

## SBAR: Epic changes for penicillin allergies

Summary of literature and proposal

February 2021

### Situation

Cefazolin is the preferred antimicrobial prophylaxis in most surgical procedures due to spectrum of activity, safety, and favorable pharmacokinetics. Use of non-beta lactam antibiotics for surgical prophylaxis is associated with greater risk of surgical site infections (SSI) and adverse reactions.<sup>1</sup>

To align with best practices of improving outcomes and reducing unneeded vancomycin use, all surgical prophylaxis order sets are being updated to replace the wording of recommendations for **severe beta-lactam allergy** to be **severe cephalosporin allergy**. This change makes it more clear on when to choose alternative agents based on allergy history. However, current Epic warnings for cross-reactivity between penicillins and cephalosporins may cause confusion among providers and pharmacists regarding safety.

### Background

Recent literature suggests cefazolin is a safe option in patients with documented penicillin allergies based on unique structural characteristics. Cross-reactivity between penicillin and cephalosporin agents are usually caused by side chain similarities. Compared to all other cephalosporins within its' class, including other first generation cephalosporins, cefazolin contains an R1 side chain that does not cross react with penicillin.<sup>2</sup> While true cefazolin allergies are still possible, these appear to be present at similar rates in both penicillin allergic and non-allergic patients.

### Assessment and Recommendation

Surgical prophylaxis with cefazolin remains safe and the preferred antibiotic in most patients. A vast majority of allergy warnings for cephalosporins are not clinically significant and yet still influence prescribing decisions toward second line therapy despite the low risk of cross reactivity with cefazolin. The studies referenced below, including a new meta-analysis, support the safety and improvement in treatment outcomes when standard of care is prescribed.

Currently all prescriptions for cephalosporins fire an alert for allergies to beta-lactams. Epic is now capable of suppressing alerts for non-severe reactions for cephalosporin orders in patients with penicillin allergies.

To minimize confusion and improve cefazolin prescribing, the Antimicrobial Stewardship Program is proposing to filter beta-lactam allergy warnings in Epic so that only severe reactions documented to penicillins are presented when prescribing other beta-lactam classes (**anaphylaxis, angioedema, SOB, "throat swelling", "trouble breathing", SJS, TEN, DRESS**).

### References

1. Blumenthal KG, Ryan EE, Li Y, et al. The impact of a reported penicillin allergy on surgical site infection risk. *Clin Infect Dis* 2018; 66(3):329-36.
2. Vorobeichik L, Weber EA, Tarshis J. Misconceptions surrounding penicillin allergy: implications for anesthesiologists. *Anesth Analg* 2018; 127:642-9.

## ***New Studies***

### **Assessment of the Frequency of Dual Allergy to Penicillins and Cefazolin: A Systematic Review and Meta-analysis**

- Meta-analysis of 77 studies which included 6147 patients to estimate the frequency of dual allergy to cefazolin and natural penicillin.
- Findings: Of 6,147 patients with a history of penicillin allergy, only 44 (0.7%) had an allergic reaction to cefazolin. Even fewer patients developed a reaction when the penicillin allergy was unknown compared to those with a confirmed history. Data was similar among surgical patients showing again 0.7% of patients with confirmed allergies to cefazolin.

Sousa-Pinto B, Blumenthal KG, Courtney L, Mancini CM, Jeffres MN. Assessment of the Frequency of Dual Allergy to Penicillins and Cefazolin: A Systematic Review and Meta-analysis. *JAMA Surg.* 2021;156(4):e210021. doi:10.1001/jamasurg.2021.0021

### **Perioperative Use and Safety of Cephalosporin Antibiotics in Patients with Documented Penicillin Allergy**

- Review of the tolerability of cephalosporin use perioperatively in patients with a documented penicillin allergy.
- Classification: 8,770 surgical patients with a documented penicillin allergy were reviewed and classified as high risk (swelling, hives, shortness of breath/wheezing, hypotension, unknown/no listed reaction) or low risk (itching, rash, abdominal pain, N/V, diarrhea and other). 55% patients were classified as high-risk reaction, 45% were classified as low risk. 9.6% had a concurrent cephalosporin allergy.
- Findings: Of these 8,870 patients, 79% of these patients received a beta lactam perioperatively. Only 0.1% (9 patients) developed a hypersensitivity reaction. Findings show that the risk of developing a hypersensitivity reaction with a history of penicillin allergy was comparable (or lower) than that with structurally dissimilar antibiotics such as clindamycin

Anstey KM, Anstey JE, Doernberg SB, Chen LL, Otani IM. Perioperative use and safety of cephalosporin antibiotics in patients with documented penicillin allergy. *J Allergy Clin Immunol Pract.* 2021 Aug;9(8):3203-3207.e1. doi: 10.1016/j.jaip.2021.03.017. Epub 2021 Mar 23. PMID: 33766583.

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

- A retrospective cohort study evaluating antibiotic selection among physicians by removing all cephalosporin alerts hospital wide in patients with a penicillin allergy.
- Findings: 4,206,480 patients total were included (2,252,525 at intervention site, 1,953,955 at comparison site) and 10,652,014 antibiotic courses were analyzed. In penicillin allergic patients, cephalosporin prescribing rates increased from 17.9% to 27% when the alert was turned off. Despite this increased use, there was no significant difference in anaphylaxis rates, allergies to new antibiotic classes, antibiotic treatment failure, or all-cause mortality. Penicillin allergic patients did however have worse outcomes compared to those without a penicillin allergy “suggesting higher rates of new antibiotic allergies among patients with a penicillin allergy who receive any antibiotic compared with patients without a penicillin allergy”.

Macy E, McCormick TA, Adams JL, et al. Association Between Removal of a Warning Against Cephalosporin Use in Patients With Penicillin Allergy and Antibiotic Prescribing. *JAMA Netw Open.* 2021;4(4):e218367. doi:10.1001/jamanetworkopen.2021.8367