Penicillin Skin Testing

Penicillin Timeline
- Penicillin discovered, Fleming 1928
- Penicillin put into widespread use, Florey and Chain 1943
- Pre-Pen® original FDA approval, 1974
- Pre-Pen® goes off the market, 2001
- Pre-Pen® back on, 2002
- Pre-Pen® off again, 2004

IgE Mediated Drug Allergy
- Antigen specific IgE mediated with mast cell degranulation
- Predicted by skin testing
- Predicted by direct measurement of antigen specific IgE
- Requires intact protein antigens (MW>5000), materials that will haptenate proteins, or bifunctional small molecules that can cross link IgE
- Requires sensitization
### Penicillin Skin Testing

- Penicillin skin testing is very useful
  - In advance of need
  - Hospitalized patients
  - Pregnant patients with group B strep
- Penicillin skin testing does not re-sensitize
- Patients with a history of penicillin allergy who are skin test negative will have a mild adverse reaction about 4% of the time to any antibiotic
- Penicillin allergy is becoming less of a problem, less than 5% of history positive are skin test positive

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### Penicillin Skin Testing

- You can not predict penicillin skin test status based on history
- Anaphylaxis to oral penicillins is extremely rare
- Cephalosporins can be safely used in patients with positive penicillin skin tests
- PPL can be used down to 4.29 X 10^{-5}M
- Oral penicillins cause less reactions than parenteral penicillins

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### Penicillin Skin Testing

- Tryptase measurements are not useful in determining the cause of mild reactions seen in most oral drug challenges
- Mild allergic reaction to a dose + miss several doses + take another dose = potential bad reaction
- Penicillin skin testing may be too sensitive. Individuals with positive penicillin skin tests often tolerate oral penicillins
Penicillin Skin Testing

- Reactions to oral penicillins in skin test positive individuals can start up to 24 hours after ingestion.

Penicillin Skin Testing

- Take a relevant history prior to penicillin skin testing.
- Document the absence of dermographism.

Who can you test?
- Patients who have a history of anaphylaxis, respiratory problems, hives, local swelling at the site of injection, other rashes, gastrointestinal symptoms, unknown index symptoms, and other mild symptoms not specifically excluded on the next slide.
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Who should not be tested?
- Anyone with a history compatible with Stevens-Johnson Syndrome, toxic epidermal necrolysis, hemolytic anemia, nephritis, hepatitis, or oral and/or skin blisters associated with or attributed to previous penicillin class antibiotic use.

Penicillin Skin Testing

- A Complete Panel of Reagents
  - Penicilloyloxylpolylysine – 6 x 10⁻⁵ molar
  - Native Penicillin – 0.01 molar
  - Native Amoxicillin – 0.01 molar
  - Penilloate – 0.01 molar
  - Penicilloate – 0.01 molar

Penicillin Skin Testing

- Storage Requirements
  - Penicilloyloxylpolylysine – 4°C
  - Native Penicillin – -70°C
  - Native Amoxicillin – -70°C
  - Penilloate – -70°C
  - Penicilloate – -70°C

Thaw frozen material once and use within 2 hours.
Penicillin Skin Testing

- A buffered saline negative control and a histamine (1 mg/ml for prick tests and 0.1 mg/ml for intradermal tests) positive control are placed at the start of each round of tests.
- Drops of each reagent are placed on the outer surface of the upper arm and pricked using a different DUOTIP-TEST® device for each drop.
- Following a 15 minute waiting period, skin prick reactions are read and recorded.
- The mean diameter of the wheal over the mean diameter of the flare or surrounding erythema is measured in millimeters.

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- Positive responses consist of a wheal of 5 mm or more in diameter with surrounding erythema greater than the wheal, a negative response to the control solution, and a positive response to histamine.
- If all tests are negative by skin prick then intradermal (ID) testing is performed using the outer surface of the other upper arm.
- Using the same reagents, 0.02 mls of each reagent is administered ID through individual 27 gauge tuberculin syringes.
- ID tests are also read and recorded after 15 minutes.

Penicillin Skin Testing

- Positive responses consist of a wheal of 5 mm or more in diameter with surrounding erythema greater than the wheal, a negative response to the control solution, and a positive response to histamine.
- If any puncture test was positive, no ID tests are done with any of the remaining negative reagents.
Penicillin Skin Testing

- Antigen specific ELISAs (Pharmacia)
  - Penicillin V
  - Penicillin G
  - Amoxicillin

Penicillin Skin Testing

- Antigen specific ELISAs (Pharmacia)
  - Patients with high IgE levels (573 kU L⁻¹) can have false positives
  - ELISAs can be positive in individuals who died of anaphylaxis
  - No studies on ELISA results in puncture positive individuals

Penicillin Skin Testing

- Antigen specific ELISAs (Pharmacia)
  - Very little recent literature on this topic if you exclude papers by Blanca.
  - We have had no positive ELISAs in a limited number of penicillin skin test positive individuals (n < 10).
Penicillin Skin Testing

- **Penicillin oral challenges**
  - 250 mg amoxicillin after negative penicillin skin testing, watch for 1 hour.
  - 10 to 25 mg for an adult followed by 250 mg ½ hour later, watch for ½ hour.

Antibiotic Skin Testing

- **Selected References**
Antibiotic Skin Testing

Selected References