Are You Really Allergic to Penicillin?
Effectively Managing Self-Reported Cases
Disclosures

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All other planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.
Objectives

• Discuss the role of penicillin skin testing as a modality for allergy clarification.
• Describe the role of penicillin skin testing for antimicrobial stewardship efforts in inpatient settings.
• Review the current literature demonstrating effectiveness of penicillin skin testing as an antimicrobial stewardship initiative.
• Develop a penicillin skin testing program for your institution.
Are You Really Allergic to Penicillin?
Effectively Managing Self-Reported Cases

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Are you allergic to penicillin?

- Yes
- No
What is the PCN allergy?

- Anaphylaxis
- Rash/Urticaria
- Unknown
- Other
Where are you currently with penicillin skin testing at your institution?

- Interested
- Planning to implement
- Implemented
- I thought this was the diabetes session
PCN “Allergy” Case

- 67 year old male admitted with presumed sepsis syndrome
- PMH: HTN, OA, GAD, GERD
- Medications PTA: Clonidine patch, Acetaminophen, Lorazepam, Hydralazine, Omeprazole
- Allergies: Penicillin (Anaphylaxis)
- Discharged from hospital 1 week prior
- Vitals: 100/60; Pulse 110; RR 20. T: 101.4°F
- Pertinent Positive Labs: SCr: 1.6 mg/dL (baseline 1.0 mg/dL); WBC 18.4 X 10^3
- Patient receives 2L NS and is hemodynamically stable for the moment
PCN “Allergy” Case

• Because of patient’s PCN allergy, the providers prescribes meropenem and vancomycin which are given after cultures are drawn and the patient is being transferred to the intensive care unit for further management.

• Is this patient a candidate for PCN skin testing?
What is Antimicrobial Stewardship?

“Antimicrobial stewardship includes not only limiting inappropriate use but also optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection while limiting the unintended consequences, such as the emergence of resistance, adverse drug events, and cost.”

Antibacterial Approvals by FDA

Approvals by the US Food and Drug Administration (FDA), 1983-2007

Systemic Agents Approved


Background

• Penicillin allergy is one of the most frequently reported drug allergies
  – Approximately 10% of patients report hypersensitivity
  – Results in limited treatment options, increased healthcare costs, and increased resistance with the use of broad-spectrum agents
• Up to 90% of patients reporting hypersensitivity do not truly have a penicillin allergy
• Many patients therefore do not receive optimal therapy for infecting pathogen

Clinical Indications where Beta-lactams are best

- Surgical Prophylaxis
- Methicillin-susceptible *Staphylococcus aureus*
  - Superior to vancomycin for MSSA bacteremia
- Severe Pseudomonas infections
  - Often backbone at many institutions
- Group A streptococcal infections
  - Including invasive necrotizing infections
- Several STIs
  - Syphilis, PID, Gonococcal infections

Implications of PCN “Allergy”

• Increased adverse effects
• Increased hospital stays
  – Approximately one-half day longer
  – 30,000 hospital days/65 million in expenditures
• Development of MDR infections
  – 23.4% increase in CDI
  – 14.1% more MRSA
  – 30.1% increased VRE

Patients who report a PCN allergy experience:

- Increased usage of broad-spectrum antibiotics
  - FQ, Clindamycin, Vancomycin
- Increased antibiotic costs
  - 63% higher than those without reported allergy
- Antibiotic regimens deviate from standard of care (as defined by national guidelines, protocols or ID consults) in ~40% of patients with a reported PCN allergy

Consequence: Increased Costs

- Mean antibiotic cost for patients allergic to penicillin is 63% higher than those not allergic to penicillin.
  - Cost of drug
  - Additional lab work
  - Nurse and pharmacist time
  - Management of side effects
  - Increased LOS
Potential Benefits of PCN Skin Testing

• Increased usage of drugs of choice where superior outcomes exist
• Decreased usage of more expensive antimicrobials
• Avoidance of broad-spectrum antimicrobials
• Acute and long-term benefit potential on resistance
• Preserve newer agents
Allergy Assessment First!

- Detailed Patient/Family Interview
  - Not all patients need testing
  - Ask Brand/Generic names (Interrogation)
  - Get specific
- Previous hospital stay medication history
- Use your pharmacist (local pharmacies)

<table>
<thead>
<tr>
<th>Cross-reactive beta-lactams</th>
<th>Penicillin</th>
<th>Amoxicillin</th>
<th>Ampicillin</th>
<th>Cephalexin</th>
<th>Cefuroxime</th>
<th>Cefoxitin</th>
<th>Ceftriaxone</th>
<th>Cefotaxime</th>
<th>Cefepime</th>
<th>Ceftazidime</th>
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</table>

Who should we test... Patient characteristics

- Type I reaction to PCN
- Superior outcomes would be produced
  - MSSA bacteremia
- $$$$...
- Frequent fliers
- Resistance pattern of organism
- Facilitation of discharge
Patient populations for PST

• Outpatient
  – Home infusion/infusion centers
  – Preoperative patients
  – Clinic

• Inpatient

• LTAC
Penicillin Allergy Skin Testing for Antimicrobial Stewardship

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Baltimore, Maryland
Antimicrobial Stewardship Guidelines

• Penicillin allergy skin testing (PAST) is now recommended
• “In patients with a history of B-lactam allergy, we suggest that ASPs promote allergy assessments and PCN skin testing when appropriate”
• Largely unstudied as primary ASP intervention
• Weak recommendation, low-quality evidence

### Table 2. Recommendations for Surgical Antimicrobial Prophylaxis

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>Recommended Agents&lt;sup&gt;ab&lt;/sup&gt;</th>
<th>Alternative Agents in Pts With β-Lactam Allergy</th>
<th>Strength of Evidence&lt;sup&gt;c&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Cardiac</td>
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<tr>
<td>Coronary artery bypass</td>
<td>Cefazolin, cefuroxime</td>
<td>Clindamycin&lt;sup&gt;a&lt;/sup&gt;, vancomycin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>A</td>
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<tr>
<td>Cardiac device insertion procedures (e.g., pacemaker implantation)</td>
<td>Cefazolin, cefuroxime</td>
<td>Clindamycin, vancomycin</td>
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<tr>
<td>Ventricular assist devices</td>
<td>Cefazolin, cefuroxime</td>
<td>Clindamycin, vancomycin</td>
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<td>Thoracic</td>
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<tr>
<td>Noncardiac procedures, including lobectomy, pneumonectomy, lung resection, and thoracotomy</td>
<td>Cefazolin, ampicillin-sulbactam</td>
<td>Clindamycin&lt;sup&gt;a&lt;/sup&gt;, vancomycin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>A</td>
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<tr>
<td>Video-assisted thoracoscopic surgery</td>
<td>Cefazolin, ampicillin-sulbactam</td>
<td>Clindamycin&lt;sup&gt;a&lt;/sup&gt;, vancomycin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>C</td>
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<tr>
<td>Gastroduodenal&lt;sup&gt;g&lt;/sup&gt;</td>
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<tr>
<td>Procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy)</td>
<td>Cefazolin</td>
<td>Clindamycin or vancomycin + aminoglycoside&lt;sup&gt;e&lt;/sup&gt; or aztreonam or fluoroquinolone&lt;sup&gt;h&lt;/sup&gt;</td>
<td>A</td>
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<tr>
<td>Procedures without entry into gastrointestinal tract (antireflux, highly selective vagotomy) for high-risk patients</td>
<td>Cefazolin</td>
<td>Clindamycin or vancomycin + aminoglycoside&lt;sup&gt;e&lt;/sup&gt; or aztreonam or fluoroquinolone&lt;sup&gt;h&lt;/sup&gt;</td>
<td>A</td>
</tr>
</tbody>
</table>

<sup>a</sup> Clindamycin or vancomycin may be appropriate if Cefazolin is contraindicated due to allergy, renal insufficiency, or other reasons.

<sup>b</sup> Vancomycin may be appropriate if Cefazolin is contraindicated due to allergy, renal insufficiency, or other reasons.

<sup>c</sup> The strength of evidence (A, B, C) is based on the level of evidence available and the balance of benefits versus risks.

<sup>d</sup> Beta-lactam allergy.

<sup>e</sup> Beta-lactam allergy.

<sup>g</sup> Gastro-duodenal.

<sup>h</sup> Beta-lactam allergy.

16 patients reporting PCN allergies skin tested pre-op

13 patients were skin test negative

11 were to receive vancomycin prophylaxis
2 were to receive ciprofloxacin and gentamicin prophylaxis

All 13 received cefazolin

No post-op infections
853 patients with reported PCN allergy

442 referred for PAST

411 not referred for PAST

405 (91.6%) had negative tests

37 (8.4%) had positive tests

Significantly reduced use of vancomycin, clindamycin and levofloxacin
Pre-operative clinic that offers same-day allergy consultation and penicillin allergy skin testing (PAST)

1,030 patients underwent PAST
43 (4%) had positive tests

91% of patients with negative tests received a beta-lactam

Emergency Department

- 2 emergency medicine physicians performed PAST in patients with self-reported allergy
- Tested 150 patients, 137 (91.3%) of which were negative
- Median cost of prescribed antibiotics was $79.40 higher than first-choice penicillin or penicillin-derivative derivative antibiotics

1 patient had a positive test (0.7%)

146 patients eligible for skin testing

145 patients had a negative test (99.3%)

$225 per patient savings from altered therapy

Annual savings of $82,000

90 patients assessed by Penicillin Allergy Consult Team

76 patients had Penicillin Allergy Skin Testing (PAST) Performed

PAST Results
- Negative 64 (84%)
- Invalid 9 (12%)
- Positive 3 (4%)

14 patients did not undergo skin testing
- Previous tolerance of beta-lactams identified during history (6)
- Patient did not consent for testing (3)
- Antibiotic plan changed prior to PST (2)
- Recent, convincing reaction to penicillin (2)
- Patient on a histamine blocker, unable to be held (1)
Antibiotic Management of Patients with negative PST

- Antibiotic change: Yes 81%, No 19%
- Change to narrower spectrum: Yes 51%, No 30%, NA/no change 29%
- Change to more effective therapy: Yes 64%, No 17%, NA/no change 19%
- Change to more cost effective therapy: Yes 49%, No 28%, NA/no change 19%
- Allergy record updated: Yes 88%, No 12%

Acute Care


Aaztreonam Use

Annual savings of $26,000
Acute Care

Annual savings of $60,000-100,000

*IA = in appropriate use

• Antimicrobial stewardship teams at 3 hospitals received training by allergists to offer skin testing in staggered 3-month intervals

827 patients with reported beta-lactam allergy, beta-lactam therapy would be preferred in 76%

Baseline Period:
50% (124/246) received preferred beta-lactam therapy

Post-implementation: 81% (313/386) received preferred beta-lactam therapy (P<0.001)
Choosing a model

IMPLEMENTATION OF SKIN TESTING
What do you foresee as being the biggest barrier to implementation?

- A. Time/Personnel
- B. Cost
- C. Pharmacy Preparation
- D. Utility of Results
Questions to ask prior to initiating PST

• Who will take ownership of the program and how will I structure it?
• Who needs to be trained?
• Who will be tested?
• Is it worth it?
PST Models

- Allergy (when available)
- Pharmacist-managed (state law dependent)
- Pharmacist-nurse
- Pharmacist – ID Fellows
- Other physician specialties
  - Emergency Medicine
  - Hospitalist
- Outpatient/Peri-operative referrals
Thinking about your own institution, what model might work for you?

• A. We have allergists, woohoo!
• B. Pharmacy power, let’s do this!
• C. Infectious Diseases consults
• D. Still unsure I can make it work
Are You Really Allergic to Penicillin?
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How do you justify financially?

• Inpatients
  – Generally bundled into the DRG
    • No direct reimbursement
  – Physicians can perform as a procedure
    • Usually allergists
    • ID attending – probably not cost effective
  – ID fellows?
## Inpatient Cost Analysis

<table>
<thead>
<tr>
<th>Total Antimicrobial Cost Savings</th>
<th>$7554.08</th>
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</thead>
<tbody>
<tr>
<td>Average Antimicrobial Cost</td>
<td>$314.75</td>
</tr>
<tr>
<td>Savings/Patient</td>
<td></td>
</tr>
</tbody>
</table>

Average cost for one test = ~$130-140

How do you justify financially?

• Outpatients - **Product**
  – Up to 9 Current Procedural Terminology (CPT®) codes can be applied to 1 test, with an additional CPT® code for oral challenge

• **95018** – Code to use to allergy test a patient to any drug or biological and is used for both the percutaneous and intradermal testing of any drug or biological

• **95076** – Code for oral drug challenge (first 2 hours (120 min) of testing)
How do you justify financially?

• Outpatients - **Office Visit**
  – Detailed patient history
  – Detailed examination
  – Medical decision with low complexity

• **99203** - Level 3 (new patient)

• **99213** - Level 3 (established patient)

PST Models

- Allergy (when available)
- Pharmacist-managed (state law dependent)
- Pharmacist-nurse
- Pharmacist – ID Fellows
- Other physician specialties
  - Emergency Medicine
  - Hospitalist
- Outpatient/Peri-operative referrals
Structure – Pharmacist with Nursing
Skin Testing Procedure at SJCHS

- Currently restricted to infectious diseases physicians or stewardship pharmacist recommendation
- Requires a physician order to complete under P&T approved protocol
- Protocol contains reaction medications in case of allergic reaction
- Complete allergy history taken
- Performed by nursing staff under the direction of clinical pharmacists

Skin Testing Procedure at SJCHS

• Supplies
  – 0.9% sodium chloride (negative control)
  – Histamine base 1 mg/ml (positive control)
  – Benzylpenicilloyl Polylsine (Pre-Pen®) (major determinant)
  – Reconstituted Penicillin G, diluted to a strength of 10,000 U/ml (minor determinant)

www.alk-abello.com/US/products/PRE-PEN/Pages/PREPEN.aspx
Skin Testing Procedure at SJCHS

- **First Step – Puncture Test**
  - Histamine
  - Saline
  - Benzylpenicilloyl Polylysine
  - Penicillin G

- **Second Step – Intradermal Test**
  - Saline
  - Benzylpenicilloyl Polylysine
  - Penicillin G

- **Third Step (optional)**
  - Amoxicillin 250mg PO x 1
Post-Procedure Follow-Up

• Patient monitored for signs of allergic reaction
• Results called to prescribing physician
• New orders for antimicrobial written (if needed)
• Patient education
• Allergies updated in the electronic medical record
Patient Education

Live Smart.

Penicillin Allergy Skin Test: PATIENT RESULTS

Name: ________________________________
DOB: ________________________________
Date of Test: _________________________

I received a penicillin allergy skin test and the results were:

- Negative: I am not allergic to penicillin.
- Positive: I am allergic to penicillin.

Information for Healthcare Providers

Previously Tolerated Beta-lactam Therapy

- Penicillin(s): ________________________________
- Cephalosporin(s): ________________________________
- Carbapenem(s): ________________________________

Skin test verified positive penicillin allergy

Healthcare provider: ________________________________

City-wide Antimicrobial Management Program (C.A.M.P.)
Savannah, GA
Post-Procedure Follow-Up

• The electronic medical record will be updated with:
  – Details of reaction for positive results
  – Removal of the penicillin allergy for negative results
• Negative results will then have an uncoded “Pre-Pen” allergy added with the comments
  – “Patient not allergic to penicillin per penicillin skin test conducted on [date], test was negative”

Penicillin Skin Test Results

Date of Test: [ ]
Ordering Provider: [ ]

Test performed by:
Pharmacist: [Bruce M. Jones, PharmD, BCPS] [ ] , PharmD
Nurse: [ ], RN

Hx: Patient is a [age] year old [white/black/hispanic/latino/other] [male/female] [poor/moderate/reliable] historian reporting an allergy to penicillin.

Reaction(s): [anaphylaxis/hives/throat swelling/urticaria/rash/unknown/other] (canned text)
Comments: [ ]

Current Antimicrobials: [ ]

Step 1 – Puncture Test Forearm, [L/R]:
1. Histamine: [positive, negative]
2. Normal Saline: [positive, negative]
3. Pre-Pen: [positive, negative]
4. Penicillin G: [positive, negative]
Comments: [ ]

Step 2 – Intradermal Test [Upper Arm/Forearm], [L/R]:
1. Normal Saline: [positive, negative]
2. Pre-Pen 1: [positive, negative]
3. Pre-Pen 2: [positive, negative]
4. Penicillin G 1: [positive, negative]
5. Penicillin G 2: [positive, negative]
Comments: [ ]

(Optional) Step 3 – Oral Challenge [Not Performed, Performed]
[Amoxicillin 250mg PO x 1 dose, other] (canned text)
If performed: [positive, negative]

Penicillin Skin Test is [POSITIVE, NEGATIVE]. Patient [IS, IS NOT] allergic to penicillin.
Role in Antimicrobial Stewardship

- Evaluation of these patients should be part of a hospital’s antimicrobial stewardship program
  - Appropriate documentation and interview is a great place to start
  - Penicillin skin testing can be performed anywhere in the hospital by properly trained staff, without an allergist
Penicillin Allergy Evaluation

Patient/Room #: ____________________________
Date/Time for PST: ____________________________

Preliminary (Assess Profile)

• What did the patient take? How long ago? What was their reaction?
  ________________________________________________________________

  □ Yes □ No: Patient has documented PCN/Cephalosporins taken during prior visits
  • If yes, __________________________________________________________

  □ Yes □ No: Patient currently taking any antihistamines, steroids, and/or vasopressors
  • If yes, __________________________________________________________

Talk to Patient

• Ask which PCN they remember taking. How long ago was it? >10 years?
  ________________________________________________________________

  • Ask, in detail: What was their reaction?
    □ Rash □ Hives □ Anaphylaxis □ Patient was hospitalized
    Localized or full body? ____________________________________________

    □ Other: _________________________________________________________

    □ Yes □ No: Patient has had an episode of anaphylaxis within the last month

    □ Yes □ No: Patient recalls taking other PCN/Cephalosporins
    Ask about common brand/generics (Keflex, Amoxicillin, Augmentin, etc.)
    • If yes, which med? When? Any reaction?
      ________________________________________________________________
Where Do We Go From Here?

• Patients Completed:
  – 188 patients @ Candler Hospital
  – 43 patients @ St. Joseph’s Hospital

• Expansion to other facilities city-wide?

• Expansion to outpatient? (i.e. elective surgery)
Key Takeaways

• Key Takeaway #1
  – Providing PST can reduce the use of carbapenems, aztreonam, vancomycin, and other broad-spectrum agents and lead to cost savings that justify the test

• Key Takeaway #2
  – Structure PST to how best fits your health system-----there is no cookie-cutter approach