Penicillin Allergy and Surgical Prophylaxis

Duke University
School of Medicine

dcasip.medicine.duke.edu

Duke Center for
Antimicrobial Stewardship
and Infection Prevention

Background

- Around 8-15% of patients report PCN allergy
  - Only **2-5%** of patients with reported penicillin allergies actually have a positive reaction to penicillin skin testing
- β-lactam antibiotics are preferred agents for treatment and prophylaxis
- Cross reactivity between penicillins and cephalosporins
  - Dependent on specific drug R1 side chain

Rimawi RH, Cook PP, Gooch M. et al. J Hosp Med 2013.
Macy E, Schatz M, Lin C, Poon K-Y. Perm J 2009.
Macy E, Ngor E. J Allergy Clin Immunol Practice 2013.
Charneski L, Deshpande G, Smith SW. Pharmacotherapy 2011.
Unger NR, Gauthier TP, Cheung LW. Pharmacotherapy 2013.
Lee CE, Zembowoer TR, Fotis MA, et al. Arch Intern Med 2000.

Implications of PCN Allergy

A retrospective, matched cohort study with reported penicillin allergy revealed:

- Cases received more fluoroquinolones, clindamycin, vancomycin ($p<0.0001$)
- Had **23.4% more *C. difficile*** (95% CI, 15.6-31.7%)
- Had **more MRSA** (14.1%) **and VRE** (30%) infection
- Had an **increased length of stay** of 0.59 days

Macy E, Contreras R. J Allergy Clin Immunol 2013.

Implications

- Impact of penicillin allergy on surgical site infections (SSI)
  - Retrospective cohort study (N=8385), 2010- 2014
  - Hip or knee arthroplasty, hysterectomy, colon surgery, and coronary artery bypass grafting
- Increase use of alternative agents
- 50% increase risk of SSI
  - SSIs account for 34% of ttl healthcare costs related to HAI, with an estattributable cost of $20,000/case

Pre-op Prophylaxis	Reported PCN Allergy	No Reported PCN Allergy	P value
Cefazolin	12%	92%	<0.001
Clindamycin	49%	3%	<0.001
Vancomycin	35%	3%	<0.001
Gentamicin	24%	3%	<0.001

KG Blumenthal, EE Ryan,Y Li, et al . CID 2018
S Sarfani, C. Stone, G Murphy, et al. JAAOS 2022

PCN allergy & Risk with Cefazolin??

Systematic review/meta-analysis of dual allergy to PCNs & cefazolin

- 77 unique studies, 6147 patients
- Cefazolin allergy identified in **44 patients with a history of PCN allergy (0.7% frequency)**
  - 0.6% in unconfirmed PEN-allergic patients vs 3% in confirmed patients

- Take-home: dual cefazolin/PCN allergy is RARE. Most PEN-allergic patients do just fine with cefazolin (no shared R1/2 side chains). Consider using some caution in recent, confirmed PEN-allergic patients with anaphylaxis

Sousa-Pinto, B et al. *JAMA Surg* 2021;156(4):1-10

Practice parameter

Drug allergy: A 2022 practice parameter update

David A. Khan, MD,[a] Aleena Banerji, MD,[b] Kimberly G. Blumenthal, MD, MSc,[b] Elizabeth J. Phillips, MD,[c,d] Roland Solensky, MD,[e] Andrew A. White, MD,[f] Jonathan A. Bernstein, MD,[g] Derek K. Chu, MD, PhD,[h,i,j] Anne K. Ellis, MD,[k] David B. K. Golden, MD,[l] Matthew J. Greenhawt, MD,[m] Caroline C. Horner, MD,[n] Dennis Ledford, MD,[o,p] Jay A. Lieberman, MD,[q] John Oppenheimer, MD,[r] Matthew A. Rank, MD,[s] Marcus S. Shaker, MD, MSc,[t] David R. Stukus, MD,[u,v] Dana Wallace, MD,[w] and Julie Wang, MD[x]

"Patients with history of anaphylaxis to penicillin, a non–cross-reactive cephalosporin (eg, cefazolin) can be administered routinely without prior testing."

Khan, DA *et al.* JACI 2022 https://doi.org/10.1016/j.jaci.2022.08.028

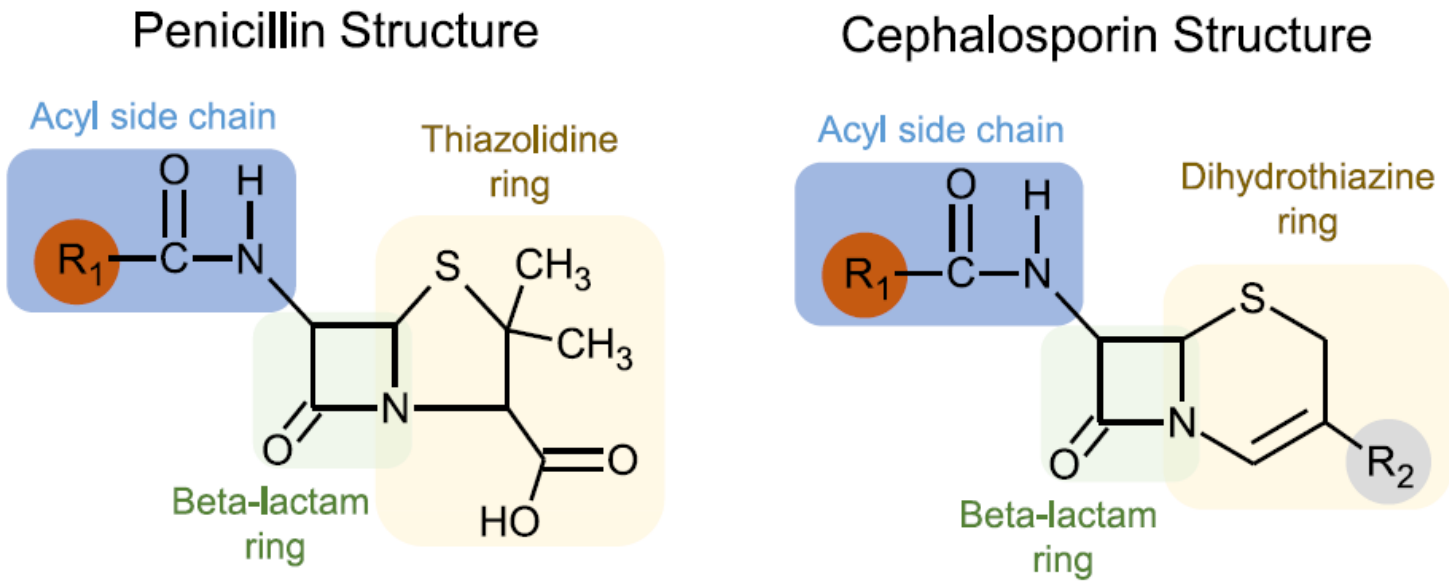


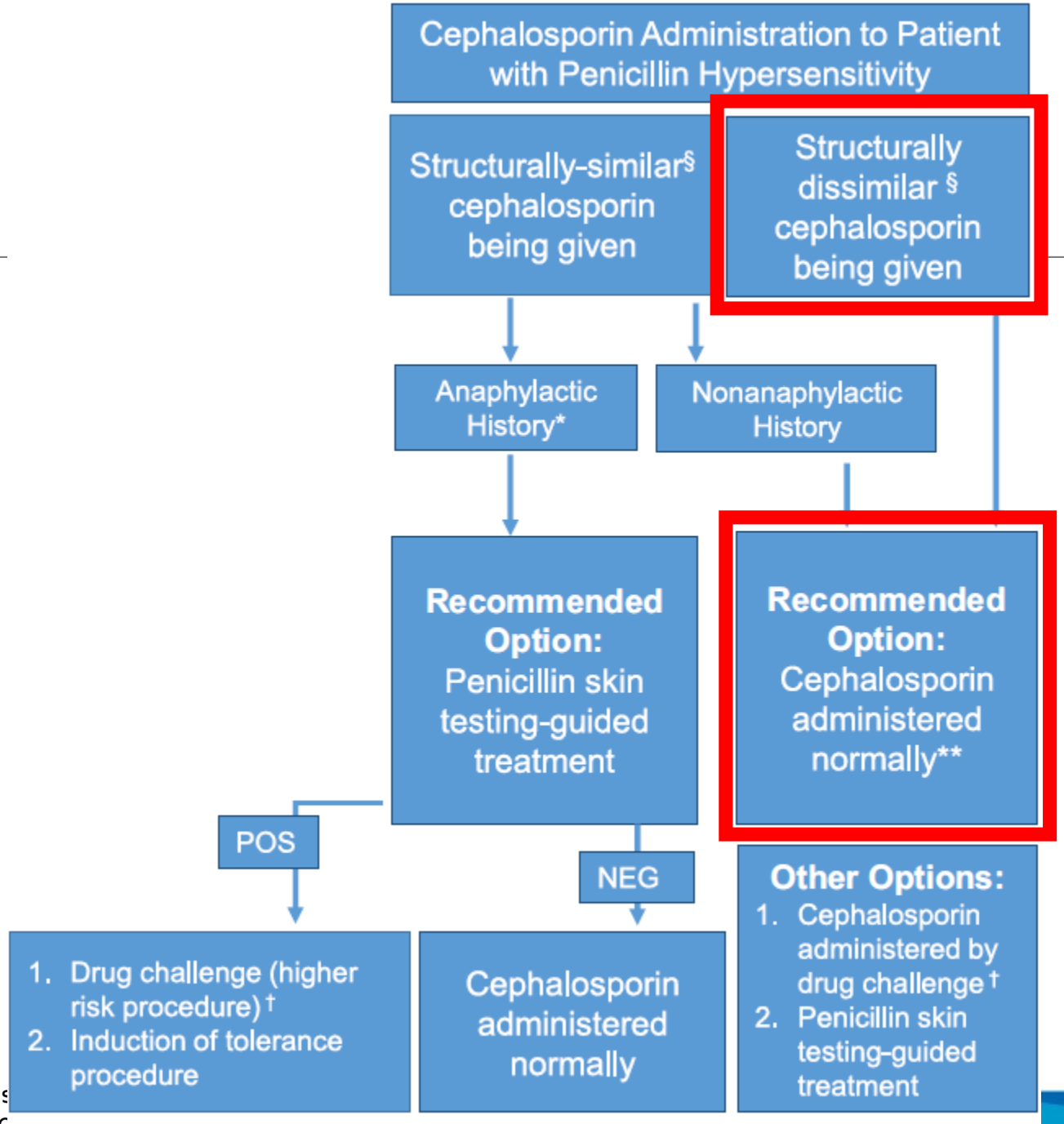
FIG 2. Penicillins and cephalosporins share common structures that are thought to be the source of cross-reactivity: (1) beta-lactam ring, shown in *green*; (2) side chain, or R group with R1 location shown in *red* and R2 location shown in *gray*. Cross-reactivity is largely based on R_1 side chains, with identical side chains in patients with IgE-mediated allergy posing the highest risk. Rarely, cross-reactivity has been demonstrated through R2 side chains and the beta-lactam ring (see Table XII).

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

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

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).

Khan, DA *et al.* JACI 2022 https://doi.org/10.1016/j.jaci.2022.08.028



Khan, DA *et al.* JACI 2022
https://doi.org/10.1016/j.jaci.2022.08.028

ASET Proposal

Update DUHS Surgical Guidance Document

1) Description in definitions

PMMC Approved April 2016, Updated June 2016, November 2016, March 2017, October 2018, May 2022, and XX 2022

Duke University Health System

ADULT PERI-OPERATIVE ANTIBIOTIC PROPHYLAXIS

ANTIBIOTIC TIMING: Antibiotics should be given within the one (1) hour preceding surgical incision. 2 hours are permitted for vancomycin and ciprofloxacin due to longer infusion times.

ANTIBIOTIC DISCONTINUATION: **Continuing antibiotic prophylaxis after closure of incision does not reduce the risk of infection and is unnecessary**. Organizations such as SCIP allow prophylactic antibiotics for up to 24 hours after surgery end time (48 hours for cardiac) but these antibiotics are unnecessary.

***PATIENTS WITH PENICILLIN/CEPHALOSPORIN (BETA-LACTAM) ALLERGIES:** ~~If patient has a documented Type 1 penicillin or cephalosporin allergy, verify that it is a true allergy (Type 1 = shortness of breath, hives, etc). Cephalosporins may be an appropriate option in non-Type 1 penicillin allergies due to limited cross-reactivity with the penicillin class. In the case of true allergy, vancomycin or clindamycin are appropriate alternatives.~~ Alternate regimen (below) recommended for patients with history of confirmed cephalosporin allergy or high-risk PCN allergy (e.g., IgE mediated (swelling of face, throat, angioedema, urticaria, difficulty breathing)); severe skin reaction (eg. SJS); history of kidney or liver injury. Patients with PCN allergy assessed as childhood reaction, intolerance, rash, or IgE mediated reaction may receive cefazolin.

VANCOMYCIN DOCUMENTATION: Reason for using vancomycin must be documented before surgery start.

INTRA-OPERATIVE ANTIBIOTIC REDOSING: Intra-operative redosing of antibiotics should occur at the intervals provided in increments after the time of the first (pre-op) dose.

***Alternate regimen (below) recommended for patients with history of confirmed cefazolin allergy, any cephalosporin anaphylaxis, or high-risk PCN/cephalosporin allergy (e.g. severe skin reaction (eg. SJS); history of kidney or liver injury). In patients with history of anaphylaxis to penicillin, a non-cross-reactive cephalosporin (eg. Cefazolin) can be administered routinely without prior testing. Caution with use of non-cefazolin cephalosporin surgical prophylaxis in patients with history of non-anaphylactic IgE-mediated cephalosporin allergy**

2) Column Header for Alternatives

~~BETA-LACTAM ALLERGY ALTERNATIVE PROPHYLAXIS~~ALTERNATIVE REGIMEN *
clindamycin + ciprofloxacin
clindamycin
vancomycin

3) Unrelated to allergy – Add Mega-prosthesis guidance to document based on review of cases

ORTHOPEDIC SURGERY	
clean operations involving hand, knee, shoulder or foot arthroscopy	prophylaxis is not recommended
total joint replacement	cefazolin
total joint replacement with MRSA risk factors or mega-prosthesis	cefazolin + vancomycin

4) Pediatric Guidelines – no updates needed

Duke University Health System

Pediatric Antibiotic Prophylaxis for Surgical Procedures

This guideline should be for all patients <18 years of age. Pediatric patients weighing more than 40 kg should still receive weight-based doses unless the dose exceeds the recommended adult dose.

ANTIBIOTIC TIMING: Antibiotics should be given within the one (1) hour preceding surgical incision. 2 hours are permitted for vancomycin due to longer infusion time.

ANTIBIOTIC DISCONTINUATION: Continuing antibiotic prophylaxis after closure of incision does not reduce the risk of infection and is associated with the development of antimicrobial resistance.[2] Organizations such as SCIP allow prophylactic antibiotics for up to 24 hours after surgery end time (48 hours for cardiac) but these antibiotics are unnecessary.

PATIENTS WITH PENICILLIN/CEPHALOSPORIN (BETA-LACTAM) ALLERGIES: If a patient has a documented Type 1 penicillin or cephalosporin allergy, verify that it is a true allergy (Type 1 = shortness of breath, hives, anaphylaxis, etc). Cephalosporins may be an appropriate option in non-Type 1 penicillin allergies due to limited cross-reactivity with the penicillin class. In the case of true allergy, vancomycin or clindamycin are appropriate alternatives for Gram positive coverage. For Gram negative coverage, gentamicin is preferred.

VANCOMYCIN DOCUMENTATION: Reason for using vancomycin must be documented before surgery start.

INTRA-OPERATIVE ANTIBIOTIC REDOSING: Intra-operative re-dosing of antibiotics should occur at the intervals provided in increments after the time of the first (pre-op) dose.