

COOMBS AND GELL CLASSIFICATION OF HYPERSENSITIVITY REACTIONS¹

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 REACTIONS¹

- ✦ 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-REACTIVITY¹

- ✦ 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%

Disclaimer: This document is intended for internal use at Sinai Health System and University Health Network. Recommendations herein are based on existing literature and clinical practice and are subject to change at any time. Please refer to the [Terms and Conditions](#) for more details.

Table 1. Groups of cephalosporins and beta-lactams with similar C3 and C7 side chains¹

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	Amoxicillin	Cefepime	Cefadroxil	Cefotetan	Cefotaxime		Cefuroxime	Cefixime	Ceftazidime
Cephalothin	Ampicillin	Cefotaxime	Cephalexin		Cephalothin		Cefoxitin		
Cefoxitin	Cefaclor	Ceftriaxone							
	Cephalexin								
	Cefadroxil								

Reference:

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

Disclaimer: This document is intended for internal use at Sinai Health System and University Health Network. Recommendations herein are based on existing literature and clinical practice and are subject to change at any time. Please refer to the [Terms and Conditions](#) for more details.