

**BREAKOUT SESSION: INTEGRATING PENICILLIN ALLERGY ASSESSMENTS INTO
YOUR PRACTICE**

INPATIENT AND HOSPITAL CURRICULUM



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Case 1 | Optimizing Cefazolin use for Surgical Prophylaxis

Narrative vignette

A hospital identifies higher-than-expected standardized infection ratio (SIR), a national, risk-adjusted metric, of surgical site infections (SSI) among patients carrying a penicillin allergy label. Alternative prophylactic agents such as clindamycin and vancomycin are frequently used instead of cefazolin. Surgeons worry that additional allergy assessments could disrupt workflow. The institution seeks a strategy to safely increase cefazolin use while reducing SSI risk and maintaining perioperative efficiency.

A 450-bed community teaching hospital noted a steady increase in its SIR over the previous 12 months. The overall SIR has increased by 40% since last year.

The Infection Prevention team performed a multidisciplinary review involving surgery, anesthesia, pharmacy, microbiology, and antimicrobial stewardship. Initial investigations found no major lapses in sterile technique, operating room ventilation, or postoperative wound care. Compliance with appropriate timing of prophylactic antibiotic administration (within 60 minutes before incision) remained above 95%.

However, a detailed audit of 300 consecutive surgical cases revealed that only 62% of patients received the guideline-recommended first-line prophylactic antibiotic (cefazolin). Instead, 38% received second-line agents such as clindamycin or vancomycin. Further reviews showed that 70% of patients receiving alternative agents had a documented penicillin allergy.

Background literature & evidence

- According to a meta-analysis of 17 studies, penicillin allergy labeled patients have a 60% increased risk of surgical site infection. Further studies demonstrate that this increased risk is due to the perioperative antibiotic choice (i.e., not using a beta-lactam antibiotic). (PMID: [40122092](#))
- Recent allergy specialist guidelines indicate that cefazolin is safe for use in all penicillin allergy histories (PMID: [36122788](#)). However, many experts will caution regarding history of immediate (e.g., anaphylaxis) and delayed (e.g., SCAR) severe reactions.
- Mass General Brigham and Mayo Clinic algorithms for cefazolin use are included below (Figure 1, 2).
- Dartmouth-Hitchcock's nurse-driven risk-stratification tool, added to the outpatient Perioperative Care Clinic to capture and clarify allergy histories ahead of the OR, significantly increased odds of cefazolin use (aOR 1.67, P = 0.019) and decreased odds of both clindamycin (aOR 0.61, P = 0.010) and vancomycin (aOR 0.56, P = 0.013), with no increase in perioperative anaphylaxis post-implementation. (PMID: [38484506](#)) The pre-op risk assessment is included below (Figure 3).

- Washington University/BJC Hospitals silenced automated penicillin cross-reactivity alerts across six hospitals and found only a modest, sensitivity-analysis-only increase in cefazolin prescribing ($P = 0.03$), with no significant change in SSI rates ($P = 0.32$). (PMID: [41020573](#))

Points for discussion

- What is the cross-reactivity between PCN and Cefazolin?
- Do PCN and Cefazolin share the same R1 side chain?
- Can cefazolin be given to a patient with a PCN reaction of anaphylaxis?
- Can cefazolin be given to a patient with a reaction of SCARS to PCN or cephalosporin?
- What is the best way for your institution to evaluate patients with a PCN allergy to see if they can receive cefazolin for surgical prophylaxis if it is a first line agent for their surgery?
- Should institutions rely on history alone, or is a formal allergy assessment needed? If history alone, who should collect the history, and should a tool or risk assessment be performed?
- Which patients can safely receive cefazolin, and how should that be decided at the point of care?
- How conservative should the institutional algorithm be?
- What is the approach to cephalosporin allergy? Both penicillin and cephalosporin allergy?
- What metrics define success: cefazolin use rate, SSI rate, allergy documentation?

Figure 1. Mass General Brigham Penicillin Allergy Pathway

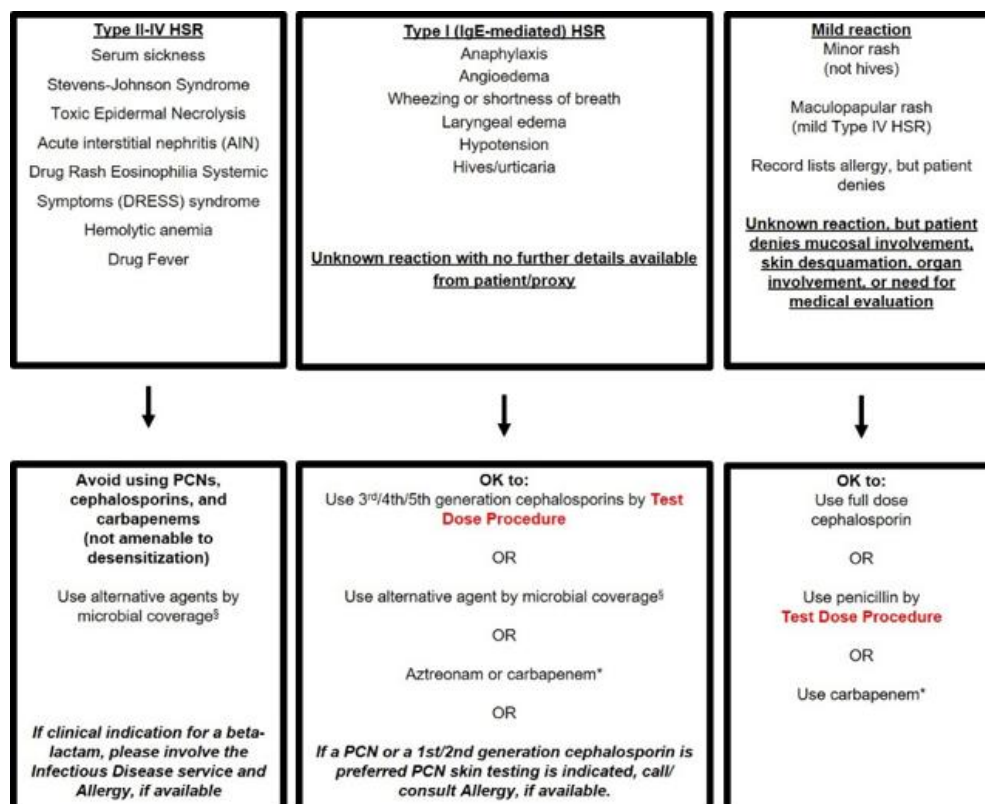


Figure 2. Mayo Clinic CEFPALS algorithm

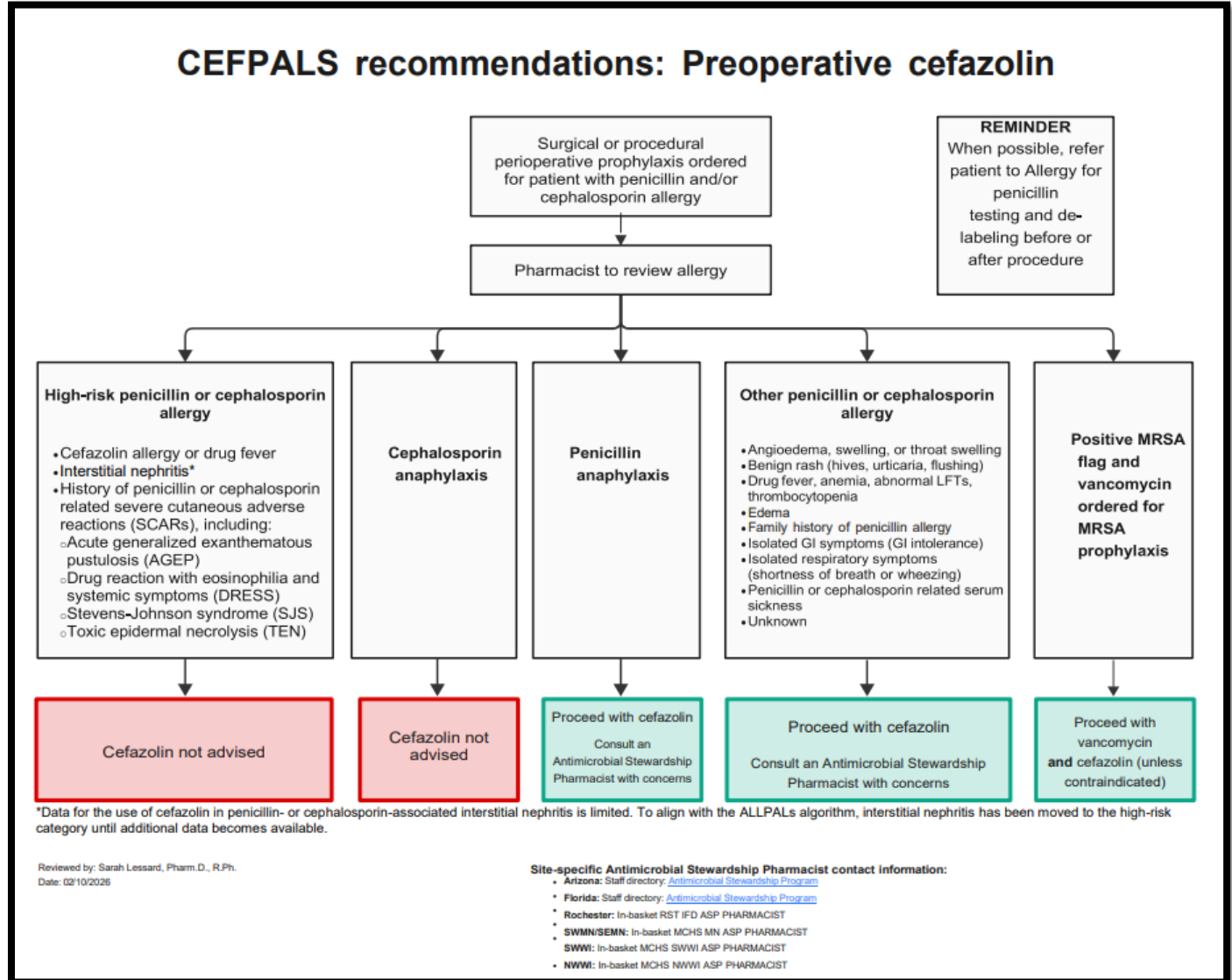


Figure 3. Dartmouth Pre-Op Nursing Allergy History Review

Dartmouth-Hitchcock Medical Center Perioperative Care Clinic Penicillin Allergy Pre-Op Risk Assessment					
1. Since your reaction to penicillin, have you taken any other "cillin" without reacting to it (examples: amoxicillin, Augmentin)? If you are uncertain, select no/unsure. <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;">Yes, I took one of those drugs and I was fine.</td> <td style="width: 50%; padding: 5px; text-align: center;">No / Not Sure</td> </tr> </table>			Yes, I took one of those drugs and I was fine.	No / Not Sure	
Yes, I took one of those drugs and I was fine.	No / Not Sure				
2. Was your reaction to penicillin within the past year? <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;">Yes [Points: +1]</td> <td style="width: 50%; padding: 5px; text-align: center;">No / Not Sure [Points: 0]</td> </tr> </table>			Yes [Points: +1]	No / Not Sure [Points: 0]	
Yes [Points: +1]	No / Not Sure [Points: 0]				
3. Did your reaction cause any other symptoms besides a rash or skin reaction? <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;">Yes [Points: +1]</td> <td style="width: 50%; padding: 5px; text-align: center;">No / Not Sure [Points: 0]</td> </tr> </table>			Yes [Points: +1]	No / Not Sure [Points: 0]	
Yes [Points: +1]	No / Not Sure [Points: 0]				
4. Was your reaction life-threatening (for example, severe anaphylaxis requiring epinephrine, an Emergency Room visit, hospitalization, or intubation)? <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;">Yes [Points: +1]</td> <td style="width: 50%; padding: 5px; text-align: center;">No / Not Sure [Points: 0]</td> </tr> </table>			Yes [Points: +1]	No / Not Sure [Points: 0]	
Yes [Points: +1]	No / Not Sure [Points: 0]				
5. Did your reaction cause blistering, ulceration, peeling of the skin, or affect the inside of your mouth, eyes, or genitals- OR - were you diagnosed with Stevens Johnson Syndrome or Toxic Epidermal Necrolysis? <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;">Yes [Points: +5]</td> <td style="width: 50%; padding: 5px; text-align: center;">No / Not Sure [Points: 0]</td> </tr> </table>			Yes [Points: +5]	No / Not Sure [Points: 0]	
Yes [Points: +5]	No / Not Sure [Points: 0]				
6. Did your reaction affect your internal organs (like your liver or kidneys), cause organ failure -OR- were you diagnosed with serum sickness, vasculitis, drug reaction with eosinophilia (DRESS/DIHS), acute interstitial nephritis, drug-induced hepatitis? <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;">Yes [Points: +5]</td> <td style="width: 50%; padding: 5px; text-align: center;">No / Not Sure [Points: 0]</td> </tr> </table>			Yes [Points: +5]	No / Not Sure [Points: 0]	
Yes [Points: +5]	No / Not Sure [Points: 0]				
7. Are you allergic to cephalosporins, like Keflex? <table border="1" style="width: 100%; border-collapse: collapse; margin-top: 10px;"> <tr> <td style="width: 33%; padding: 5px; text-align: center;">Yes [Points: +1]</td> <td style="width: 33%; padding: 5px; text-align: center;">No [Points: 0]</td> <td style="width: 33%; padding: 5px; text-align: center;">Not Sure [Nurse Review Allergy List]</td> </tr> </table>			Yes [Points: +1]	No [Points: 0]	Not Sure [Nurse Review Allergy List]
Yes [Points: +1]	No [Points: 0]	Not Sure [Nurse Review Allergy List]			
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%; padding: 2px;">Person filling out form:</td> <td style="width: 33%; padding: 2px;">Relationship to patient:</td> <td style="width: 33%; padding: 2px;">Date:</td> </tr> </table>			Person filling out form:	Relationship to patient:	Date:
Person filling out form:	Relationship to patient:	Date:			
_____ Patient questionnaire complete. Do not write below this line.					
Total Points: 					

Case 2 | Inpatient Treatment Decisions: Empiric Antipseudomonal Coverage

Narrative vignette

A patient with septic shock and a reported penicillin allergy requires empiric antipseudomonal therapy. Due to the allergy label, the team defaults to aztreonam. The antimicrobial stewardship team raises concerns regarding susceptibility, delayed optimal therapy, and cost.

A 56-year-old man with a history of type 2 diabetes mellitus and hypertension presents to the emergency department with fever, productive cough, confusion, and weakness. He appears critically ill.

Vital Signs

- Temperature: 39.4°C (102.9°F)
- Heart rate: 132 beats/min
- Blood pressure: 82/48 mmHg
- Respiratory rate: 30 breaths/min
- Oxygen saturation: 90% on room air

Laboratory Results

- WBC: $22.8 \times 10^3/\mu\text{L}$
- Serum lactate: 5.6 mmol/L
- MAP: 59 mmHg

Allergies

- Amoxicillin anaphylaxis
- Cephalexin anaphylaxis

Blood and sputum cultures are obtained and are pending. The patient is diagnosed with septic shock secondary to suspected pneumonia. Aztreonam, vancomycin, and azithromycin are started on the patient. The provider is concerned about *Pseudomonas* due to recent hospitalization and recent use of IV antibiotics. Your hospital antibiogram susceptibility for pseudomonas are below.

Inpatient Antibiogram 2026 (1/1/2025-12/31/2025) Includes ED						
<i>Pseudomonas aeruginosa</i> (715)	Aztreonam 74%	Cefepime 95%	Ciprofloxacin 77%	Meropenem 87%	Tobramycin 96%	Piperacillin/tazobactam 81%

Background literature & evidence

- 106 hospitals with 10,992 inpatients submitted inpatient data on patients with penicillin or cephalosporin allergy labels being treated for neutropenic fever. Patients with documented beta-lactam allergy were less likely to receive first-line neutropenic fever antibiotic agents (36% vs 63%). Compared to patients without documented beta-lactam allergy, patients with allergies had lower cefepime use (36% vs 63%) and higher meropenem use (35% vs 11%). (PMID: [34010699](#))
- Empiric aztreonam use in patients who subsequently grow *Pseudomonas* has been associated with worse outcomes than an antipseudomonal beta-lactam, with one cohort finding empiric therapy failure in 77.8% of the aztreonam group versus 41.9% of the beta-lactam group. (PMID: [30464539](#)) A separate study in septic shock specifically found empiric aztreonam associated with increased mortality compared with beta-lactams. (PMID: [34004470](#))
- Delayed time-to-effective antibiotics are independently associated with increased mortality in septic shock, with each hour of delay linked to roughly a 7.6% rise in mortality. (PMID: [16625125](#), PMID: [28528569](#)) One study of 403 patients in the emergency department found that the average time to first dose of antibiotic treatment for patients with a penicillin allergy was prolonged compared with those without a penicillin allergy (236.1 vs 186.6 minutes; $P = 0.03$), resulting in an approximately 50-minute delay. (PMID: [29032850](#))
- Cross-reactivity between penicillin and cephalosporins depends on side-chain similarity rather than the shared beta-lactam ring; cefepime and ceftazidime do not have similar side chains to penicillin making it a reasonable option for many labeled patients, including those with more severe reaction histories. (PMID: [25930196](#)) Recent allergy specialist guidelines indicate that cephalosporins with dissimilar side chains are safe for use in all penicillin allergy histories. (PMID: [36122788](#))
- Local antibiogram data matter clinically: at one institution, *Pseudomonas* susceptibility was roughly 74% to aztreonam versus 95% to cefepime, meaning an aztreonam-based regimen may under-cover a meaningful share of patients from the outset.
- Aztreonam-based regimens carry hidden costs: because aztreonam lacks gram-positive coverage, patients typically also receive vancomycin, raising antibiotic burden, cost, and *C. difficile* risk relative to a cefepime-based regimen.
- Pharmacist-led screening interventions targeting aztreonam use in labeled patients have shifted prescribing toward more appropriate, antibiogram-guided therapy. A study at a 528-bed tertiary referral community teaching facility reviewed 496 aztreonam orders before and after implementation of a multipronged intervention by the antimicrobial stewardship team and clinical pharmacists, combining a penicillin allergy screening tool, provider education, and order set decision support. Both total and inappropriate aztreonam use decreased significantly (total: 9.5 vs. 4.4; inappropriate: 4.0 vs. 0.8 days of therapy per 1,000 patient-days), with an estimated cost avoidance of \$60,000–\$100,000. (PMID: [26896502](#))
- EHR modifications that silence or redesign cross-reactivity alerts (rather than relying on manual override) have been shown to shift prescribing patterns toward first-line beta-lactam

therapy in both the inpatient and perioperative settings. (PMID: [33914051](#), PMID:[41020573](#))

Points for discussion

- As the inpatient antimicrobial stewardship pharmacist, you are reviewing restricted antimicrobial agents the next day.
- Based on allergy profiles and antibiograms, what antipseudomonal agents would you recommend?
- When is cefepime or ceftazidime preferred over aztreonam? Is there still a role for aztreonam in some patients with penicillin allergy histories?
- What role should pharmacists play in flagging and redirecting aztreonam orders in labeled patients?
- Should EHR alerts be redesigned rather than simply silenced, and if so, what alerts would we want to still have?
- How should local susceptibility (antibiogram) patterns influence institutional policy on broad antibiotic use for labeled patients?
- Are there any allergy histories that give you pause using cephalosporins in penicillin allergy labelled patients?

TABLE XII. Groups of beta-lactam antibiotics that share side chains

R1—Identical side chains					
Amoxicillin	Ampicillin	Ceftriaxone Cefotaxime	Cefoxitin	<i>Cefamandole</i>	Ceftazidime
Cefadroxil	Cefaclor Cephalixin	Cefpodoxime Cefditoren Cefepime	<i>Cephaloridine</i>	<i>Cefonicid</i>	Aztreonam
Cefprozil	<i>Cephadrine</i>	<i>Ceftizoxime</i>	<i>Cephalothin</i>		
<i>Cefatrizine</i>	<i>Cephaloglycin</i>	<i>Cefmenoxime</i>			
R2—Identical side chains					
Cephalexin	Cefotaxime	Cefuroxime	Cefotetan	Cefaclor	Ceftibuten
Cefadroxil	<i>Cephalothin</i>	Cefoxitin	<i>Cefamandole</i>	<i>Loracarbef</i>	<i>Ceftizoxime</i>
<i>Cephadrine</i>	<i>Cephaloglycin</i>		<i>Cefmetazole Cefpiramide</i>		
	<i>Cephapirin</i>				

Italic indicates the drug is not available in United States or manufacturing has been discontinued.
Similar side chains may also be a source of cross-reactivity, see cross-reactivity matrix (see [Fig E2](#)).

Case 3 | Institution-Wide De-labeling Programs

A healthcare system recognizes that penicillin allergy labels contribute to broader-spectrum antibiotic use, higher costs, and longer hospital stays. Leadership must decide between two program models: preemptive de-labeling, which evaluates and clears patients proactively in advance of any specific antibiotic need and reactive de-labeling, which evaluates the allergy only when a therapeutic decision requires it. The two branches below let each table work through the evidence and trade-offs for both models before comparing notes.

Case 3A | Preemptive De-labeling

Narrative Vignette

A health system commits to evaluating and clearing patients before any specific antibiotic need arises, rather than waiting for an acute trigger. Leadership must decide which population to start with and which model to build on.

Background literature & evidence

- Vanderbilt's ICU program used a pharmacist-driven direct oral amoxicillin challenge to safely remove penicillin allergy labels at the point of care in low-risk, critically ill patients including immuno-compromised and multiple-drug-allergy-labeled patients without waiting for a specific therapeutic trigger. (PMID: [35131513](#))
- UT Southwestern built a proactive inpatient penicillin skin-testing service that flagged eligible patients daily through the EMR and tested them ahead of any specific need, reducing use of costly beta-lactam alternatives. This system had a prioritization schema whereby patients were given increased priority if they were currently receiving high-value broad-spectrum agents such as carbapenems or aztreonam or had an immunocompromising condition (diabetes mellitus, HIV infection, active malignancy, or use of immunosuppressant medication) that increased their risk of subsequent infection. (PMID: [27888034](#))

Points for discussion

- Which patients should be prioritized for proactive evaluation: ICU, oncology, broad-spectrum antibiotics, or a broader inpatient population?
- Is universal preemptive de-labeling feasible at your institution, or does it need to start narrowing?
- How should return-on-investment be measured for a preemptive program: cost savings, avoid alternative-antibiotic days, or something else?

Case 3B | Reactive De-labeling

Narrative vignette

Rather than building a proactive program, a system continues to evaluate the allergy only when a specific therapeutic decision requires the traditional "give them what they need clinically and deal with the allergy label later" posture. Leadership wants to understand what this default costs before deciding whether to change it.

Background literature & evidence

- High-cost, high-need patients with a reported penicillin allergy show significantly higher healthcare resource utilization and much greater odds of receiving a beta-lactam alternative than similar patients without the label (adjusted odds ratio 3.84 for alternative antibiotic use). (PMID: [32270982](#))
- MD Anderson Cancer Center targeted immunocompromised cancer patients already receiving aztreonam for a reported penicillin allergy, performing penicillin skin testing followed by an oral amoxicillin challenge. Of those tested, 94% tested negative, and 72% of these were subsequently transitioned to beta-lactam therapy. This intervention significantly reduced aztreonam use (10.0 vs. 8.0 days of therapy per 1,000 patient-days, $P = .005$) and generated \$63,192.61 in projected cost savings. (PMID: [31660339](#))
- Adult inpatients with a penicillin allergy label have a longer average stay length and higher hospital charges than matched patients without it. (PMID: [24188976](#))
- Pediatric data complicates the reactive-vs-preemptive case: one large cohort study found no significant difference in length of stay, readmission rates, or total antibiotic-days between children with and without a beta-lactam allergy label once compared directly, suggesting the adult-population length-of-stay effect may not generalize evenly across ages. (PMID: [32938517](#)) Yet, there is evidence that children with pneumonia labeled with a penicillin allergy with matched children without a PCN allergy label, PCN allergy label was associated with a higher risk of hospitalization (relative risk [RR], 1.15; 95% confidence interval [CI], 1.07-1.23), acute respiratory failure (RR, 1.27; 95% CI, 1.17-1.39), and need for intensive level of care (RR, 1.46; 95% CI, 1.15-1.84). The PCN allergy label resulted in overutilization of broader-spectrum antibiotics and increased complications including cutaneous drug reactions (RR, 2.43; 95% CI, 1.31-4.52) and *Clostridioides difficile* infection (RR, 2.25; 95% CI, 1.14-4.44). (PMID: [36948494](#))
- Pathways implemented across Mass General Brigham used two-step drug challenges to the indicated beta-lactam, rather than prioritizing de-labeling. Studies to date have shown this algorithm led to good antibiotic switches (from vancomycin to a beta-lactam, for example), increased first line therapy for some specific infections, and was safe. Yet, the label likely stayed present for most patients but was modified with information such as tolerance of a specific antibiotic. (PMID: [26070805](#), PMID: [25991471](#), PMID: [30915929](#))
- Similar approaches were done at Dartmouth-Hitchcock (PMID: [35339433](#)), University of California San Francisco (PMID: [37182569](#)) and Mayo Clinic (PMID: [30465860](#)).

Points for discussion

- Should reactive evaluation remain at the default? Is this only appropriate for lower resource settings? How do you consider evidence for children and ICU patients?
- How should the cost/length-of-stay case for preemptive programs be weighed against populations where the effect appears smaller or absent?
- Should the reactive-vs-preemptive decision differ between inpatient and outpatient settings?

Case 4 | The Pharmacist's Perspective: Scope of Practice

Narrative vignette

An inpatient pharmacist encounters a patient with a documented penicillin allergy and must decide how far their own role extends: taking a more detailed allergy history, communicating a recommendation to the ordering physician, doing the de-labeling or starting allergy referrals, or acting as a liaison who bridges the gap between the two.

Background literature & evidence

- Pharmacist-led screening tools targeting aztreonam use in labeled patients have shifted prescribing toward more appropriate, antibiogram-guided therapy: an example of the pharmacist acting past history-taking and into active recommendation. (PMID: [26896502](#))
- A physician-pharmacist team model for inpatient penicillin skin testing and oral challenge effectively removed inaccurate allergy labels, with the pharmacist positioned as the point of contact for both identifying eligible patients and communicating results back to the care team. (PMID: [27888034](#))
- A hospital-based penicillin allergy screening algorithm paired with pharmacist-administered skin testing successfully transitioned hospitalized patients to first-line antibiotic therapy, formalizing the pharmacist's role as liaison between allergy history and prescribing decision. (PMID: [29242142](#))

Points for discussion

- What is the realistic ceiling for pharmacist-led de-labeling at your institution, given your state's scope-of-practice rules?
- Where does the outpatient or community pharmacist fit into a hospital-based de-labeling initiative?
- What activities can pharmacists realistically perform today, what barriers stand in the way, and how should a program be sustained and measured over time?