Disclosures

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ALK Abello: Advisory Board, Consultant, Grant Recipient; Merck: Speaker's Bureau

Emily Heil

ALK Abello: Research Support

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ALK Abello: Advisory Board, Consultant, Grant Recipient

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.

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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.

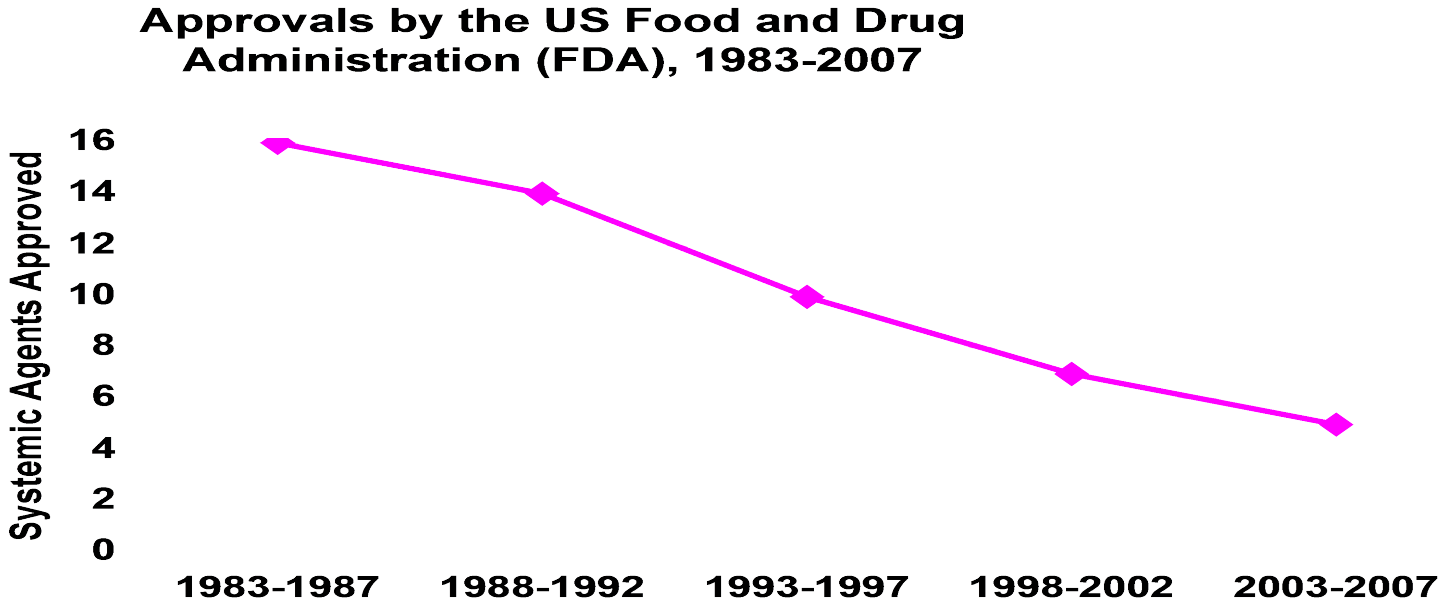
- Is this patient a candidate for PCN skin testing?

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*."

Dellit TH et al. *Clin Infect Dis*. 2007;44:159-77.

Antibacterial Approvals by FDA



Spellberg B, et al. *Clin Infect Dis* 2008;155-164.

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

***Ann Allergy Asthma Immunol*. 2010; 105:259-273.; *Mayo Clinic Proc.* Mar 2005; 80(3):405-410.; *Ann of Allergy, Asthma, and Immunology*. 2007; 98: 355-359.**

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

Blumenthal KG et al. Clin Infect Dis. 2015;61:741-9.

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

MacFadden DR et al. Clin Infect Dis. 2016;63:904-10.
Macy E et al. J Allergy Clin Immunol 2014;133:790-6.

PAST for ASP – A Natural Partnership

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

MacLaughlin EJ et al. Arch Fam Med 2009;9:722-6.; Charneski L et al. Pharmacother 2011;31:742-7.; Macy E. er al. J Allergy Clin Immunol 2014;133:790-6.

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)

Staicu ML, et al. AJHP 2016;73:298-306.

Cross-reactive beta-lactams	Penicillin	Amoxicillin	Ampicillin	Cephalexin	Cefuroxime	Cefoxitin	Ceftriaxone	Cefotaxime	Cefepime	Ceftazidime
Penicillin		X	X	X		X				
Amoxicillin	X		X	X						
Ampicillin	X	X		X						
Cephalexin	X	X	X							
Cefuroxime						X	X	X		
Cefoxitin	X				X					
Ceftriaxone					X			X	X	X
Cefotaxime					X		X			X
Cefepime							X			
Ceftazidime							X	X		

Campagna, et al. J Emerg Med 2012;42(5):612-620.

Antunez et al. J Allergy Clin Immunol 2006;117:404-10.

DePestel et al. J Am Pharm Assoc. 2008;48(4):530-40.

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

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Penicillin Allergy Skin Testing for Antimicrobial Stewardship

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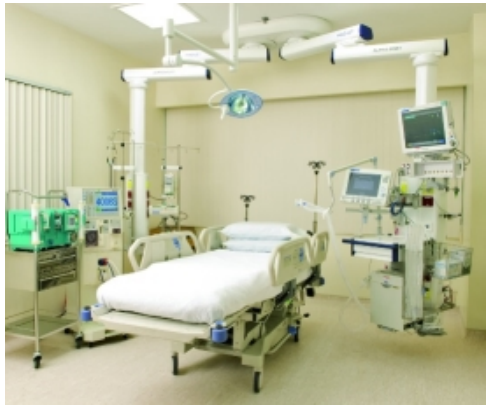
Antimicrobial Stewardship Guidelines

- 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

Barlam TF, et al. Clin Infect Dis 2016;62:e51-77.




EMERGENCY

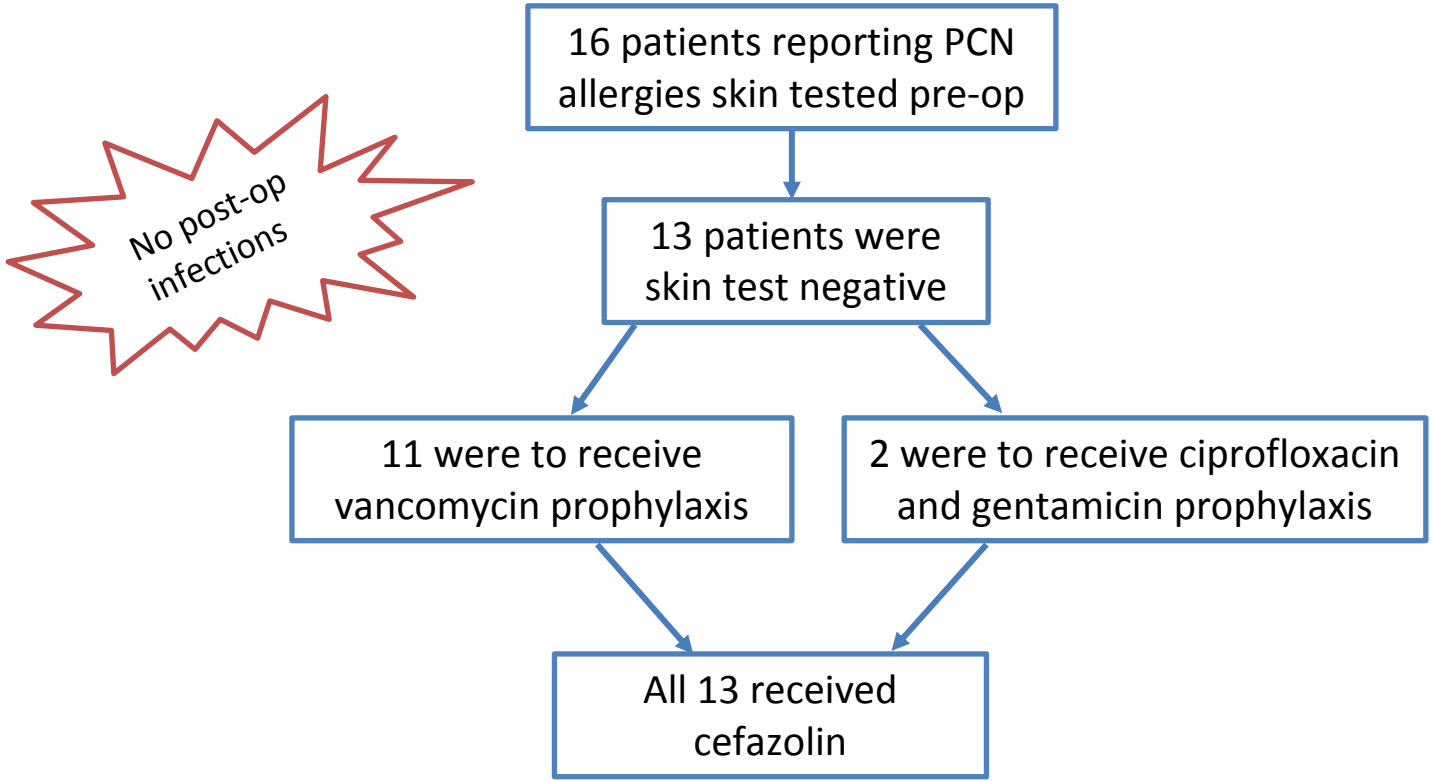
Pre-op

Table 2.
Recommendations for Surgical Antimicrobial Prophylaxis

Type of Procedure	Recommended Agents[a,b]	Alternative Agents in Pts With β-Lactam Allergy	Strength of Evidence[c]
Cardiac			
Coronary artery bypass	Cefazolin, cefuroxime	Clindamycin,[d] vancomycin[e]	A
Cardiac device insertion procedures (e.g., pacemaker implantation)	Cefazolin, cefuroxime	Clindamycin, vancomycin	A
Ventricular assist devices	Cefazolin, cefuroxime	Clindamycin, vancomycin	C
Thoracic			
Noncardiac procedures, including lobectomy, pneumonectomy, lung resection, and thoracotomy	Cefazolin, ampicillin–sulbactam	Clindamycin,[d] vancomycin[e]	A
Video-assisted thoracoscopic surgery	Cefazolin, ampicillin–sulbactam	Clindamycin,[d] vancomycin[e]	C
Gastroduodenal[f]			
Procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy[f])	Cefazolin	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h,i]	A
Procedures without entry into gastrointestinal tract (antireflux, highly selective vagotomy) for high-risk patients	Cefazolin	Clindamycin or vancomycin + aminoglycoside[g] or aztreonam or fluoroquinolone[h,i]	A

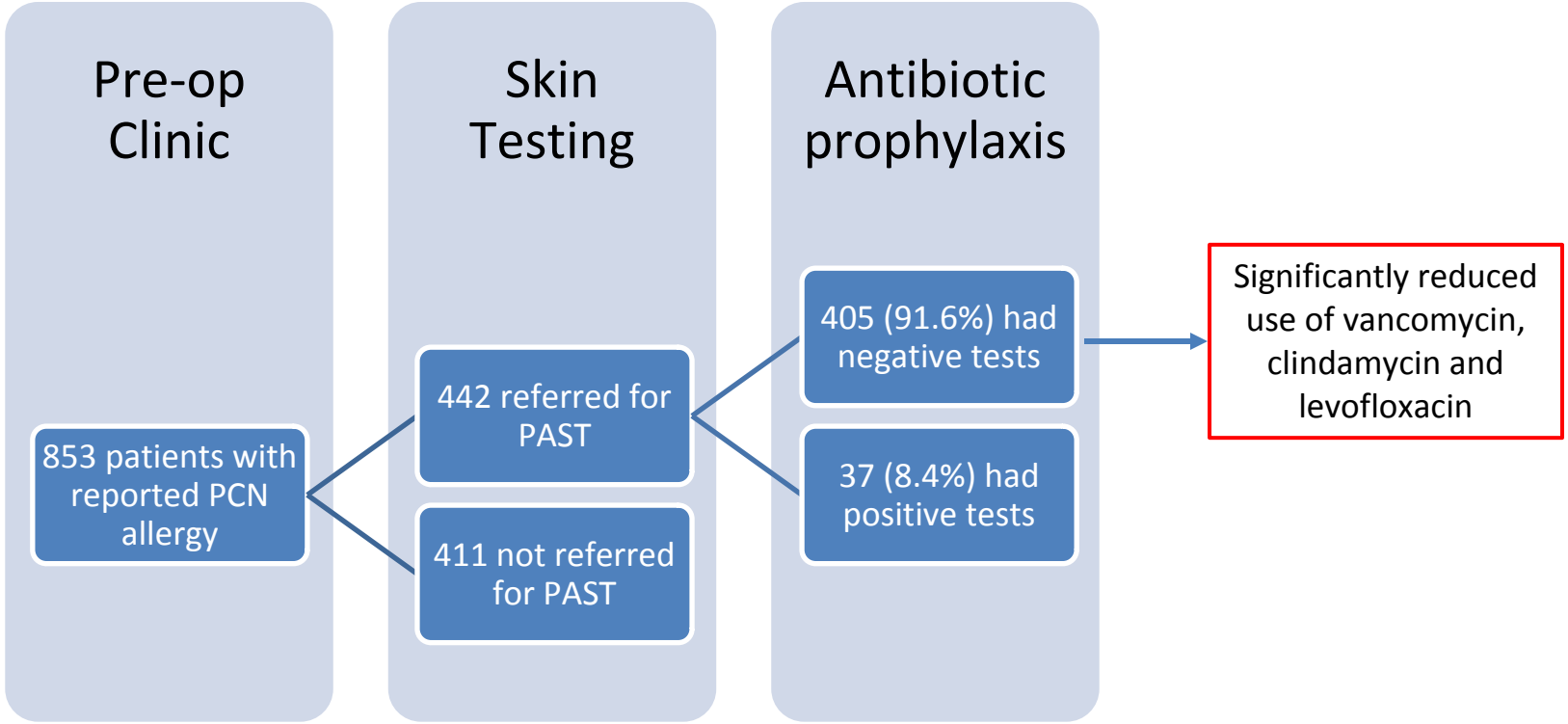
Bratzler DW et al. Am J Health Syst Pharm 2013;70:195-283.

Pre-op



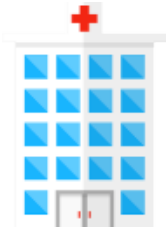
Harris AD, et al. Am J Med 1999;107:165-8.

Pre-op



Sacco KA, et al. J Allergy Clin Immunol 2017.

Pre-op



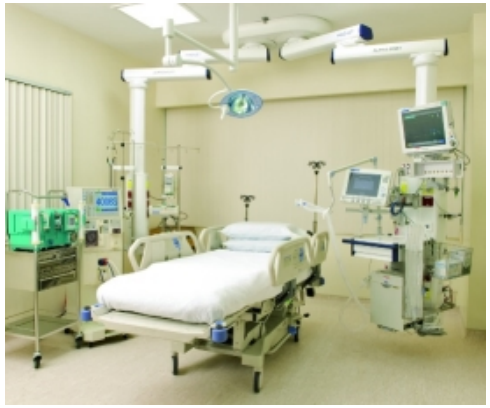
Pre-operative clinic that offers same-day allergy consultation and penicillin allergy skin testing (PAST)

1,030 patients underwent PAST

43 (4%) had positive tests

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

Park M, et al. Ann Allergy 2006;97:681-7.

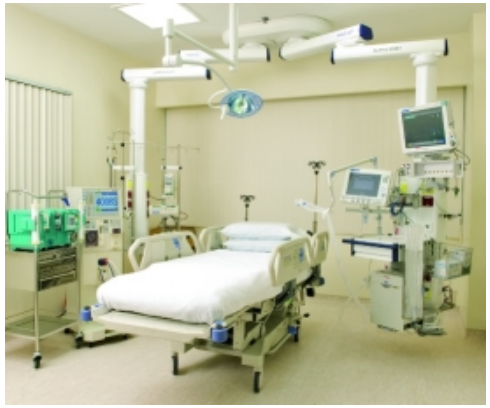



EMERGENCY

Emergency Department

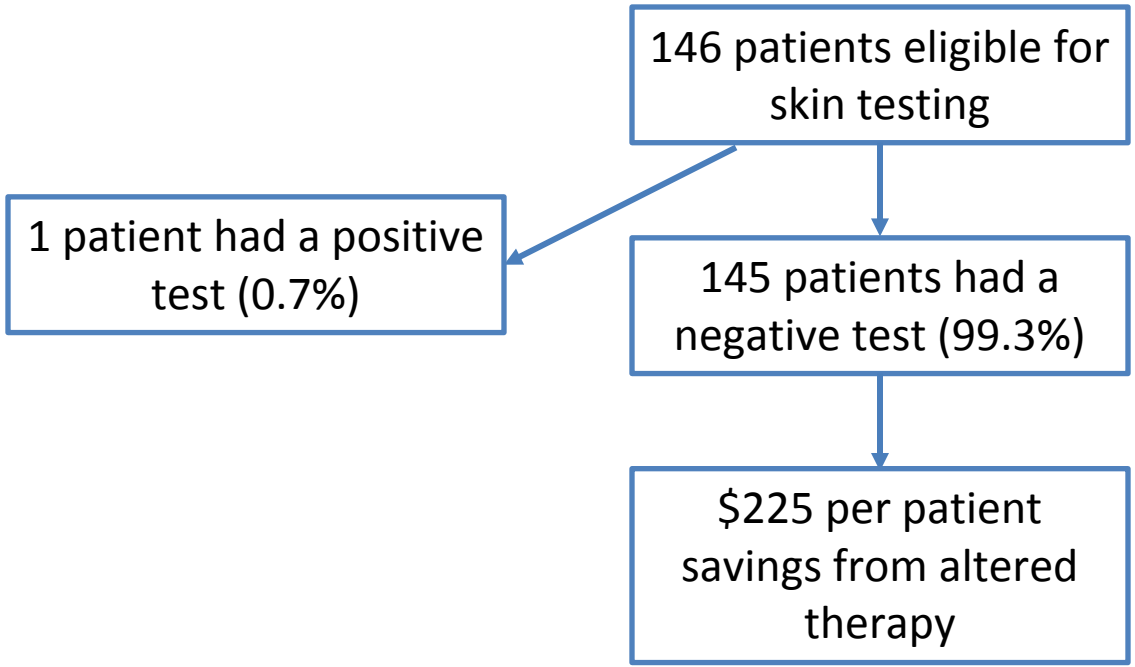
- 2 emergency medicine physicians performed PAST in patients with self-reported allergy
- Tested 150 patients, 137 (91.3%) of which were negative
- Median cost of prescribed antibiotics was $79.40 higher than first-choice penicillin or penicillin-derivative derivative antibiotics

Raja AS, et al. Ann Emerg Med 2009;54:72-8.




EMERGENCY

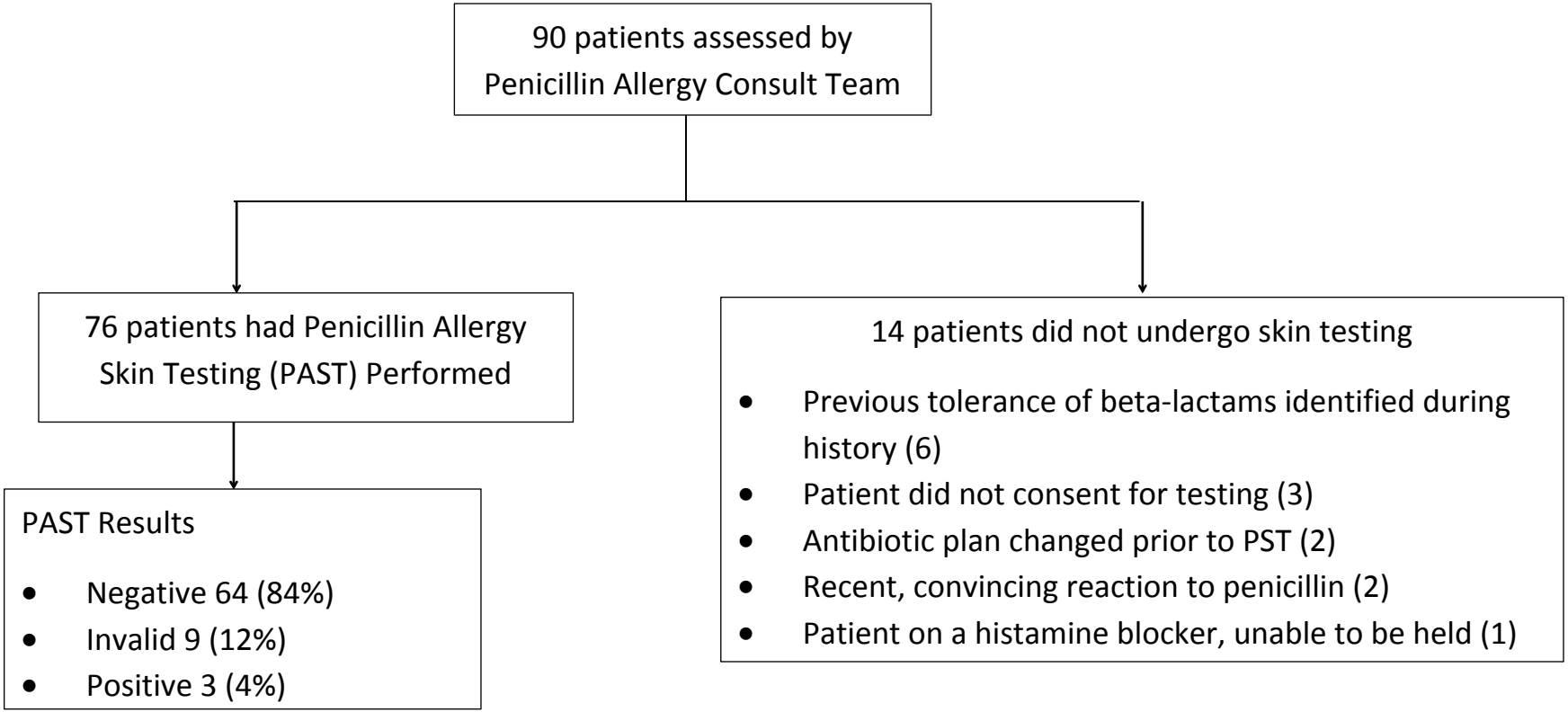
Acute Care



Annual savings of $82,000

Rimawi RH, et al. J Hosp Med 2013;8:341-5.

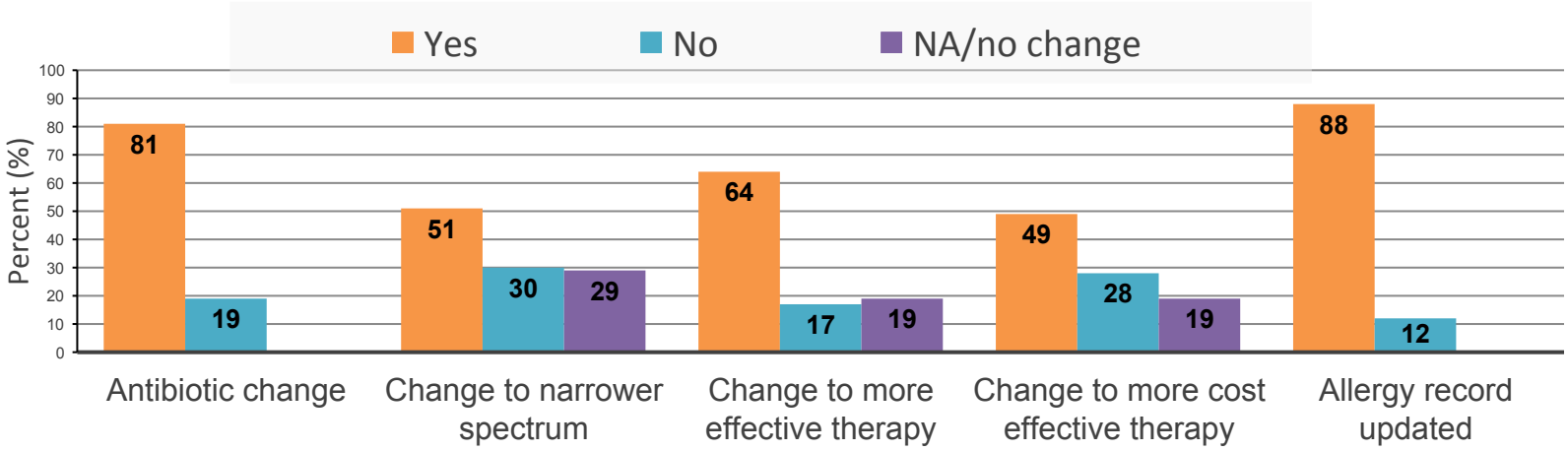
Acute Care



Heil EL, et al. Open Forum Infect Dis 2016.

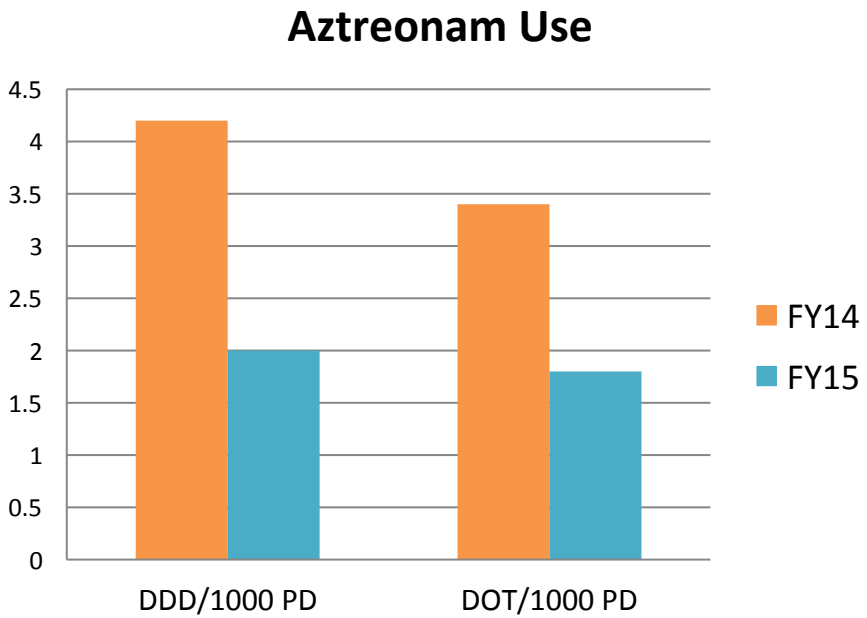
Acute Care

Antibiotic Management of Patients with negative PST



Heil EL, et al. Open Forum Infect Dis 2016.

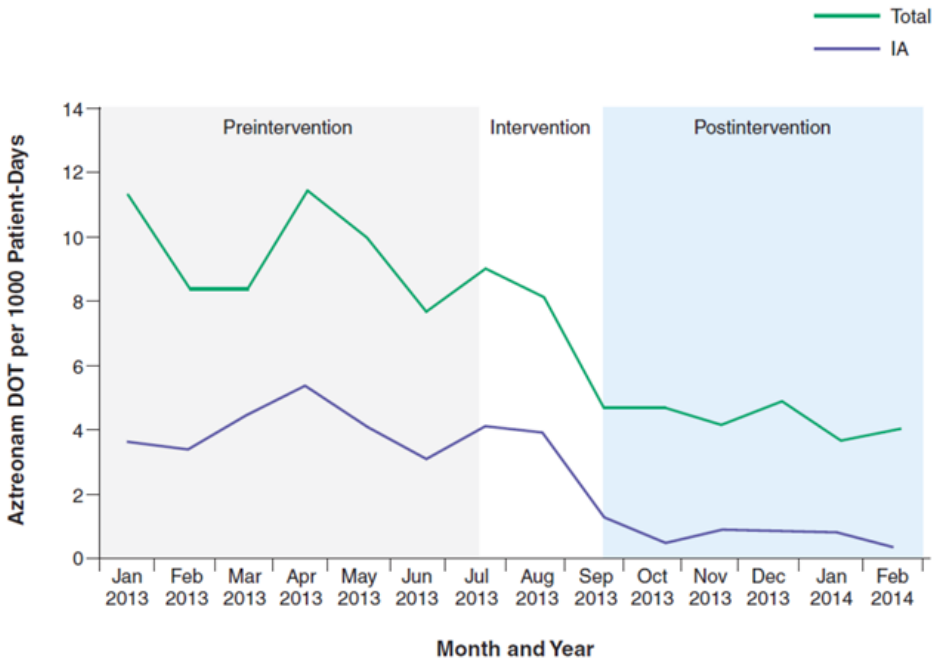
Acute Care



Annual savings of $26,000

Heil EL, et al. Open Forum Infect Dis 2016.

Acute Care



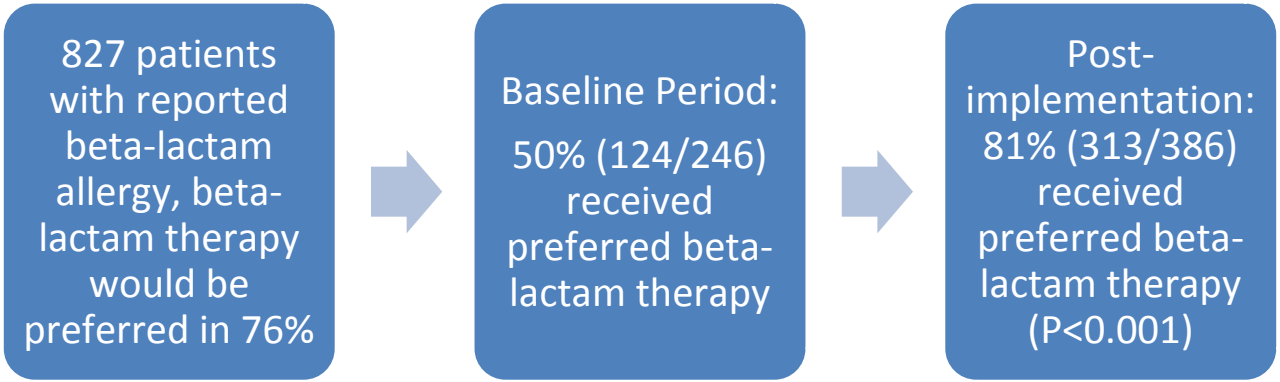
Annual savings of $60,000-100,000

*IA = in appropriate use

Staicu ML. Am J Health Syst Pharm 2016;73:298-306.

Acute Care

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



Leis JA, et al. Clin Infect Dis 2017 [epub ahead of print]

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

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

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Clinical Adjunct Assistant Professor
University of Georgia College of Pharmacy

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

Total Antimicrobial Cost Savings	$7554.08
Average Antimicrobial Cost Savings/Patient	$314.75

Average cost for one test = ~$130-140

Jones, BM. Am J Health Syst Pharm. Feb 2017, 74 (4) 232-237.

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)

www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Management/finances-coding/Coding-for-Penicillin-Testing.pdf

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)

http://www.aafp.org/fpm/2003/0900/p33.html

PST Models

- Allergy (when available)
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- Other physician specialties
  - Emergency Medicine
  - Hospitalist
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Structure – Pharmacist with Nursing

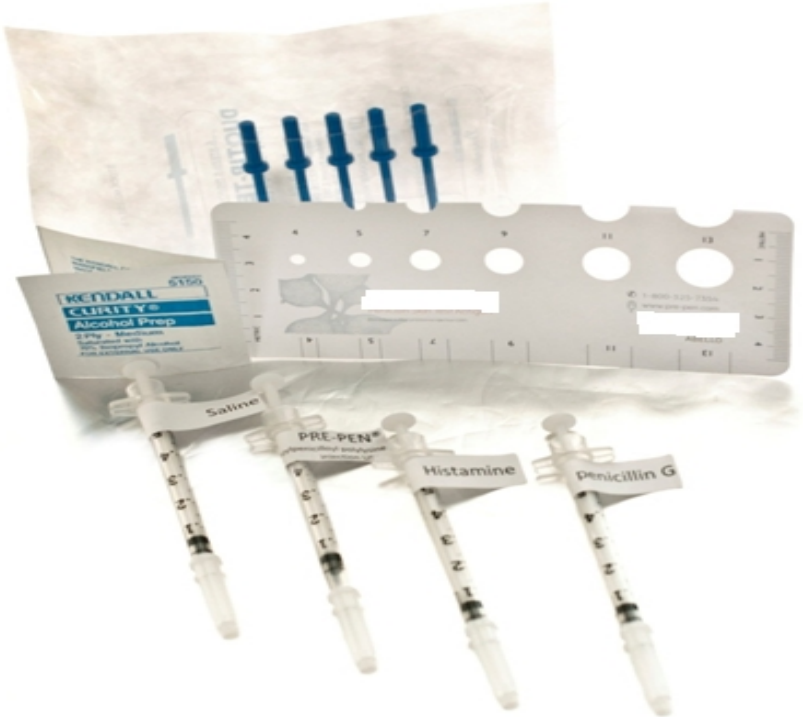
Skin Testing Procedure at SJCHS

- 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

Jones, BM. Am J Health Syst Pharm. Feb 2017, 74 (4) 232-237.

Skin Testing Procedure at SJCHS

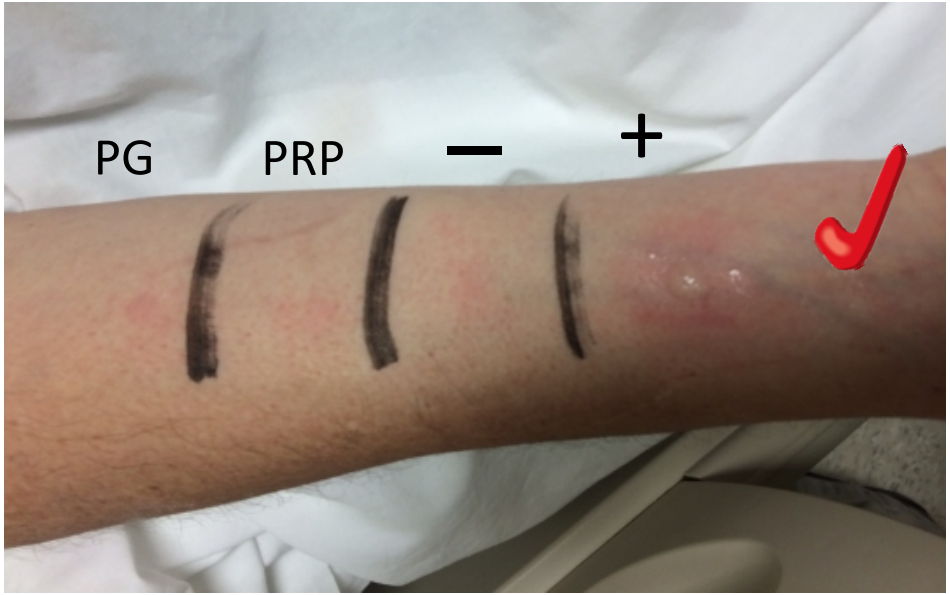
- Supplies
  - 0.9% sodium chloride (negative control)
  - Histamine base 1 mg/ml (positive control)
  - Benzylpenicilloyl Polylysine (Pre-Pen®) (major determinant)
  - Reconstituted Penicillin G, diluted to a strength of 10,000 U/ml (minor determinant)



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



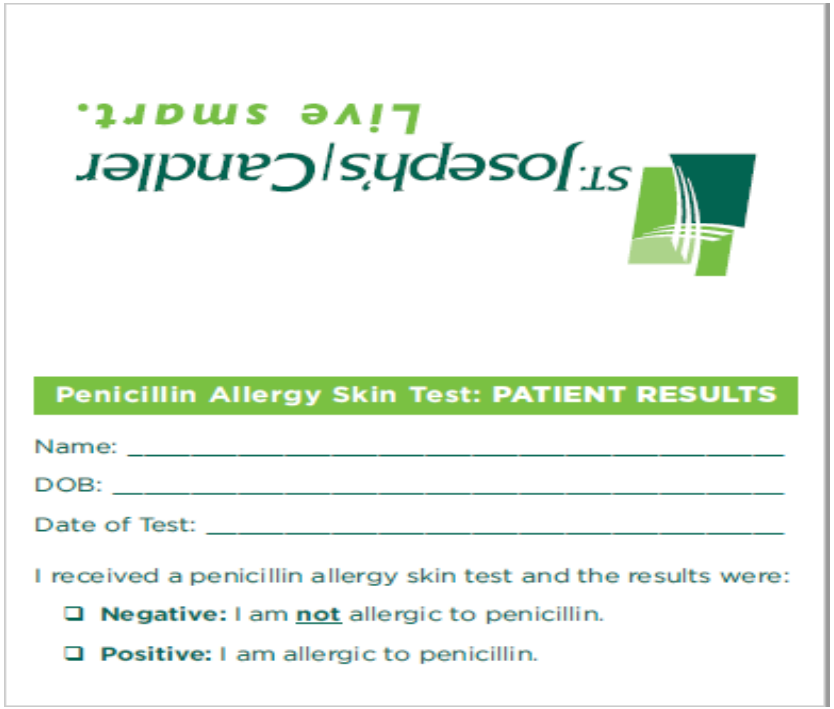
www.alk-abello.com/US/products/PRE-PEN/Pages/PREPEN.aspx

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

Jones, BM. Am J Health Syst Pharm. Feb 2017, 74 (4) 232-237.

Patient Education



St. Joseph's/Candler 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”

Date ▲	Exam/Report	Rpt	Img	Status	Tissue/Code	Dictated By	Dictated	Hx
01/08/16 07:11	General Surgery Progress Note			Signed			01/08/16	
01/08/16 04:44	Infectious Disease Progress Note			Signed			01/08/16	
01/07/16 15:08	Skin Test Results			Signed		Jones,Bruce	01/07/16	
01/07/16 13:48	Chest X-Ray			Signed			01/07/16	
01/07/16 08:44	Consultation			Signed			01/07/16	

Jones, BM. Am J Health Syst Pharm. Feb 2017, 74 (4) 232-237.

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