Antibiotic Allergy

-A practical approach to an important but frustrating problem

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Background/Disclaimer

I’m a virologist, not an allergist! (Last BIDN Grand Rounds on Pandemic Flu.)

I was the last of the Glover ER moonlighters

I am a loyal Needhamite, coming up on 20 yr

I have no conflicts to disclose.
The Problem

Most Patients report some “allergy” history.

Most of these are not true.

Most of the alternative abx are worse.

Predicting true reactions remains mysterious.
Definitions

- **Type I**: Immediate, IgE, Mast Cells/Basophils
- **Type II**: Delayed, Antibody Directed Cell Killing
- **Type III**: Delayed, Antibody/Antigen deposition
- **Type IV**: Delayed, T-cell mediated
- **Pseudoallergy**
- **Non-allergic adverse reactions**
Pseudo-allergy

- Direct, non-IgE activation of Mast Cells (Vanco, Cipro, Contrast)
- Prostaglandin mediated (ASA, NSAIDs)
Non-allergy

Pt’s can be invested in their allergy hx.

Almost never useful to struggle over this

Seek alternative meds, objective findings

Document specific complaints and avoid putting “allergy” in medical record.
Allergy Risks

- Most important risk for allergy is allergy
- Multiple allergy syndrome: narrow definition
- Increased exposure
- Female sex - menopause
- Atopy
- AIDS
- Atyps
- Genetics
Genetics

- Clear familial associations
- Special cases: HLA-B*5701 - Abacavir
- Likely many more
- Rapidly approaching time of whole genome sequencing
Penicillin Allergy

- Most common of “reported” allergies: 5-10%
- 80-90% have negative skin tests
- For Staph and Strep Infections, alternatives have higher failure rates
- Anaphylaxis ~1-4:10,000 doses
- Skin test reagents now available
PCN Allergy

- Large majority to penicilloyl (major determinant) -> Class-wide allergy
- Minority to intact beta-lactam or other breakdown products (minor determinants, not necessarily minor reactions)
- Less than 10% to side chains -> drug-specific allergy
Risk Factors

- Repeated use
- Parenteral/IM route
- Multiple drug allergy syndrome
- Genetics - 10x higher if 1st degree relative allergic
- Other Allergic conditions - PCN allergy not more common, but once sensitized, higher risk of severe reaction.
Why it Matters

- Non-lactam antibiotics have higher failure rates vs. sensitive organisms (endocarditis, pneumonia, surgical site infections, etc.)
- Issues of cost and driving multidrug resistance
- Taoism: You can’t make water better
- ID: You can’t make penicillin better
History

- When they got it: >50% neg after 5 yr
- What happened: Immediate, delayed, viral, non-allergic
- “Unknown Reactions”: No one forgets anaphylaxis.
- Importance of purging incorrect allergy info from medical records - role of PCP’s.
- Futility of talking pts out of their “allergies”.

Wednesday, April 9, 14
Strategy and Tactics

I) Flat rash only (immediate or delayed), OK to give cephalosporins.

II) Dubious Allergy: Graded Challenge, covering with another antibiotic

III) Life-threatening infection: desensitize

IV) Likely future need for abx:

Allergist referral for skin testing.
Cephalosporin Allergy

- Mostly to side-chains, not lactam core
- For rash only, OK to challenge with another cephalosporin
- Aztreonam and Ceftazidime
Skin Testing

- Reagents once again available (Major determinant)
- Very safe and effective (zero deaths)
- Should be done by Allergy specialist
- 1st challenge dose can be done in ED
- Non-standardized variants for other lactams
- Worth considering for all pt w/ uncertain or distant allergy hx.
- Major potential clinical benefits
Meet Our Team

Anna Kovalszki, MD
Clinical Director, Division of Allergy & Inflammation
Board-Certified in Allergy and Immunology

Clinical Interests: Immunodeficiency, Asthma, Hypersensitivity Lung Disorders, Allergic Rhinitis, Atopic and Contact Dermatitis, and Mast Cell Disorders

Dr. Kovalszki's profile -
Examples

- Pt at high risk for future infections, e.g. chronic steroids, DM
- Pt requiring long abx course, e.g. osteo, endocarditis
- Elective surgery
- Life-threatening infection
Desensitization

- Very effective, mechanism remains mysterious
- Only for Type I reactions. Allergy returns after d/c.
- Protocols available for most lactams, trim/sulfa
- Often done in ICU but can be done with tele
- No reported deaths when properly done.
- Logistics are key.

Table II: Oral penicillin desensitization protocol.

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<thead>
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<th>Dose* (units/ml)</th>
<th>Penicillin V Suspension (ml)</th>
<th>Amount* (units)</th>
<th>Cumulative Dose (units)</th>
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*Interval between doses, 15 min (elapsed time, 3 h and 45 min) total dose, 1.3 MU. *Specific amount of drug is diluted in approximately 30 ml of water and then given p.o.
Scenarios

- Severe Pneumococcal or Staph PNA
- MSSA or enterococcal endocarditis
- Orthopedic infection with retained hardware
- Neurosyphilis
- Severe PJP
Logistics

- Protocols on file with pharmacy (oral, IV)
- Procedures on file with ICU
- Buy-in beforehand from nursing
- Defined chain of command: ID rec., Attending approves, nursing supervisor clears.
Graded Challenge

- Use for unlikely allergy
- NOT desensitization
- 1/1000, 1/100, 1/10, 1 q30 min
- Does not need ICU
- No reported deaths
Conclusions

- Allergy histories exert a large, often negative effect on the treatment of serious infection.

- PCP’s have a key role in clarifying history and purging incorrect data.

- Use of alternative agents is frequently associated with significantly worse outcomes.

- Allergist referral is useful for many patients with likely need for future antibiotics.

- Desensitization and graded challenge are underused but preparation is essential.
So, until next time...

...Adios, Amoebas!