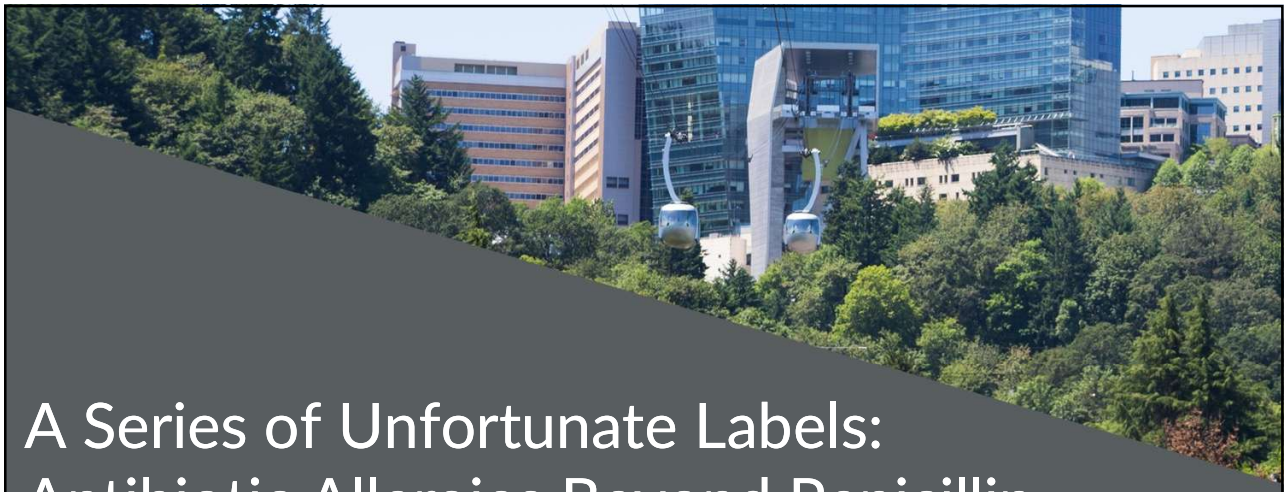

A Series of Unfortunate Labels: Antibiotic Allergies Beyond Penicillin

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Disclosures

- None

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We will talk about…

- Cephalosporin allergies
- Sulfonamide allergies
- Fluoroquinolone allergies
- And some one offs we've done!

Cephalosporin allergies

Case 1

WH is a 50 yo woman who had an allergic reaction to penicillin 4 years ago. She reports that she developed angioedema and her throat started to close up after a dose of ampicillin-sulbactam. She now requires surgery and the first line surgical prophylaxis antibiotic is cefazolin. What would be the most reasonable way to proceed?

1. Prophylaxis with second line, non-beta lactam antibiotic
2. Penicillin Skin Testing, followed by oral challenge
3. Directly to graded oral challenge
4. Give therapeutic dose cefazolin without challenge



Case 2

BN is a 55 yo male who has an allergy of angioedema to cephalosporins in his chart. He is currently neutropenic and has developed a fever. The first line agent for empiric therapy for neutropenic fever at your institution is cefepime, but the team is understandably reluctant given his allergies. You talk to the patient after a detailed chart review and you find that the index reaction was to cephalexin, which he received for cellulitis 10 years ago. What would be the most reasonable way to proceed?

1. Avoid cephalosporins, treat with carbapenem
2. Avoid beta lactams, treat with fluoroquinolone
3. Intravenous challenge with cefepime
4. Give therapeutic dose cefepime without challenge



Cephalosporin allergy evaluation

- Which cephalosporin caused initial reaction?
- How long has it been?
- What cephalosporin are we trying to give?

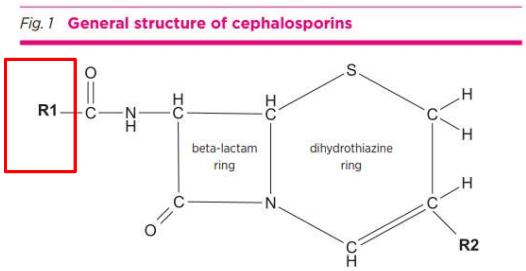
Cross-reactivity for cephalosporins

Loosely grouped into two categories

- Penicillin allergies → cephalosporins
- Cephalosporin allergies → other cephalosporins

Cephalosporin allergies

- Cephalosporin allergies are not a class effect
- Detailed interview can be helpful in narrowing down cephalosporin allergies



Yuson et al. Australian Prescriber Vol 41, N 2. April 2018

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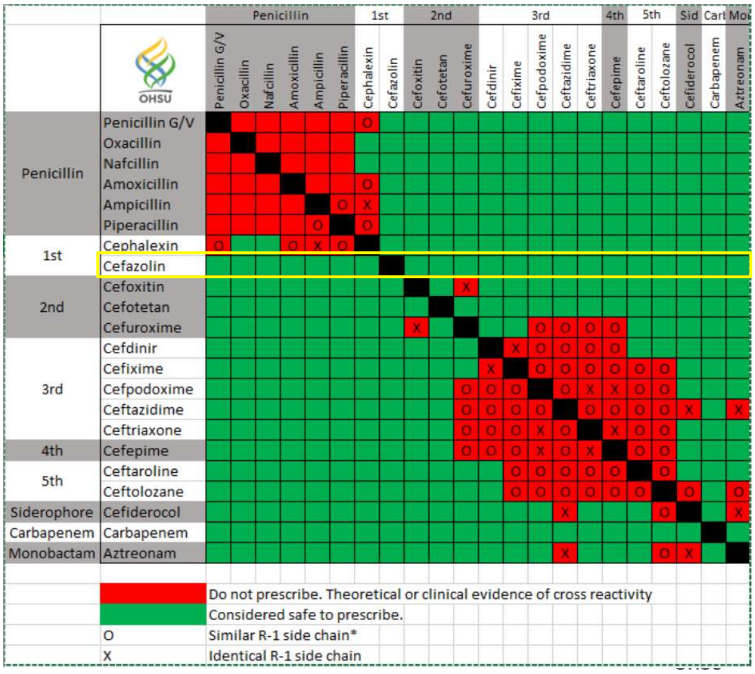
Cross-reactivity

- Early studies were confounded by contamination
- Not a class effect
- Depends on the side chain
- Where's cefazolin?



Systemic interventions

JAMA Network | Open

Original Investigation | Allergy

Association Between Removal of a Warning Against Cephalosporin Use in Patients With Penicillin Allergy and Antibiotic Prescribing

Eric Macy, MD, MS; Thomas A. McCormick, PhD; John L. Adams, PhD; William W. Crawford, MD; Myngoc T. Nguyen, MD; Liem Hoang, PharmD, MS; Victoria Eng, MD; Anna C. Davis, PhD; Elizabeth A. McGlynn, PhD

- Retrospective cohort: 4.2 million patients and 10.7 million antibiotic courses across two Kaiser Permanente regions (2017–2018).
- Intervention: Removed EHR warnings against cephalosporin use in patients with penicillin allergies; compared with region retaining warnings.

JAMA Network | Open

Original Investigation | Allergy

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- Increased cephalosporin use: Prescribing increased from 17.9% to 27.0% of antibiotic courses in penicillin-allergic patients (adjusted relative increase 47%; 95% CI, 38–56%).
- No significant increase in adverse outcomes: No significant differences in anaphylaxis, new allergy labels, treatment failure, mortality, hospitalizations, or C. difficile infections.

Macy E, et al. JAMA Netw Open. 2021;4(4):e218367.

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293 Breaking the Allergy Label: Safety of Inpatient Cefepime Challenges

Shyam Joshi, MD FAAAAI[1], **Tanush Sistla**[2], YoungYoon Ham, PharmD[1]; [1]Oregon Health and Science University, [2]Oregon State University.

- 14 patients undergoing three-step IV graded cefepime challenges (10/100/1000 mg or 20/200/2000 mg).
- 12/14 oncology patients, including 10 with AML.

Joshi S, et al. J Allergy Clin Immunol. 2026;157(2 Suppl):AB102.

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293 **Breaking the Allergy Label: Safety of Inpatient Cefepime Challenges**

Shyam Joshi, MD FAAAAI[1], **Tanush Sistla**[2], YoungYoon Ham, PharmD[1]; [1]Oregon Health and Science University, [2]Oregon State University.

- 13/14 (93%) tolerated challenges, including patients with historical anaphylaxis to another cephalosporin
- 11 patients received cefepime again, with 1 delayed morbilliform rash reported and no additional reactions.

Joshi S, et al. J Allergy Clin Immunol. 2026;157(2 Suppl):AB102.

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Cephalosporin takeaways

- Cephalosporin allergies are not a class effect
- Clarifying which cephalosporin caused the reaction is helpful in deciding which cephalosporins can be given without a challenge
- Challenges are often done with the target cephalosporin

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Sulfonamide allergies

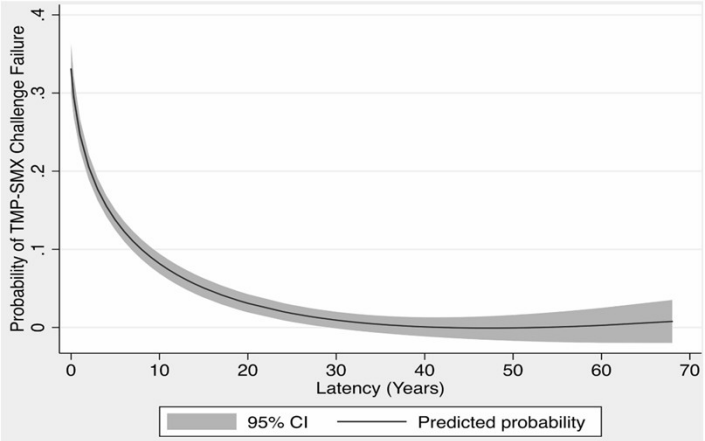
Sulfonamide allergies

- Delayed rashes more common
- Data does suggest high rate of non-reactivity
  - 94% tolerated a single dose oral challenge in one study
- Little concern for cross reactivity between different sulfa agents
  - Sulfasalazine/sulfamethoxazole exception

Krantz MS, Stone CA Jr, Abreo A, Phillips EJ .J Allergy ClinImmunol.2019;143(2):AB209

Reactions fade over time

- Less than 10% after 10 years



Krantz MS, Stone CA Jr, Abreo A, Phillips EJ .J Allergy ClinImmunol.2019;143(2):AB209

Sulfamethoxazole/trimethoprim challenge at our institution

- 2 dose challenge to rule out immediate reaction
- Desensitization can happen on the floor if needed
  - 7 hour process, one dose per hour

P-2118. Pharmacist Led Trimethoprim-Sulfamethoxazole (TMP-SMX) Oral Challenges in a Largely Immunocompromised Population Post Transplant with a Listed Sulfa Allergy

Andrea Chin[1]; Kendall J. Tucker, PharmD, MS[2]; Shyam Joshi, MD[3]; YoungYoon Ham, PharmD[3]; [1]Oregon State University/Oregon Health and Science University, Portland, OR; [2]Oregon State University College of Pharmacy, Portland, Oregon; [3]Oregon Health & Science University, Portland, Oregon

- 88 patients underwent challenge with TMP-SMX
- 75% immunocompromised
- 94% passed initial challenge
- 85% completed treatment or prophylaxis course

Chin A, et al. Open Forum Infect Dis. 2026;13(Suppl 1):ofaf695.2282.

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Fluoroquinolone allergies

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Immediate Hypersensitivity to Fluoroquinolones: A Cohort Assessing Cross-Reactivity

Sara F. Azimi,[a] Vincent Mainella,[a] and Meghan N. Jeffres[b]

Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

- Retrospective cohort of 321 patients with documented allergy to a quinolone who subsequently received a different one.
- Overall cross-reactivity was low: 2.5% (8/321) reacted to the alternative fluoroquinolone.
- Cross-reactivity by index allergy: Ciprofloxacin 2.5%, levofloxacin 2.0%, and moxifloxacin 5.3%.

Azimi SF, et al. Open Forum Infect Dis. 2022;9(4):ofac106.

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So where do we go from here?



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One offs we've done

- Dolutegravir
- Minocycline
- Posaconazole
- Azithromycin
- Vancomycin

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