

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 exanths 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%

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 is possible | | | Similar C-3 side chain. Cross reactions between agents within one group is 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

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