxil, cefamandole). Only 4/252 (1.5%) patients reacted to cephalosporins that have dissimilar side chains to penicillin-based antibiotics (ceftriaxone, cefuroxime, cefotaxime).[1]

214 patients with history of delayed hypersensitivity (T-cell mediated) to penicillin underwent skin testing with six beta-lactams, three with similar side chains to penicillins, and three with dissimilar side chains. Cross-reactivity was found in 40 (19%) of patients; all reactions were from the three cephalosporins with side chains similar to penicillin derivatives. Cefaclor and cephalexin have similar side chains to ampicillin and resulted in positive skin tests in 39 and 31 patients respectively. Cefadroxil has a similar side chain to amoxicillin and resulted in positive skin tests in 17 patients.[2]

Note that a patient could have an allergic reaction to a dissimilar beta-lactam; however this likely represents a second allergic reaction, not cross-reactivity of the parent allergen.

Penicillins and Carbapenems Clinical Studies

Two well-done studies have evaluated the risk of cross-reactivity for penicillin allergic patients with a history of immediate reactions [3] and delayed reactions.[4] Over 400 patients were skin tested and received IV challenges against imipenem, meropenem, and ertapenem. No patients reacted to either the skin test or IV challenge. These data support the safe use of carbapenems in patients with a known penicillin allergy.

Medical Liability Concerns

- Fear of litigation has been identified as a potential reason clinicians avoid using β -lactams in a patient with a penicillin allergy.
- Since 1959, 27 medical malpractice or negligence cases have been published in which a patient with a penicillin allergy received a β -lactam and experienced an adverse reaction.
- Defendants (providers) were found liable in 3 of 7 cases in which a penicillin-based antibiotic was prescribed to a patient with a known penicillin allergy.
- Defendants were not found liable in any cases in which a cephalosporin or carbapenem was prescribed excluding 1 case in which physicians settled out of court.
- Judges have cited a lack of scientific evidence demonstrating cephalosporins or carbapenems are contraindicated for patients with a penicillin allergy.
- Legal Case Reference: Systematic review of professional liability when prescribing β-lactams for patients with a known penicillin allergy. *Ann Allergy Asthma Immunol. 2018;121(5):530-536.*

Selected References

1. Romano A, Valluzzi RL, Caruso C, Maggioletti M, Quaratino D, Gaeta F. Cross-Reactivity and Tolerability of Cephalosporins in Patients with IgE-Mediated Hypersensitivity to Penicillins. J Allergy Clin Immunol Pract **2018**; 6(5): 1662-72.
2. Romano A, Gaeta F, Valluzzi RL, Maggioletti M, Caruso C, Quaratino D. Cross-reactivity and tolerability of aztreonam and cephalosporins in subjects with a T cell-mediated hypersensitivity to penicillins. J Allergy Clin Immunol **2016**; 138(1): 179-86.
3. Gaeta F, Valluzzi RL, Alonzi C, Maggioletti M, Caruso C, Romano A. Tolerability of aztreonam and carbapenems in patients with IgE-mediated hypersensitivity to penicillins. J Allergy Clin Immunol **2015**; 135(4): 972-6.
4. Romano A, Gaeta F, Valluzzi RL, et al. Absence of cross-reactivity to carbapenems in patients with delayed hypersensitivity to penicillins. Allergy **2013**; 68(12): 1618-21.