The Role of the ID Pharmacist, Physician, and Allergist in Penicillin Allergy and Skin Testing

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CIDRAP
September 18th, 2019
Learning Objectives

• Describe how a collaborative, multidisciplinary approach can augment penicillin allergy reconciliation and skin testing

• Identify and discuss potential barriers to penicillin allergy initiatives

• Outline strategies for successful implementation of penicillin allergy reconciliation and skin testing
Background

• Penicillin allergy assessments and skin testing are important tools to optimize care in penicillin allergic patients

• Wide variability of resources between facilities
  • Creative approaches and interventions
  • Diverse penicillin skin testing models
  • Multi- and interdisciplinary collaboration
Aztreonam Optimization
Aztreonam Optimization

Increased Aztreonam Utilization

Declining *P. aeruginosa* Susceptibilities

ASP Intervention

Aztreonam DOTs decreased by 55%

Aztreonam DOTs decreased by 89%

2008 - 2011

2012

2013

2014

2019

Second most expensive unrestricted antibiotic

Susceptible to aztreonam

2009 – 83%

2012 – 71%

Education

PAST is Present

ASP PAF

9.5 to 4.4

DOT/1,000 PD

$60-100K annual cost-avoidance

9.5 to 1.0

DOT/1,000 PD

>$100K annual cost-avoidance

PAF, prospective audit and feedback; PAST, penicillin allergy screening tool; DOT, days of therapy; PD, patient days

Penicillin Allergy Screening Tool

What is the Penicillin allergy?

- Mild to moderate allergy or intolerance
  - i.e. immediate or delayed rash, itching, GI
  - Recommend a cephalosporin (or PCN if intolerance)

- Severe allergy: immediate or life-threatening
  - i.e. anaphylaxis, SOB, hives, angioedema, facial swelling, blistering, SJS

- Undocumented
  - Has the patient tolerated a cephalosporin in the past?
    - No: Continue aztreonam
    - Yes: Recommend a cephalosporin

- Unknown
  - Can the patient provide a reliable history?
    - No: Assess allergy with family
    - Yes: Refer to appropriate algorithm based on allergy severity

  - Family can confirm reaction?
    - No: Continue aztreonam
    - Yes: Refer to appropriate algorithm based on allergy severity

EMR Allergy Documentation
68% of penicillin allergy histories were inconsistent with EMR documentation.
Penicillin Allergy History Algorithm

When did your penicillin allergy occur?

- Flat, itchy, non-hive-like rash < 5 years ago?  
  - Avoid penicillin
  - No

  Evaluate for Severe Adverse Reaction
  - Blistering or peeling of skin
  - Blistering or sores of mucus membranes
  - Joint pain or joint swelling associated with penicillin administration
  - Avoid penicillin
  - Yes
  - No

  Evaluate for IgE Mediated Reaction
  - Hives
  - Itching
  - Swelling (angioedema)
  - Passing out
  - Shortness of breath
  - Low blood pressure (hypotension)
  - Skin test
  - Yes
  - No

Non specific rash >5 years ago with no other history?

- Gastrointestinal symptoms only? e.g. nausea, vomiting, diarrhea
  - Give penicillin
  - Yes
  - No

Family history of a reaction without a personal history of a reaction?

- Other history not mentioned
  - Avoid penicillin or consult Allergy
  - Yes
  - No

Unable to describe reaction

- Patient declining skin test or unable to be skin tested?
  - Avoid penicillin or consult Allergy
  - Yes
  - No

Have you taken/tolerated a penicillin since?
Clinician Survey
<table>
<thead>
<tr>
<th>Survey Assessment</th>
<th>Answered Correctly (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pharmacists</td>
<td>APPs and MDs</td>
</tr>
<tr>
<td><strong>Antibiotic Cross-Reactivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin and imipenem</td>
<td>23/33 (70)</td>
<td>133/238 (56)</td>
</tr>
<tr>
<td>Penicillin and aztreonam</td>
<td>27/33 (82)</td>
<td>114/238 (48)</td>
</tr>
<tr>
<td>Penicillin and cephalosporins</td>
<td>27/33 (82)</td>
<td>120/241 (50)</td>
</tr>
<tr>
<td><strong>Clinical Vignettes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid penicillin</td>
<td>13/33 (39)</td>
<td>116/236 (49)</td>
</tr>
<tr>
<td>Penicillin skin test</td>
<td>19/33 (58)</td>
<td>91/238 (38)</td>
</tr>
<tr>
<td>Re-challenge penicillin</td>
<td>33/33 (100)</td>
<td>209/237 (88)</td>
</tr>
<tr>
<td>Temporary induction of drug tolerance</td>
<td>11/33 (33)</td>
<td>40/234 (17)</td>
</tr>
</tbody>
</table>

Staicu ML. Ann Allergy Asthma Immunol 2017;119:42.
Lessons Learned

• A thorough penicillin allergy history is the first step to evaluating management options
  • Determines management strategy
  • Antibiotic therapy optimization

• Universal opportunities for all facilities

• Allergy and ID live together in perfect harmony
The Role of the (ID) Pharmacist

Pre-Prescription
• Development of allergy tools
• Obtain and document medication allergy histories

Order Entry
• Review prior antibiotic administration data and tolerability
• Early identification of patients that may benefit from penicillin skin testing

Post-Prescription
• Penicillin skin testing
• Patient education
Because ID is consulted more than allergy...

...ID is in a key position to promote the importance of penicillin skin testing (PST)...

...and clarify MD misconceptions about the timing, setting, and safety of allergy testing.
Clinical scenario

“Severe orbital cellulitis:

• Symptoms are improving with IV antibiotics over the last 2 days.

• MSSA growing on cultures, continue vancomycin and clindamycin.

• Appreciate ophtha consult, patient may not need surgery.

• Considering her penicillin allergy, will request ID consult for antibiotic selection.”
Canterbury Allergy Immunology Consultations

Canadian study: 84% never referred to allergy
U.K study: 64% never referred

Staicu, *Ann Allergy Asthma Immunol* 2017
Elkhalifa, *Allergy* 2017
Myths about PCN Allergy

Dialogue of the ID Consultant

Benefits of β-lactam antibiotics
Benefits of β-lactam antibiotics

- Better clinical outcomes
- Safer than 2nd-line antibiotics
- Antibiotic pipeline benefits
### Pathogens for which β-lactams are the First-Line

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Beta-Lactam Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococci spp.</td>
<td>First-line</td>
</tr>
<tr>
<td>Methicillin-sensitive <em>Staphylococcus aureus</em></td>
<td>First-line</td>
</tr>
<tr>
<td>Methicillin-sensitive coagulase-negative <em>Staphylococcus</em> spp.</td>
<td>First-line</td>
</tr>
<tr>
<td>Ampicillin-sensitive <em>Enterococcus</em> spp.</td>
<td>First-line</td>
</tr>
<tr>
<td><em>Actinomyces</em> spp.</td>
<td>First-line</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Clostridium pefringens</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Lactobacillus</em> spp.</td>
<td>First-line</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Pasteurella multocida</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Capnocytophaga canimorsis</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Neisseria meningitides</em></td>
<td>First-line</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td>First-line</td>
</tr>
</tbody>
</table>

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**63 IDSA Guidelines**

**29 w/ antibacterial recommendations**

**23 recommend a β-lactam as first-line**

**6 recommend non-β-lactams as first-line**
59% of non-ID providers surveyed did **not** consider PCN skin testing in the event of β-lactam clinical superiority.

Staicu, Ann Allergy Asthma Immunol 2017
Challenging a PCN allergy and promoting β-lactam use positively impacts the Antibiotic pipeline:

- **Uses current resources**
  - Optimizes use of the antibiotics we already have

- **Preserves antibiotic reserves**
  - Often broader than needed
  - More toxic
  - Save them for when really needed

- **Newer agents**
  - Most are β-lactam derivatives anyway
MYTH #1: A PCN allergy is lifelong.

Does the PCN allergy resolve over time?

<table>
<thead>
<tr>
<th></th>
<th>Providers (n=276)</th>
<th>Patients (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>58%</td>
<td>28%</td>
</tr>
<tr>
<td>No</td>
<td>42%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Only 53% of providers respond that they always ask how long ago an allergic reaction occurred.

FACT: Penicillin allergies fade with time.

- 50% of patients will outgrow their allergy within 5 years
- 80% will outgrow their allergy within 10 years

Staicu, Ann Allergy Asthma Immunol 2017
Drug Allergy Practice Guidelines. Ann Allergy Asthma Immunol 2010
MYTH #2: A PCN allergy label is harmless.

Patient survey:
- 55% did not believe a PCN allergy is associated with an increased risk of an infection with resistant bacteria.
- 67% disagreed that PCN is less costly compared to other antibiotics.

FACT: The PCN allergy label has many implications across the healthcare spectrum.

- ↑ Abx exposure
- ↑ MDRO
- ↑ Adverse reactions
- ↑ Drug costs
- ↑ LOS, Readmits

HR 1.84 MRSA
HR 1.37 C diff
Nephrotoxicity
Neurotoxicity
Tendonitis
$0-$609/px

Staicu, Ann Allergy Asthma Immunol 2017
Van Dijk, J Allergy Clin Immunol Pract 2016
Blumenthal, BMJ 2018
Blumenthal, Ann Allergy Asthma Immunol 2015
McFadden, Clin Infect Dis 2016
Blumenthal, Clin Infect Dis 2015
Macy, J All Clin Immunol 2014
Mattingly, J Allergy Clin Immunol Pract 2018
<table>
<thead>
<tr>
<th>Myth #3: My patient is _________, so PST can’t be done today.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elkhalifa et al. Provider survey 60% agree with the statement: “Regardless of the details of the allergy history, it is always better to “play it safe” and avoid β-lactams in patients with a PCN-allergy label.”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PCN allergy label assoc w/: ↑LOS, post-op wound infection</td>
</tr>
<tr>
<td>• PST prospectively evaluated and reported safe in two studies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunocompromised</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PCN allergy → worse outcomes, ↑LOS, ↑costs</td>
</tr>
<tr>
<td>• PST QI initiative at MD Anderson: 95/99 negative PST and oral challenge</td>
</tr>
</tbody>
</table>
| Huang, *Clin Infect Dis* 2018  
Taremi, *J Allergy Clin Immunol Pract* 2019 |

<table>
<thead>
<tr>
<th>Too stable/Ready for discharge so can get PST as an outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient survey: 52% were more likely to undergo PST if conducted in the hospital</td>
</tr>
<tr>
<td>Brown, Upcoming Poster, ID Week 2019</td>
</tr>
</tbody>
</table>
Underrecognition of the benefits of a β-lactam

Knowledge gap in the safety of the PST

ASP-Allergy Collaboration

Overestimation of 2nd line antibiotics efficacy, safety

Underestimation of PCN allergy label risks

Antimicrobial Stewardship Program (ASP) Recommendations

The ASP team would like to make the following suggestions for your patient’s antimicrobial therapy.

Please consider placing an order for an Allergy consult

Microbiologic data and other considerations such as site of infection, antimicrobial efficacy, drug costs and dosing characteristics have been factored into our suggestions. We have not seen the patient; therefore, our suggestions should be considered in conjunction with all other patient factors. Our review is not intended to provide a clinical diagnosis and treatment plan, but to provide assistance in optimizing antimicrobial therapy once the primary clinical team has made a diagnosis and initiated therapy.

Based on a review of the above data, it was noted that your patient is receiving *** with the indication of ***. Microbiologic workup ***. Upon chart review, it was noted that the patient has a documented penicillin allergy. Based on this information, the ASP team would like to make the following suggestions for your patient’s antimicrobial therapy.

Approximately 80% of patients with an IgE-mediated reaction to penicillin (i.e., anaphylaxis, angioedema, hives, itching) lose their sensitivity within 10 years. The use of penicillin skin testing to de-label patients that are no longer allergic has been shown to reduce healthcare exposure (LOS and readmission rates) and use of second-line antibiotic therapy.

Therefore, please consider calling Allergy (922-8350) for a penicillin allergy evaluation.
Collaboration with Allergy

Allison Ramsey, MD
Allergy/Immunology
FAAAAI, FACAAI

Drug Allergy History and Management Expertise

Experience with Recognition and Management of Anaphylaxis

Experience with Recognition and Management of Hypersensitivity Reactions
Penicillin Allergy – Skin Prick Testing
Penicillin Skin Testing – Intradermal Test
**Interpretation of Penicillin Skin Testing**

<table>
<thead>
<tr>
<th>Result</th>
<th>Change of IgE-Mediated Reaction</th>
<th>Penicillin Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>50/50 change of reaction</td>
<td>Avoid</td>
</tr>
<tr>
<td>Negative</td>
<td>Risk of reaction same as the baseline population</td>
<td>Give</td>
</tr>
</tbody>
</table>

Note: Penicillin skin testing does not address other types of reactions

Purpose

To identify PCN allergic patients receiving vancomycin, linezolid, daptomycin, moxifloxacin, or aztreonam to undergo penicillin skin testing
47/50 patients with negative skin testing

<table>
<thead>
<tr>
<th>Clinical Characteristics of Patients Undergoing Skin Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
</tr>
<tr>
<td>Average age in years ± SD</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
</tr>
<tr>
<td>Caucasian</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Primary service, n (%)</td>
</tr>
<tr>
<td>Internal medicine</td>
</tr>
<tr>
<td>General surgery</td>
</tr>
<tr>
<td>Vascular surgery</td>
</tr>
<tr>
<td>Cardiothoracic surgery</td>
</tr>
<tr>
<td>Plastic surgery</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
</tr>
</tbody>
</table>
Direct cost savings = $70 per patient (conservative measure)

Days of Second-Line Antibiotics Avoided Based on Clinical Indication

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam</td>
<td>66</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>40</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>13</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>863</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>962</td>
</tr>
</tbody>
</table>

FIGURE 3. A, Antibiotic therapy before PST. B, Antibiotic therapy after PST. NOTE: Percentages exceed 100% because of some subjects receiving more than 1 antibiotic/antibiotic class. IV, Intravenous; PST, penicillin skin testing.

Raising Awareness Among Colleagues

<table>
<thead>
<tr>
<th>Inpatient</th>
<th>Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hospital Medicine</td>
<td>• Pediatrics</td>
</tr>
<tr>
<td>• Hematology/Oncology</td>
<td>• Internal Medicine / Family Medicine / Geriatrics</td>
</tr>
<tr>
<td>• Critical Care</td>
<td>• Dentistry</td>
</tr>
<tr>
<td>• Surgery</td>
<td>• Urology</td>
</tr>
<tr>
<td>• Urology</td>
<td>• APPs from all Specialties</td>
</tr>
<tr>
<td>• Ob/Gyn</td>
<td></td>
</tr>
</tbody>
</table>
Results of Raising Awareness!

>400% increase in consults between 2016 and 2018

- Aztreonam Initiative
- EMR Review
- PST Second-line Agents
- Clinical Survey
- Tele-medicine
- Graded Challenges
Allocating Resources: Telemedicine
# Use of Telemedicine for Penicillin Allergy Skin Testing

**Question**

What is your overall impression of telemedicine consult for penicillin skin testing? n (%)  

<table>
<thead>
<tr>
<th>Rating</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fair</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Neutral</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Good</td>
<td>18 (37)</td>
</tr>
<tr>
<td>Excellent</td>
<td>26 (53)</td>
</tr>
<tr>
<td>Average Rating</td>
<td>4.4</td>
</tr>
</tbody>
</table>

**Statement**

<table>
<thead>
<tr>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly Agree</th>
<th>Average rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall, I was very satisfied with my telemedicine encounter, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>21 (43)</td>
<td>27 (55)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly Agree</th>
<th>Average rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>I would have preferred to discuss penicillin skin testing with the allergy doctor in person, n (%)</td>
<td>6 (12)</td>
<td>11 (22)</td>
<td>26 (53)</td>
<td>4 (8)</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

Allocating Resources: Incorporating Direct Challenges

When did your penicillin allergy occur?

Flat, itchy, non-crease-like rash < 1 years ago? Yes → Avoid penicillin GC to cephalosporin

Evaluate for Severe Adverse Reaction
- Blistering or peeling of skin
- Blisters or sores of mucus membranes
- Joint pain or joint swelling associated with penicillin administration

No → Avoid penicillin

Evaluate for Moderate to Severe Ig-E Mediated Reaction
- Swelling (angioedema)
- Passing out (syncope)
- Shortness of breath (dyspnea)
- Low blood pressure (hypotension)

No → Skin test to PCN GC to 3/4th cephalo

Non specific rash >1-20 years ago with no other history? Yes → Skin test to PCN GC to cephalo

No → Graded challenge to penicillin

Skin rash, hives, itching or unknown reaction >20 years ago without emergency medical attention?

No → Give penicillin/cephalo

Gastrointestinal symptoms only?
- e.g. nausea, vomiting, diarrhea

Yes → Give penicillin/cephalo

Family history of a reaction without a personal history of a reaction?

No → Avoid penicillin or consult Allergy

Other history not mentioned

Yes → Avoid penicillin or consult Allergy

Unable to describe reaction and reaction time frame

Yes → Avoid penicillin or consult Allergy

Patient declining skin test or unable to be skin tested?

Yes → Avoid penicillin or consult Allergy

Have you taken/tolerated a penicillin since?
### Outcomes of Randomized Penicillin Allergy Evaluations

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Penicillin SPT (n=80)</th>
<th>DC (n=79)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PST Positive/DC fail, n (%)</td>
<td>10 (12.5)</td>
<td>3 (3.8)</td>
<td>8.7% (P = .70)</td>
</tr>
<tr>
<td>PST Negative/DC pass, (n%)</td>
<td>70 (87.5)</td>
<td>76 (96.2)</td>
<td></td>
</tr>
<tr>
<td>Time (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>72.7 ± 5.3</td>
<td>66.7 ± 4.8</td>
<td>6.0 (P &lt; .001)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>73.5 (68.8 – 75.3)</td>
<td>66.0 (62 – 70)</td>
<td>7.5 (P &lt; .001)</td>
</tr>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Each</td>
<td>$393.66</td>
<td>$53.66</td>
<td>$340.00</td>
</tr>
<tr>
<td>Total</td>
<td>$29,092.80</td>
<td>$4,239.14</td>
<td>$24,853.66</td>
</tr>
</tbody>
</table>

Allocating Resources: E-consults

- Review of chart and data
- Possible discussion with healthcare providers
- May not require in person or telemedicine visit
Conclusions

A multidisciplinary team has been key to our success

We have benefitted from key expertise from pharmacy, infectious disease, and allergy/immunology specialists

There are significant individual, institutional, and public health benefits to be gained from penicillin allergy evaluations

We employ multiple strategies to improve institutional antibiotic use and penicillin allergy evaluations
Thank you

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