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 1<sup>st</sup> and 2<sup>nd</sup> generation cephalosporins. When no similarity in side chain exists, the potential for cross-reactivity is likely very low, such as between pencillins and 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins.

In cases where the allergy to penicillin is not anaphylaxis, 3<sup>rd</sup> and 4<sup>th</sup> 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.”

![Penicillin Core Structure](image)

**Figure: Penicillin Core Structure**

**Selected References:**
## Potential for Cross-Reactivity

### Offending Agent:

<table>
<thead>
<tr>
<th>Penicillins (ampicillin, amoxicillin, piperacillin)</th>
<th>1st Gen Cephalosporins (Cefazolin)</th>
<th>2nd Gen Cephalosporins (Cefuroxime)</th>
<th>3rd and 4th Gen Cephalosporins (Ceftazidime, Cefepime)</th>
<th>Azytreonam</th>
<th>Quinolones (ciprofloxacin, levofloxacin, moxifloxacin)</th>
<th>Vancomycin</th>
<th>Clindamycin</th>
<th>Aminoglycosides (gentamicin, tobramycin)</th>
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<tbody>
<tr>
<td>5-10%</td>
<td>&lt; 5%</td>
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<td>&lt; 1-3% if ceftazidime allergy</td>
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<td>1st Gen Cephalosporins (Cefazolin)</td>
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<td>2nd Gen Cephalosporins (Cefuroxime)</td>
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<td>3rd and 4th Gen Cephalosporins (Ceftaxone, ceftazidime, ceftepime)</td>
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<td>&lt; 1-3% if ceftazidime allergy</td>
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<td>Carbapenems (ertapenem, meropenem)</td>
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<td>Quinolones (ciprofloxacin, levofloxacine, moxifloxacin)</td>
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**KEY:**

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

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Approved by UCDH Pharmacy Therapeutics Committee 6/2017.