β-Lactam Allergy

COOMBS AND GELL CLASSIFICATION OF HYPERSENSITIVITY REACTIONS[1]

Type	Mediator	Onset	Clinical Reaction	Comments
I Immediate and accelerated hypersensitivity	IgE antibodies	< 1 hour (rarely 1-72 hours)	Anaphylaxis, urticaria, angioedema, hypotension, bronchospasm, laryngeal edema, pruritus	Anaphylaxis with penicillins: ~ 0.01-0.05% Anaphylaxis with cephalosporins: ~0.0001-0.1% Patients with anaphylaxis should not be given the offending drug again.
II Delayed cytotoxic antibody-mediated hypersensitivity	IgG and IgM antibodies	> 72 hours	Hemolytic anemia, thrombocytopenia, neutropenia	These reactions are drug-specific, so the offending drug should be avoided in the future.
III Antibody complex-mediated hypersensitivity	IgG and/or IgM complexes	> 72 hours	Serum sickness (fever, cutaneous eruptions, lymphadenopathy, arthralgias, myalgias), Glomerulonephritis Small vessel vasculitis Drug Fever	The antibody-antigen complexes can precipitate in tissues and potentially affect any end organ.
IV Delayed type hypersensitivity	T-cells	> 72 hours	Contact dermatitis Pustulosis	Incidence is low Eosinophilia, bullous exanthems and immune hepatitis may be due to T-cell activation as well

IDIOPATHIC REACTIONS[1]

- Not clearly immune mediated
- Non-pruritic morbilliform and maculopapular rash (which occur in 3-7% of children that take amoxicillin) → if occurs, not a contraindication to taking the antibiotic again
- 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, the culprit antibiotic should be avoided.

CROSS-REACTIVITY[1]

- Between Penicillins and Cephalosporins
  - The widely cited risk of cross-reactivity between penicillins and cephalosporins of 8-10% is based on studies from the 1970s and is now known to be flawed.
  - Cross-reactivity between penicillin or amoxicillin and cephalosporins is due to similarities in side chains so there will only be significant risk of cross-reactivity between those with a similar side chain at C-3 or C-7 (see Table below). For example, cefazolin is not expected to cross-react with any penicillin or cephalosporin as it does not have a similar side chain to any other beta-lactam, hence its absence from the table.
- Between Cephalosporins
  - Cross-reactivity amongst cephalosporins is low due to the significant heterogeneity of side chains (C-3 and C-7).
  - Therefore, if your patient has a cephalosporin allergy, you can safely prescribe another cephalosporin that has dissimilar side chains (both C-7 and C-3 side chains must be different).
- Between Penicillins and Carbapenems
  - Cross-reactivity is ~ 1%

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Table 1. Groups of cephalosporins and beta-lactams with similar C3 and C7 side chains[1]

Similar C-7 side chain. Cross reactions between agents within one group are possible.			**Similar C-3 side chain. Cross reactions between agents within one group are possible.**						
Group 1	**Group 2**	**Group 3**	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**	**Group 7**
Penicillin Cephalothin Cefoxitin	Amoxicillin Ampicillin Cefaclor Cephalexin Cefadroxil	Cefepime Cefotaxime Ceftriaxone	Cefadroxil Cephalexin	Cefotetan	Cefotaxime Cephalothin		Cefuroxime Cefoxitin	Cefixime	Ceftazidime

Reference:

Lagace-Wiens P, Rubinstein E. Adverse reactions to beta-lactam antimicrobials. Expert Opin Drug Saf 2012;11:381-399.