Approach to the Patient with Penicillin Allergy

Penicillin reactions – Incidence

- 80-90% of patients who report they are “allergic” to penicillin (PCN) actually have negative skin tests and are not at increased risk of an IgE-mediated allergic reaction.
- Penicillin reactions of some type occur in 0.7 to 10% of all patients who get the drug.
    - BUT: The incidence of anaphylactic reactions is 0.004% to 0.015%.
- Rates of cross-reactive IgE-mediated allergic reactions to cephalosporins in PCN-allergic patients appear to be uncommon (<5%), but do occur.
- Rates of PCN and carbapenem skin test cross reactivity are 47%, although clinical rates of hypersensitivity reactions in patients with reported PCN allergy who receive carbapenems are 9–11%.
- Cross reactions to monobactams (Aztreonam) do NOT appear to occur.

Penicillin skin testing

- When done correctly, PCN skin testing is highly predictive of serious, anaphylactic reactions.
- Patients with a negative skin test are NOT at risk for anaphylactic reactions.
- Rarely (1-3%), skin test negative patients may get mild hives and itching following penicillin administration but these RESOLVE with continued treatment.
- Skin test positive patients are at high-risk (50-75%) for serious IgE-mediated reactions with PCN exposure, and should avoid PCN agents or undergo a PCN desensitization procedure if no alternative agent exists.
- Skin tests cannot predict non-IgE mediated dermatologic reactions (delayed morbilliform rash or SJS/TEN), GI disturbances, or drug fevers.

Penicillin reactions—Types

- **Immediate** (Type 1/IgE-mediated) – Urticaria, angioedema, pruritus, flushing, anaphylaxis, hypotension, laryngeal edema, wheezing.
    - Typically occurs within minutes and nearly always within 4 within 1 hours of administration.
    - Potentially fatal if anaphylaxis, hypotension, respiratory distress occurs
    - Hypotension always occurs soon after administration
    - Can be predicted by skin tests
- **Accelerated** – Laryngeal edema, wheezing, angioedema, urticaria (NOT hypotension)
    - Occur within 1-72 hours of administration
    - Can be predicted by skin tests
- **Late** – Rash (maculopapular or morbilliform or contact dermatitis), destruction of RBC, WBC, platelets, serum sickness

    - Generally develops days to weeks into drug
    - Almost always occurs after 72 hours of administration
    - Morbilliform rashes sometimes resolve despite continued treatment
    - Maculopapular and morbilliform rashes generally DO NOT progress to Stevens-Johnson syndrome
    - Late reactions are NOT predicted by skin tests
- **Stevens-Johnson Syndrome** – exfoliative dermatitis with mucous membrane involvement
    - Generally occurs 1-3 weeks after drug administration.
    - May evolve from initial erythroderma, purpuric target lesions, or blisters
    - Almost always occur after 72 hours of administration
    - NOT predicted by a history of morbilliform rash OR by skin tests

Approach to the patient with reported penicillin allergy

- Brief, focused history can be VERY helpful.
- Questions to ask:
    1. How long after beginning penicillin did the reaction occur?
    2. Was there any wheezing, throat or mouth swelling, urticaria, or angioedema?
    3. If a rash occurred, what was the nature of the rash? Where was it and what did it look like? Did the rash include any blistering or exfoliative features?
    4. Was the patient on other medications at the time of the reaction?
    5. Since then, has the patient ever received another penicillin or cephalosporin (ask about trade names like: Augmentin, Keflex, Ceftin, Vantin)?
    6. If the patient received a beta-lactam subsequent to the initial reaction, what happened?
- The skin test nurse can be contacted (x5-4369) to perform PCN skin testing.

Interpreting the history of the patient reporting penicillin allergy

- **ANY patient who has a history consistent with an immediate reaction (any symptoms of urticaria, angioedema, laryngeal edema, wheezing, hypotension) SHOULD NOT receive beta-lactams without undergoing skin testing first EVEN IF they have received beta-lactams with no problems after the serious reaction.**
    - Patients who report non-immediate (non-IgE) reactions and have received other penicillins without problems DO NOT have penicillin allergy and are not at increased risk for an allergic reaction compared to the general population.
    - Patients who report non-immediate reactions and have received cephalosporins can get cephalosporins but not necessarily PCNs.
    - Patients who report a history of a non-urticarial rash that is NOT consistent with Stevens-Johnson syndrome (target lesions with mucous membrane inflammation) after more then 72 hours of getting penicillin are not at increased risk for a serious hypersensitivity adverse reaction. They should, however, be watched closely for development of rashes.
    - Patients who report reactions consistent with serum sickness (rare) can receive either penicillins or cephalosporins with careful monitoring for recurrence.
    - Patients who report PCN-related GI symptoms (diarrhea, nausea) in the absence of other allergy symptoms are unlikely to have penicillin allergy and do not appear to be at increased risk for hypersensitivity adverse reactions. They should

be closely observed for recurrent symptoms and be given supportive therapy if they occur.

References:

JAMA 2001;285:2498.
Use of carbapenems in patients with PCN allergy: J Antimicrob. Chemother 2004;54: 1155–7.
Ann Intern Med 2007;146:266–9.