

## β – LACTAM ALLERGY

### IMPORTANT INFORMATION TO COLLECT FOR ALLERGY ASSESSMENT<sup>1</sup>:

- Source of reported allergy history (patient, family member, healthcare provider)
- Indication of inciting drug
- Dose/route of medication
- Signs/symptoms experienced
- Timing of onset of reaction in relation to initiation of medication
- Any concurrent medications (prescription or non-prescription), change in detergent used or changes in diet?
- Reaction required hospitalization?
- Treatment given for the reaction and response
- Did the patient take the medication again since prior reaction
- If yes, did any recurrent signs or symptoms occur with subsequent exposure?

### IDIOPATHIC REACTIONS<sup>2</sup>

- Not clearly immune mediated
- Maculopapular rash → if occurs, not a contraindication to taking the antibiotic again

### CROSS-REACTIVITY<sup>2</sup>

- If anaphylaxis to one beta lactam, avoid antibiotic class if clinically possible and contact Infectious Disease Service for alternate therapeutic options
  - Between Penicillins and Cephalosporins: estimated cross-reactivity ~5%
  - Between Penicillins and Carbapenems: estimated cross-reactivity is ~ 1%
  - Between Cephalosporins: cross-reactivity low due to the significant heterogeneity of side chains (C-3 and C-7)
  - Mechanism for cross-reactivity: occurs between various penicillins and cephalosporins as a result of similar side chains at C-3 or C-7 (see Table 1). For example, cefazolin has a unique side chain and therefore would not cross react with cephalixin

Table 1. Groups of cephalosporins and beta-lactams with similar C3 and C7 side chains<sup>2</sup>

C-7 SIDE CHAIN			
Similar side chain cross-reactivity possible WITHIN these 3 groups*			Completely dissimilar side chains make cross-reactivity unlikely**
Cefoxitin Cephalothin Penicillin	Amoxicillin Ampicillin Cefaclor Cephalexin	Cefepime Cefotaxime Ceftriaxone	Cefotetan Cefazolin Cefuroxime Cefixime Cefprozil Ceftazidime

**How to use this table:** check the antibiotic your patient is allergic to for possible cross-reactivity with other antibiotics based on both the 7-position (C-7) and 3-position (C-3) side chains. Avoid drugs that share structural similarity of either side chain position. Antibiotics that do not share similarity of either side chain are unlikely to exhibit cross-reactivity and can be recommended.

\*For example, based on the 7-position side chain structure similarity, allergy cross-reactivity might occur among cefoxitin, cephalothin and penicillin.

\*\* Based on the 7-position side chain structure uniqueness, allergic cross-reactivity would be highly unlikely for all of these cephalosporins with each other and with other cephalosporins and/or penicillins

**C-3 side chain:**

Similar side chain cross-reactivity possible between cefuroxime and cefoxitin

**Testing for Penicillin/Beta-Lactam Allergy:**

Skin testing is available at HHS and SJH through Immunology department. It is primarily used for determination of IgE-mediated reactions.

Penicillin is the only drug class with a valid skin test. Penicillin skin testing has a high negative predictive value since 97-99% of patients with a negative skin test to both the major and minor determinants will not have an immediate type 1 reaction (e.g. anaphylaxis).

For patients who are deemed to be skin-test positive, all penicillin compounds should be avoided. For those individuals for whom an alternative class of antibiotics cannot be substituted, desensitization may be required.

Type of Reaction	Coombs and Gell Classification	Onset	Mediator
Idiopathic reactions including maculopapular rash	n/a	Delayed usually 7 days	unclear
Anaphylaxis, urticarial (hives), angioedema, hypotension, bronchospasm, laryngeal edema, pruritus	Type I Immediate and accelerated hypersensitivity	< 1 hour (rarely 1-72 hours)	IgE antibodies
Hemolytic anemia, thrombocytopenia, neutropenia	Type II Delayed cytotoxic antibody-mediated hypersensitivity	> 72 hours	IgG and IgM antibodies
Serum sickness (fever, cutaneous eruptions, lymphadenopathy, arthralgias, myalgias), glomerulonephritis, small vessel vasculitis, drug fever	Type III Antibody complex-mediated hypersensitivity	> 72 hours (7-14 days)	IgG and/or IgM complexes
Contact dermatitis, exfoliative dermatitis, maculopapular or morbilliform drug eruptions, pustulosis	Type IV Delayed type hypersensitivity	> 72 hours	T-cells
Stevens-Johnson Syndrome, toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and erythema multiforme are rare with beta-lactams but because of the severity, antibiotic should be avoided	n/a	>72hours	unclear

**REFERENCE**

1. Pichichero ME. J Family Practice; 2006;55:106-112.
2. Lagace-Wiens P, Rubinstein E. *Expert Opin Drug Saf* 2012;11:381-399.
3. Li, James T., M.D., PH.D., Mayo Clinic and Foundation, Rochester, Minnesota *Am Fam Physician*. 2002 Aug 15;66(4):621-625.
4. Lasley MV, Shapiro GG. *Pediatr Rev*. 2000;21:39-43.