β-LACTAM ALLERGY

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Penicillin Allergy

Incidence:
- 1-10% of patients treated with penicillin will have an adverse reaction, including allergy.
- 0.01% of patients experience life-threatening anaphylactic reactions to penicillin, of which 10% are fatal.

History of Penicillin Allergy:
- It is very important to determine the nature of the patient's reaction, in order to differentiate between allergic and other adverse reactions, and the onset of the allergic reaction, which will help to classify the reaction (see below).
- Only about 10% of patients with a history of penicillin allergy actually have an IgE mediated allergy (skin test positive).

Classification of Penicillin Allergic Reactions:

Type of Reaction	Clinical Manifestations	Usual Onset
I **Immediate**	Anaphylaxis, bronchial asthma, allergic rhinitis, early onset urticaria, angioedema	within 1 hour (anaphylaxis) < 24 hours
II **Cytotoxic**	Hemolytic anemia, agranulocytosis, leukopenia, thrombocytopenia	5-12 hours
III **Immune Complex**	Serum sickness, drug-induced fever, allergic vasculitis, interstitial nephritis	7-14 days
IV **T-cell mediated**	Contact dermatitis	24-48 hours
Idiopathic	Exfoliative dermatitis, maculopapular drug eruptions, fever, late onset urticaria	> 72 hours

Risk Factors for Penicillin Allergy:
- <u>History of previous reaction to penicillin</u> - Six times more likely to react on subsequent exposure than patients with a negative history.
- <u>Route of administration</u> - More likely with the parenteral route than with the oral route.
- <u>Age</u> - Most common in patients between 20 and 49 years. True penicillin allergy is uncommon in the pediatric population.

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Cross Reactivity:

- Cephalosporins - The incidence of cross reactivity **is less than 2%.**
- Third-generation cephalosporins - Less cross reactivity with penicillin than first and second generation cephalosporins because of their structural differences.
- Imipenem - **Extensive cross reactivity** with penicillins. Use same degree of caution as if penicillin was to be given.

Management of β-Lactam Allergy:

- Avoid all β-lactams (penicillins, cephalosporins, carbapenems) in patients with a documented history of severe allergic reactions to penicillin, such as:
  - urticaria/angioedema
  - serum sickness
  - hemolytic anemia
  - exfoliative dermatitis
  - organ dysfunction.

Alternative antibiotics should be chosen.

- ***Penicillin Skin Testing:***
  - The clinical role of skin testing for penicillin allergy is unclear. While it is 99% effective in predicting penicillin allergic reactions if both the major and minor determinants are used, skin testing has several limitations to its use:
    - Only predictive of IgE-mediated allergic reactions to penicillin.
    - The minor determinant mixture needed for the test is not commercially available.
    - Although usually safe, fatalities have occured when done improperly. Therefore, penicillin skin testing should only be performed and interpreted by a qualified allergist.

- ***Desensitization:***
  - Indicated when the patient has a history of IgE mediated penicillin allergy and/or is skin test positive, and has a serious infection where alternatives to penicillin are not suitable, e.g. syphilis in pregnancy.
  - Will **not** prevent non-IgE mediated reactions.
  - Once complete, treatment with penicillin must be started immediately.
  - Usually lost within two days after cessation of penicillin therapy.
  - An oral method of penicillin desensitization has been approved by the Regional Antimicrobial Advisory Subcommittee and P&T. For the complete guidelines, contact pharmacy.