

Allergic Cross-reactivity of Select Antimicrobials

Definition

Type I hypersensitivity reactions are IgE-mediated responses that manifest clinically as urticaria, angioedema, anaphylaxis, or anaphylactic shock and are potentially fatal. These are true hypersensitivity reactions caused by specific antibodies to drugs. Onset is usually within 30-60 minutes of drug administration.

Many antibiotics can cause a non-urticarial rash that is not IgE-mediated and this does not necessarily preclude subsequent exposures.

Assessment of Allergy

In order to adequately assess the patient, history must be obtained from the patient and/or family members regarding:

- The exact nature of the reaction (i.e. nausea, rash, shortness of breath, anaphylaxis etc)
- If these reactions are considered Type I hypersensitivity reactions
- Whether or not the patient has received similar agents in the past without reaction. Patient medication histories can be searched in the medication tab in EMR and filtered by medication name to see if similar agents have been administered.

Penicillin Cross-Reactivity

In cases of true penicillin allergy, the source of the reaction is thought to be due to formation of antibodies against metabolites of the penicillin molecule, specifically the R₁ side chains of the beta-lactam ring, and not the penicillin molecule or the presence of the beta-lactam ring. Similarity in side chains between different beta-lactam antibiotics may be the source of cross-reactivity between penicillins and 1st and 2nd generation cephalosporins. When no similarity in side chain exists, the potential for cross-reactivity is likely very low, such as between penicillins and 3rd and 4th generation cephalosporins.

In cases where the allergy to penicillin is not anaphylaxis, 3rd and 4th generation cephalosporins can be considered with close monitoring.

Additional Decision Support

Lexi-comp (online.lexi.com) has a drug allergy and idiosyncratic reactions database that is searchable by drug class. For example, for levofloxacin allergy search “fluoroquinolone allergy.” There is also a review of penicillin cross reactivity under “penicillin allergy.”

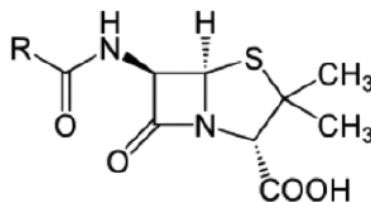


Figure: Penicillin Core Structure

Selected References:

1. Terico, A T, & Gallagher, J C. (2014). Beta-lactam hypersensitivity and cross-reactivity. *Journal of pharmacy practice*, 27(6), 530-44. PMID: 25124380
2. Romano, A, Gaeta, F, Valluzzi, R L, et al. (2010). IgE-mediated hypersensitivity to cephalosporins: cross-reactivity and tolerability of penicillins, monobactams, and carbapenems. *Journal of allergy and clinical immunology*, 126(5), 994-9. PMID: 20888035
3. Campagna, J D, Bond, M C, Schabelman, E, et al. (2012). The use of cephalosporins in penicillin-allergic patients: a literature review. *The Journal of emergency medicine*, 42(5), 612-20. PMID: 217

Potential for Cross-Reactivity

Offending Agent: ↓	Penicillins (ampicillin, amoxicillin, piperacillin)	1st Gen Cephalosporins (Cefazolin)	2nd Gen Cephalosporins (cefuroxime)	3rd and 4th Gen Cephalosporins (Ceftioxone, ceftazidime, cefepime)	Carbapenems (ertapenem, meropenem)	Aztreonam	Quinolones (ciprofloxacin, levofloxacin, moxifloxacin)	Tetracyclines (doxycycline, minocycline)	Vancomycin	Clindamycin	Aminoglycosides (gentamicin, tobramycin)
Penicillins (ampicillin, amoxicillin, piperacillin)		5-10%	< 5%	< 5%	< 5%						
1st Gen Cephalosporins (Cefazolin)	*		X	X	*						
2nd Gen Cephalosporins (cefuroxime)	*	X		X	*						
3rd and 4th Gen Cephalosporins (Ceftioxone, ceftazidime, cefepime)	*	X	X		*	< 1-3% if ceftazidime allergy					
Carbapenems (ertapenem, meropenem)	*	*	*	*							
Aztreonam	*	*	*	< 1-3% if ceftazidime allergy	*						
Quinolones (ciprofloxacin, levofloxacin, moxifloxacin)											
Tetracyclines (doxycycline, minocycline)											
Vancomycin											
Clindamycin											
Aminoglycosides (gentamicin, tobramycin)											

For choices of antibiotics in penicillin-allergic patients requiring surgical prophylaxis, see recommendations in the following UCDMC guidelines on the CRC website under the Drug Use Guidelines tab:**

[Cardiothoracic and Vascular](#)

[Gastrointestinal](#)

[Head and Neck](#)

[Neurosurgical](#)

[OB/GYN](#)

[Ortho](#)

[Urologic](#)

KEY:

X	Do not give, high potential for cross-reactivity
*	May consider using if NON-ANAPHYLACTIC reaction
	OK to give, low potential for cross-reactivity

For specific questions, please call the central pharmacy at 3-4084, option 2

**To get to the CRC, type "CRC" in the address bar of Internet Explorer, click "guest login" and then click on the Drug Use Guidelines tab. The above guidelines are below the Infectious Disease heading labeled surgical prophylaxis