

Breaking the Allergy Barrier: Optimizing Delabeling with Cefazolin Test Doses and Amoxicillin Challenge

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Objectives

- Describe the epidemiology and clinical impact of inaccurate β -lactam allergy labels
- Differentiate risk categories for penicillin allergies
- Apply evidence-based protocols for conducting cefazolin test doses and oral amoxicillin challenges
- Implement practical strategies to integrate test-dose–based delabeling into hospital policies and interdisciplinary care pathways.
- Evaluate operational barriers solutions for de-labeling programs
- Discuss key lessons learned from regarding clinical implementation, patient safety, and operational efficiency when introducing cefazolin test dosing and oral amoxicillin challenge protocols for penicillin-allergy delabeling



Background

Quick facts: inaccurate labels

Studies indicate that over 90% of penicillin allergy labels are inaccurate

Childhood allergies often low risk

Cross sensitivity between beta-lactams is often low

Remain on medical record without evaluation

Negative impacts



Suboptimal prescribing



Higher cost



Greater risk for adverse effects



Increased resistance

Allergy risk stratification



Low risk

Childhood, family history of, headache, GI symptoms, mild rash/urticaria(>5 yr)



Moderate risk

Systemic hypersensitivity or rash/urticaria(<5 yr)



High risk

Anaphylaxis, severe cutaneous reactions, angioedema, acute interstitial nephritis, drug induced liver injury, serum sickness or isolated drug fever(<5 yr)

*factors may vary based on study

Cross sensitivity risk

Beta-lactam Antibiotic Cross-Reactivity

		Allergy history																						
		Penicillin	Oxacillin	Dicloxacillin	Amoxicillin (Amox/Clav)	Ampicillin (Amp/Sulb)	Piperacillin/Tazo	Cephalexin	Cefazolin	Cefoxitin	Cefuroxime	Cefdinir	Ceftazidime	Ceftriaxone	Cefotaxime	Cefepime	Ceftaroline	Ceftolozane/Tazo	Meropenem	Ertapenem	Imipenem	Aztreonam		
Desired Beta-lactam	Penicillins	Penicillin	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	
	Oxacillin	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	
	Dicloxacillin	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	
	Amoxicillin (Amox/Clav)	X	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	
	Ampicillin (Amp/Sulb)	X	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	
	Piperacillin/Tazo	X	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	1st Gen	Cephalexin	X	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Cefazolin	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	2nd Gen	Cefoxitin	X	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Cefuroxime	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Cefdinir	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	3rd Gen	Ceftazidime	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Ceftriaxone	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Cefotaxime	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	4th Gen	Cefepime	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Non-Gen	Ceftaroline	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Carbapenem	Ceftolozane	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Meropenem	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Ertapenem	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
	Imipenem	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△
Mono	Aztreonam	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	△	

THE POSSIBILITIES



Reactivity linked to side chain



Many beta-lactam pose low risk of reaction

Terico AT et al. J Pharm Pract. 2014;27(6):530-44.
Gaeta F et al. J Allergy Clin Immunol. 2015;135:972-976.



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Optimizing Antibiotic Selection: Safety, Stewardship, and Cost

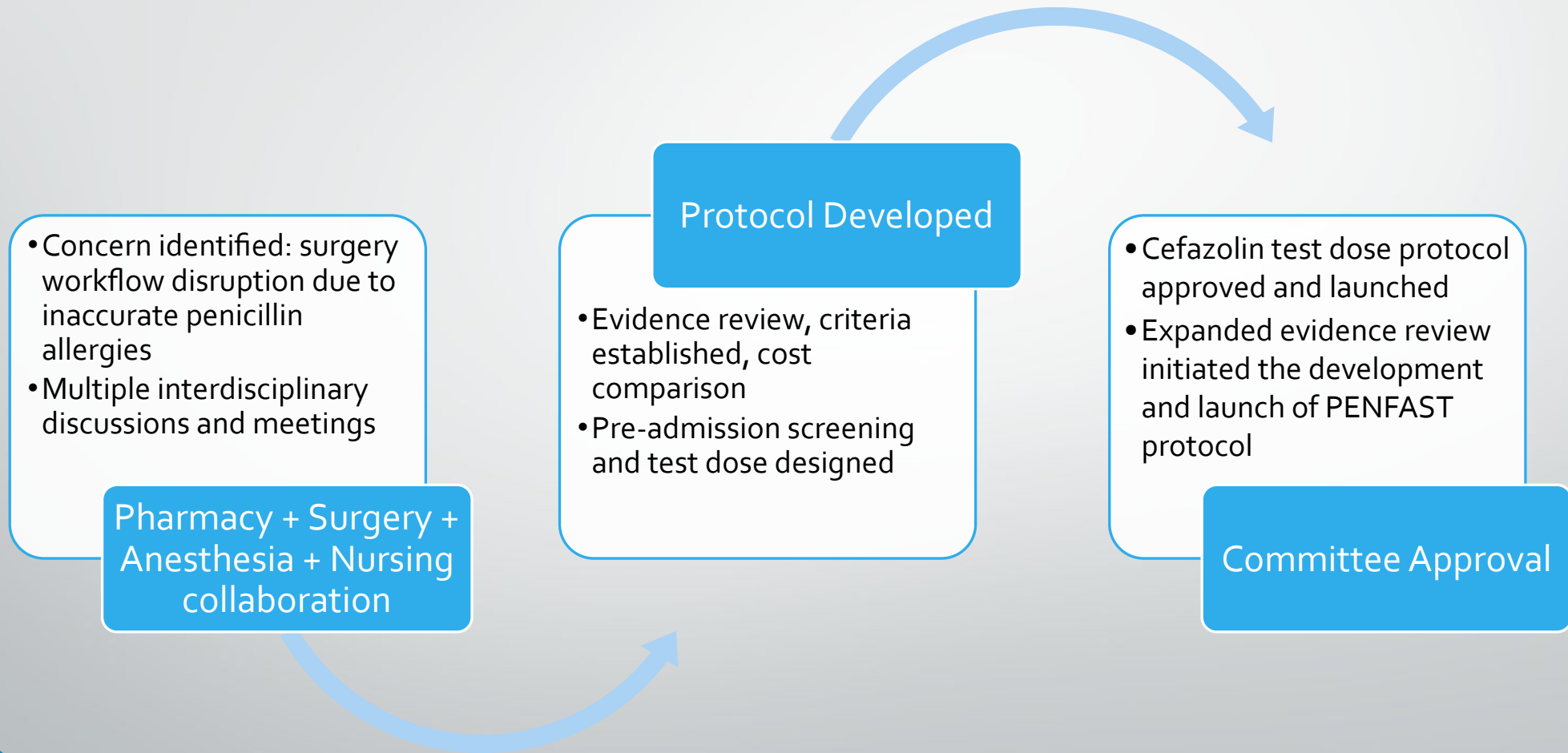
- Guidelines support use of oral and/or skin test doses to enable beta-lactam use in low-risk patients
- Regimens used in patients with penicillin allergies often include 2nd line alternatives or agents with higher risk profiles
 - Vancomycin, clindamycin, fluoroquinolones, aminoglycosides
- Cost of using alternative agents can range from 1.5-6x higher than beta-lactam 1st line monotherapies



AMS projects


WRH

Process for Developing Test Dose Protocols



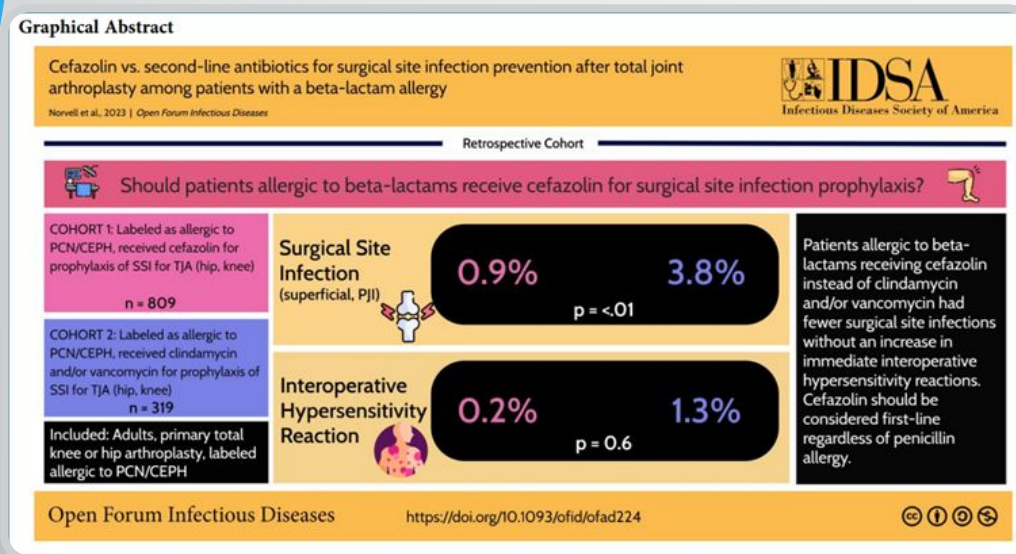
Two Projects

- Perioperative cefazolin skin-testing
- PEN-FAST questionnaire and oral amoxicillin challenge in low-risk patients



Project #1: Perioperative cefazolin skin testing

Antibiotic Selection for Surgical Prophylaxis in Penicillin-Allergic Patients



<https://doi.org/10.1093/ofid/ofad224>

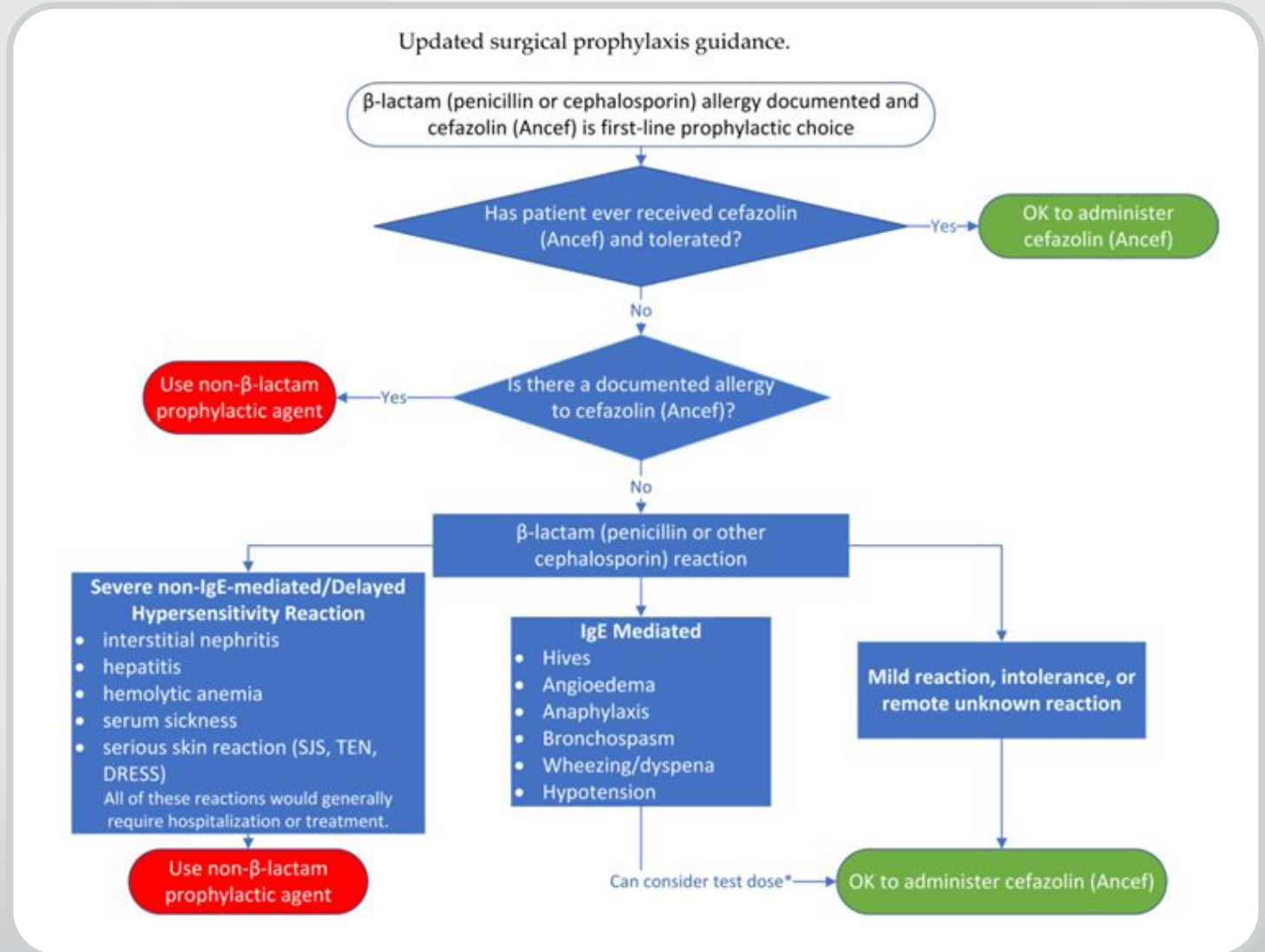
- Patients with beta-lactam allergies often receive clindamycin or vancomycin due to concerns about hypersensitivity reactions (HSRs) to cefazolin.
- Cefazolin use in patients labeled as beta-lactam allergic during TJA reduces postoperative SSIs without increasing the risk of interoperative HSRs

Project #1: Perioperative cefazolin skin testing

- To increase perioperative cefazolin usage and decrease vancomycin usage our facility implemented a cefazolin skin test protocol
- Patients with beta-lactam allergies were challenged with a cefazolin skin test prior to procedure where cefazolin was the preferred planned perioperative antibiotic

Cefazolin test dose protocol

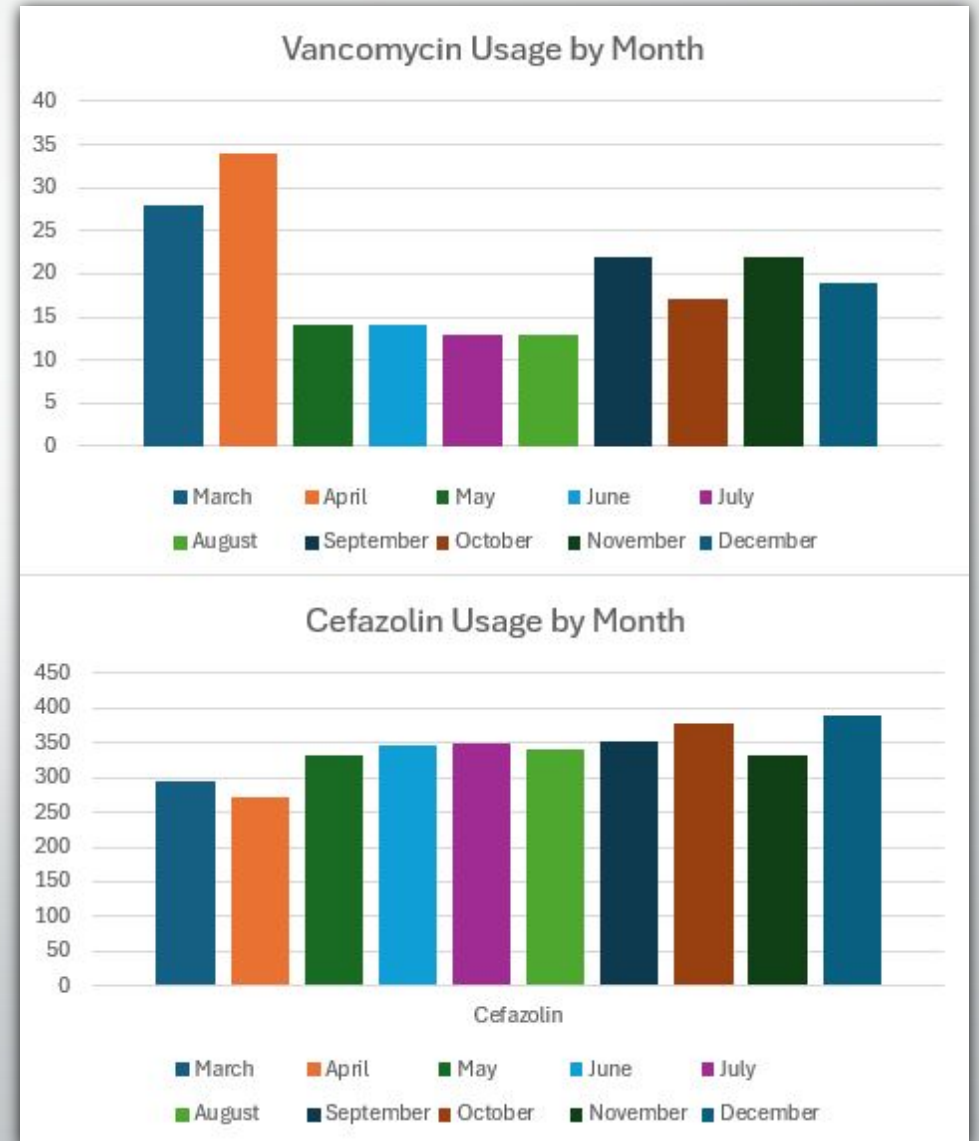
- During preoperative workflow nurse identifies patients with allergies listed
- Algorithm is used to determine if cefazolin is safe to give or if skin test indicated
- Patients that qualify are given intradermal skin test
- Negative skin test results are captured in the chart via special indicator and allergy label comments




Cefazolin test dose protocol outcomes

- Test dose protocol launch 4/21/25
- Before time 3/1/25-4/20/25, after time 4/21/25-12/31/25
- Results indicated a
 - 50% decrease in vancomycin use and
 - 21% increase in cefazolin use

Total Usage for Each Time Frame	Before	After
	3.1-4.20	4.21-12.31
Vancomycin	55	142
Cefazolin	478	2947





Project #2: PEN-FAST questionnaire and
oral amoxicillin challenge in low-risk
patients

Penicillin allergy de-labeling with oral challenge

- Multiple studies indicate penicillin de-labeling utilizing risk stratification and challenges can be safe and effective
- Palace trial(Vanderbilt)
 - Penfast+oral amox challenge vs. skin testing
 - Outcomes indicated non-inferior, as safe as standard testing in low-risk patients
- Facility implemented de-labeling protocol utilizing PENFAST and oral amox challenge
 - Oracle trial
 - Supported safety and feasibility of protocol implementation
 - Propel trial
 - Palace trial protocols, education and health record tools enabled expansion of protocol across facility(Vanderbilt)

PEN	Penicillin allergy reported by patient	<input type="checkbox"/> If yes, proceed with asse
F	Five years or less since reaction ^a	<input type="checkbox"/> 2 points
A	Anaphylaxis or angioedema	<input type="checkbox"/> 2 points
	OR	
S	Severe cutaneous adverse reaction ^b	
T	Treatment required for reaction ^a	<input type="checkbox"/> 1 point
		<hr/> <input type="checkbox"/> Total points

Interpretation

Points

- | | |
|------------------------------|--|
| <input type="checkbox"/> 0 | Very low risk of positive penicillin allergy test <1% (<1 in 100 patients reporting penic |
| <input type="checkbox"/> 1-2 | Low risk of positive penicillin allergy test 5% (1 in 20 patients) |
| <input type="checkbox"/> 3 | Moderate risk of positive penicillin allergy test 20% (1 in 5 patients) |
| <input type="checkbox"/> 4-5 | High risk of positive penicillin allergy test 50% (1 in 2 patients) |

Project #2: PEN-FAST questionnaire and oral amoxicillin challenge in low-risk patients

- Patients with reported penicillin allergies admitted to the PCU were evaluated using the PEN-FAST questionnaire
- The questionnaire stratifies patients into categories of having an immediate hypersensitivity to penicillin from
 - <1% (very low risk) up to
 - 50% (high risk)
- Patients with low risk were invited to have their allergy history challenged by ingesting 250 mg amoxicillin and be monitored for signs and symptoms of reaction
- Patients that don't have a reaction after 24 hours are able to have their penicillin allergy delabeled

Progressive care unit statistics



30-bed PCU

Typically, at full capacity

The unit manages a diverse spectrum of internal medicine diagnoses



On average, 1 patient per day admitted to PCU has a documented penicillin allergy

Procedure overview

- Nursing PENFAST assessment completed with routine allergy assessment, which generates alert for pharmacy review
- Clinical Pharmacy review includes pharmacist confirmation of score, patient interview and consent
- Oral challenge administered to patients that meet all criteria
 - Patient monitoring for immediate(30 min x2), and again at 24 hr post admin
- Negative oral challenge results in allergy removal, pharmacy challenge chart documentation and special indicator addition

Nursing Assessment

- Nurse completes on initial allergy assessment
- Generates report to pharmacy to review for interview and potential amoxicillin challenge

		Tue Sep 2 13:08 by TW
Interventions	PENFAST	✓
Assessments	PENFAST Assessment	✓
Pre-PENFAST Questions		
*Does patient have a documented penicillin allergy?	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	
*Is the penicillin allergy nausea/vomiting/diarrhea/headache?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Unknown	
*Does the patient penicillin allergy involve acute interstitial nephritis, drug-induced liver injury, serum sickness or isolated drug fever?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Unknown	
PENFAST Questions		
*Has it been 5 or fewer years since the allergic reaction?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Unknown	
*Did the patient experience anaphylaxis or angioedema OR severe cutaneous reaction?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Unknown	Severe cutaneous reactions include - Stevens-Johnson Syndrome, - Toxic Epidermal Necrolysis, - severe delayed rash with mucosal involvement
*Was treatment required for any reaction that occurred (eg antihistamines, steroids, or epinephrine)?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Unknown	
PENFAST Result		
*PENFAST Score	0	
*PENFAST Result Interpretation	Very low risk of positive penicillin allergy test <1%	

What is PEN-FAST?

PEN-FAST is a simple scoring tool doctors use to figure out if a penicillin allergy is **likely to be real**.

It asks questions like:

- Did your reaction happen in the last **5 years**?
- Was the reaction **serious**, like needing treatment or hospital care?
- Did the symptoms include **severe rash, swelling, or breathing trouble**?

Your score was **low**, which means you're **very unlikely** to have a dangerous reaction to penicillin now.

Because of your low score, it's **safe to try an oral amoxicillin challenge** to help remove the penicillin allergy label.

Pharmacy Interview

Orders

Acute **Test, Allergic-To-Pcn**
 56, M · 01/01/1970
 MRN# WM00000774

ADM IN, WV FLR2E 2102 -A

Acc # WV0000041998 Resus Status Not Ordered No Hx Avail

Search Patient's Chart

Conflicts

Allergies

Penicillins childhood allergy

Problems

No Data to Display

Pharmacies

No Pharmacies on File

Home Meds

[Prescription Monitoring Program](#)
 No Data to Display

My Widget

No Data to Display

Amoxicillin Capsule [Amoxil] 250 mg PO ONCE ONE capsule 02/10/26 15:10 02/10/26 15:11 New

Provider: Oster, Caleb

Source: Provider

Reflexed Orders from Amoxil

Anaphylaxis Kit Orders

Anaphylaxis Kit

Epinephrine

> EPINEPHrine

Fluid

> Normal Saline 0.9% - BOLUS

Albuterol for bronchospasm

> Albuterol Sulfate [Albuterol Sulfate Updraft]

Adjunctive Therapies

> diphenhydRAMINE HCl [Benadryl]

> Famotidine [Pepcid]

> methylPREDNISolone SOD SUCC [SOLU-Medrol]

Amoxicillin Suspension PO [Similar Order Selected](#)

Amoxicillin/Clavulanate Potas PO

Penicillin Allergy De-labeling

Penicillin Allergy De-labeling Add Content Rapid

Oral Amoxicillin Challenge Rapid

PENFAST Score 0

Date consent form uploaded to chart: 12/16/25

Oral Amoxicillin Challenge Education:

Education provided: risks, benefits, and procedure explained to the patient. Nature of penicillin allergy de-labeling, importance of accurate allergy documentation, low-risk profile based on PEN-FAST score, steps of the oral challenge procedure, possible outcomes and what constitutes a reaction.

Amoxicillin Administration:

Date and Time:
 Dose: 250 mg
 Route: PO
 The patient was observed post administration at 30 minutes, 60 minutes, and 24 hours.

Result Rapid

PEN-FAST Result Interpretation

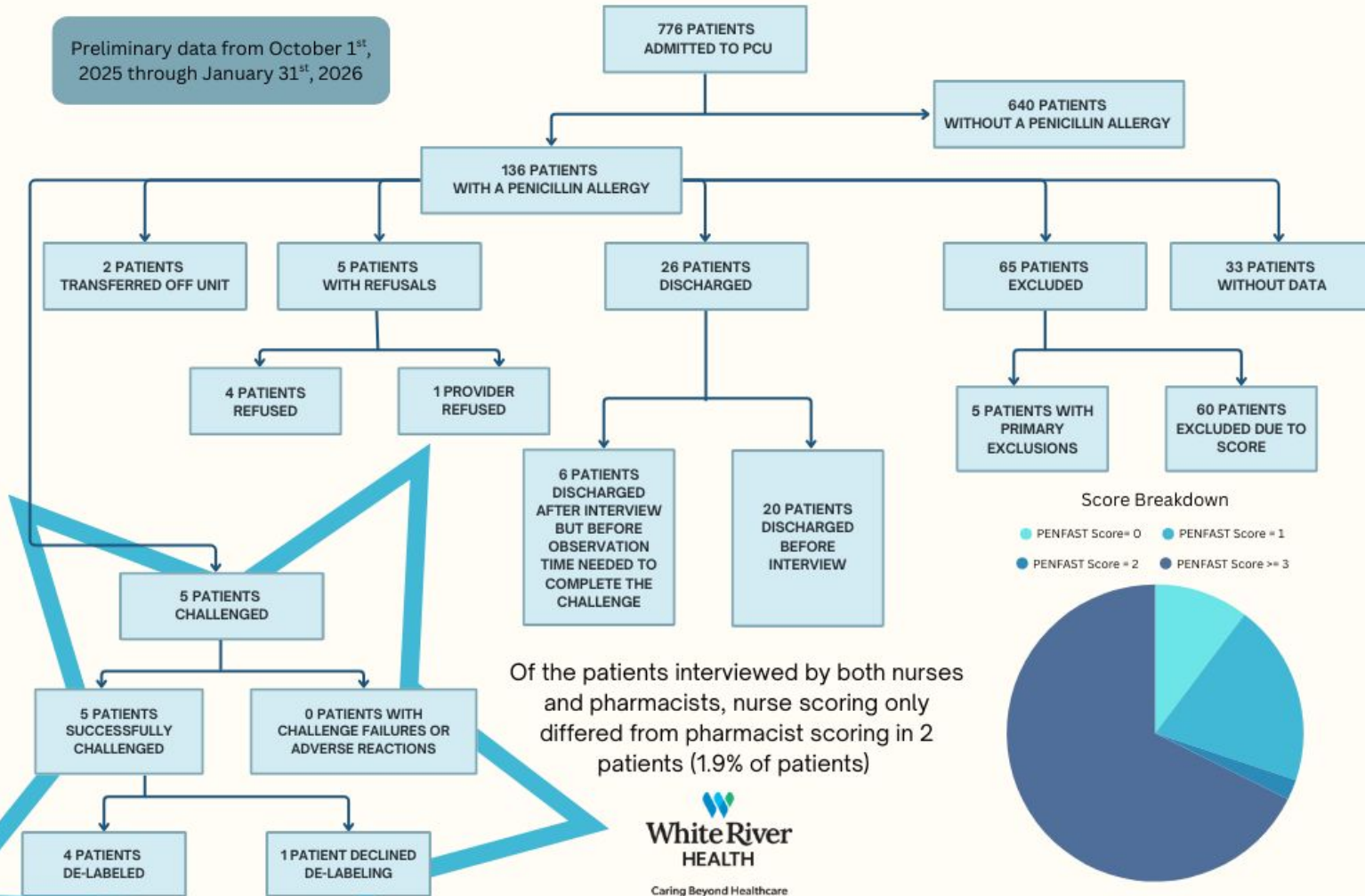
- No reaction observed
- Penicillin allergy negative
- Patient provided with discharge education, allergy removed with special indicator added.

Orders and documentation

De-labeling protocol results

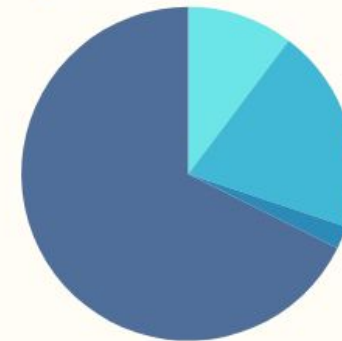
PENICILLIN ALLERGY DE-LABELING PROJECT

Preliminary data from October 1st, 2025 through January 31st, 2026



Score Breakdown

- PENFAST Score = 0
- PENFAST Score = 1
- PENFAST Score = 2
- PENFAST Score >= 3





Implementation debriefing

Implementation debriefing

- What barriers did we have?
- What lessons did we learn?
- How might you implement this at your site?

Barriers	Actions
Protocol development time and resources	Researched established protocols and guidance
IT/system process refinement	Reformatting of logic flow, implementing flow sheet of protocol into system
Nursing workflow/hesitation	Initial and on-going education Real time support and feed back

Barriers

Cefazolin test dose procedure

Barriers	Actions
Assessment/IT issues (clocks, verbiage truncated, LPN view access, transfers issues, print out issues, order entry issues),	All IT related issues were resolved within the initial weeks through close collaboration between IT, nursing and pharmacy departments to troubleshoot and implement necessary fixes.
Nursing workflow/hesitation	Dedicated on-floor support was provided.
Patient hesitation	Additional scripting and education points
Pharmacy band width	Additional pharmacists and residents have been trained to provide support as needed. Efforts to fill existing staffing gaps are underway to enable greater allocation of clinical pharmacist resources and ensure sustained operational efficiency.

Barriers

Penicillin allergy de-labeling

Lessons learned



Multidisciplinary buy-in is critical

Success depends on alignment among all teams involved (management, nursing, pharmacy, etc.)



Operational burden differs by protocol

Resource needs (staffing, monitoring, space)



Clear protocols and procedures are essential

Standardized processes ease transition of new workflows



Education reduces hesitation



Feasibility and sustainability goals must remain flexible

- At present, house-wide implementation is unlikely to be feasible within the band width constraints of a pharmacy-driven protocol.
- Continuation at PCU and ICU level is reasonable for data collection through 3/31/26. After this time frame, reassess for transition to a provider consult-based protocol.
- Shift from proactive pharmacy driven to provider consult driven in conjunction with pharmacy, nursing, etc.



Future
forecast

Tips for implementing protocols

- **Start with low-risk patients**
- **Use simple, standardized protocols**
- **Define clear eligibility and exclusion criteria**
- **Engage key stakeholders early**
- **Integrate protocols into the EHR**
- **Provide targeted clinician education**
- **Streamline documentation**
- **Plan for monitoring and staffing needs**
- **Pilot before scaling**
- **Track outcomes and feedback**
- **Communicate clearly with patients**
- **Remain flexible and adaptable**

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CARING BEYOND HEALTHCARE