54 - Penicillin Allergies

Speaker: Sandra Nelson, MD

INFECTIOUS DISEASE BOARD REVIEW — IDBR — AUGUST 20-24 2022

Penicillin Allergies

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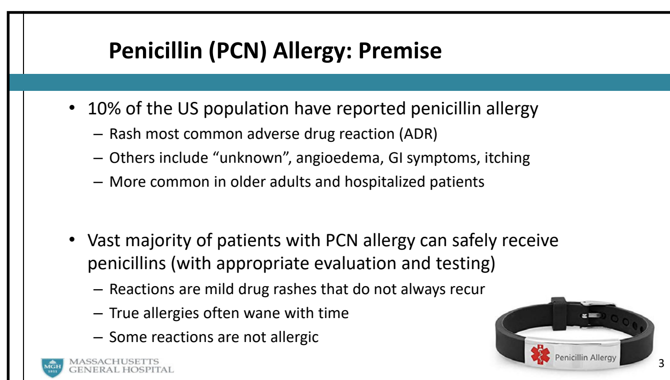
Disclosures of Financial Relationships with Relevant Commercial Interests

- None



PCN Allergy: Consequences

- Alternative antimicrobial use
  - Less effective, more toxic, higher cost, broader spectrum
- Associated with:
  - increased risk of MRSA infection and VRE colonization
  - increased risk of *C. difficile* colitis
  - increased risk of surgical site infection
  - increased mortality
- An important target of stewardship efforts

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Case #1

A 73-year-old woman undergoing chemotherapy for cholangiocarcinoma is hospitalized with bacteremia and sepsis due to ampicillin-susceptible *Enterococcus faecalis*. She has a history of allergy to penicillin that is listed in the records as rash; the family recalls that she went to the ED when the rash occurred several years earlier. She is delirious and not able to corroborate the history; no additional documentation of the reaction is available. Two of her daughters have allergies to penicillin.

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Case #1: Vote

You are asked about optimal antibiotic treatment. What do you advise?

A. Administer IV ampicillin without prior testing
B. Skin test for penicillin reaction; if negative then administer full dose ampicillin
C. Skin test for penicillin reaction; if negative then administer test dose ampicillin followed by full dose ampicillin
D. Desensitize to ampicillin
E. Administer vancomycin

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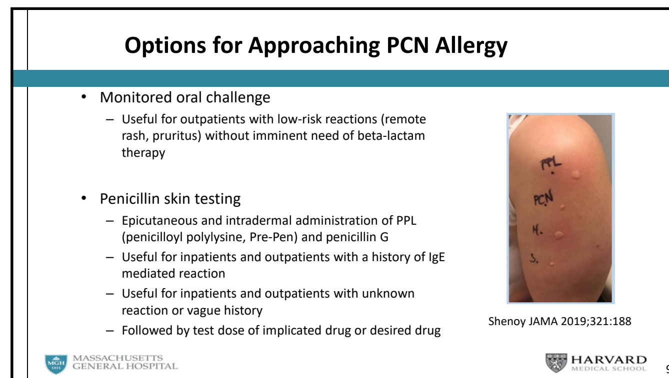
Classification of Drug Allergy (Gell and Coombs)

Type	Immune mechanism	Clinical example
I: Immediate (usually within one hour)	IgE-mediated Mast cell degranulation	Anaphylaxis, Urticaria, Angioedema, Bronchospasm
II: Often <72 hours, but up to 2 weeks	Antibody-dependent (IgG) Cytotoxicity	Hemolytic Anemia Thrombocytopenia Neutropenia
III: Days to weeks	Immune Complex (IgM/IgG) Complement activation	Serum Sickness Vasculitis
IV: Days to weeks	Cell mediated (T-cell activation)	Cutaneous drug reactions - Mild maculopapular - Severe (DRESS, SJS, TEN) Interstitial nephritis Hepatitis

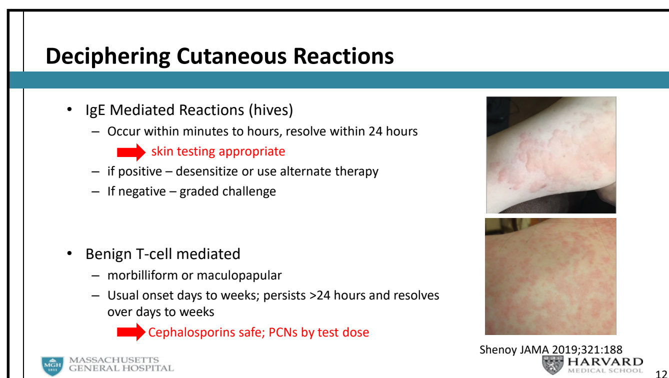


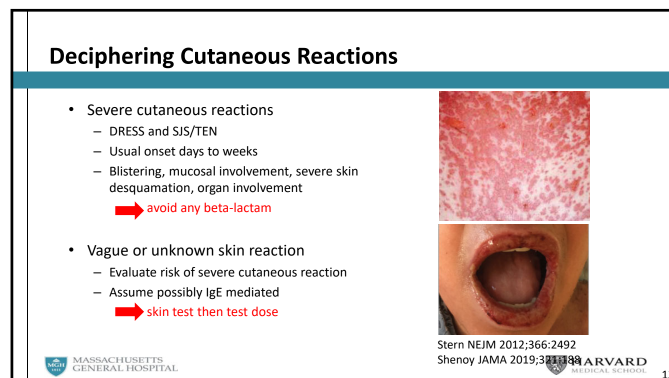
Options for Approaching PCN Allergy

- Graded Challenge (oral of IV drugs)
  - 1/4th to 1/10th dose, followed by full dose 30-60 minutes later
  - As a first step if suspicion for immediate reaction is low
  - After negative PCN skin testing
- Desensitization
  - Sequential administration of increasing dilutions of PCN every 15-30 minutes until therapeutic dose is reached
  - Positive skin test and/or confirmed immediate reaction, when a penicillin is the best therapy for an important infection
  - Desensitization wanes with missed doses (3 half-lives)
- Use of alternate therapy

Classification of Drug Allergy, revisited (Gell and Coombs)

Type	Immune mechanism	Clinical example	Management
I: Immediate (usually within one hour)	IgE-mediated	Anaphylaxis, Urticaria, Angioedema, Bronchospasm	Penicillin skin testing followed by graded challenge
II: Often <72 hours, but up to 2 weeks	Antibody-dependent (IgG)	Hemolytic Anemia Thrombocytopenia Neutropenia	No testing; if severe avoid re-use
III: Days to weeks	Immune Complex	Serum Sickness Vasculitis	No testing; generally avoid re-use
IV: Days to weeks	Cell mediated	Cutaneous drug reactions Interstitial nephritis Hepatitis	Varies; for severe reactions and organ involvement avoid re-use





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Case #2

A 43-year-old man with diabetes is hospitalized with a closed tibial fracture. Three years ago when he was being treated for a foot infection with piperacillin-tazobactam he developed a very itchy rash after several weeks of treatment. The anesthesiologist calls to ask advice about surgical antibiotic prophylaxis prior to operative fixation.

Case #2: Vote

What do you do counsel?

A. Administer clindamycin
B. Administer cefazolin
C. Administer cefazolin after intraoperative test dose
D. Administer ceftriaxone
E. Administer vancomycin

PCN Allergy and other beta-lactams

- Cephalosporins:
  - Significant cross reactivity 2%
  - Higher risk with earlier generation cephalosporins
  - If suggestive type I PCN allergy:
    - use 3rd/4th gen (graded challenge preferred)
    - use 1st/2nd after PCN skin testing
  - If mild type IV reaction:
    - any cephalosporin OK
  - Avoid if severe reaction to PCN
- Carbapenems <1%
- Aztreonam: no cross reactivity in PCN-allergic

Penicillin

Cephalosporin

Cephalosporin Allergy

- Allergy often arises from side chains
  - More common than beta-lactam ring
- Probability of reaction higher when cephalosporins with similar side chains used (R1 > R2)
- Side chain tables are available to guide cross-reactivity

Similar Side Chain Groups (R1)
Amoxicillin, Cefadroxil, Cefprozil
Ampicillin, Cefaclor, Cephalexin
Cefepime, Ceftriaxone, Cefotaxime, Cefpodoxime
Ceftazidime and Aztreonam

A few more testable points

- A patient that tolerates penicillins may still be allergic to aminopenicillins, while a patient that tolerates aminopenicillins is not allergic to PCN.
- Cefazolin has different side chains from all other cephalosporins
- Ceftazidime does not share side chains with ceftriaxone or cefepime
- Aztreonam can be safely used in individuals with beta-lactam allergy save ceftazidime

Thank you and good luck!

"The penicillin looks good."

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