

# β-Lactam Exposure Outcome in Patients with a Documented Allergy to Penicillins Post-Implementation of a New Electronic Medical Record System and Alerting Rules at Lions Gate Hospital



Brittany Buffone, Pharm.D. Candidate; Jonathan Schwarz, Pharm.D. Candidate; Jennifer Grant, M.D.; Salomeh Shajari, B.Sc.; Yu-Chen Lin, Pharm.D.

## Background

- In April 2018, Lions Gate Hospital (LGH) transitioned from paper charts to a new electronic medical record (EMR) system. Simultaneously, the alerting rules for β-lactam antibiotic prescribing were adjusted.
- Previously, prescribers were alerted when prescribing any penicillin, cephalosporin or carbapenem for a patient with an allergy to penicillins.
- The new alerting rules are triggered when a prescriber orders any penicillin, cefadroxil, cephalixin or cefoxitin for a patient with an allergy to penicillins. This reflects recent studies suggesting that type-1 hypersensitivity cross-reactivity between penicillins and other β-lactam antibiotics is due to side chain similarity and not core β-lactam rings as previously hypothesized.
- Note: cephalothin, cefaclor and cefprozil were not built into the alerting rules as they are off market or rarely used.*

## Objective

- To assess and confirm the safety of the new alerting rules
- Primary:** Determine the prevalence of anaphylaxis secondary to β-lactam antibiotic exposure in patients with documented allergies to penicillins
- Secondary:** Document reports of non-anaphylactic adverse reactions

## Methods

- Design:** Retrospective chart review of EMR at LGH
- Study Period:** April 2018 to July 2019
- Inclusion Criteria:** Patients who were prescribed a β-lactam antibiotic and had a documented allergy to penicillins
- Exclusion Criteria:**
  - Prescribed a β-lactam antibiotic prior to allergy documentation
  - Allergy status changed to “cancelled” prior to β-lactam antibiotic exposure
  - Prescribed a β-lactam antibiotic but never received it according to the Medication Administration Record (MAR)
- Chart Review:** Performed for the first β-lactam antibiotic exposure post-documentation of an allergy to penicillins. Given the anticipated volume of eligible patients, a 25% sample was randomly selected for 30-day chart review post-exposure.
- Sample Validation:** To validate the 25% sample, prescribing patterns of alerted versus non-alerted β-lactam antibiotics were compared between the sample and total population. To approximate prescribing patterns in the total population, the first β-lactam antibiotic ordered for all patients with a documented allergy to penicillins was recorded. Unlike the sample population, administration was not confirmed against the MAR.
- Statistical analysis:** Statistical analysis performed with Microsoft Excel.

Figure 1: Type-1 Hypersensitivity Cross-Reactivity of β-Lactam Antibiotics & New Prescribing Alerting Rules

	Penicillin	Amoxicillin	Ampicillin	Cloxacillin	Piperacillin	Ticarcillin	Cefadroxil	Cefazolin	Cephalixin	Cephalothin	Cefaclor	Cefprozil	Cefuroxime	Cefoxitin	Cefixime	Cefotaxime	Ceftazidime	Ceftriaxone	Cefepime	Meropenem	Imipenem	Ertapenem	Aztreonam
Penicillin	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆				◆									
Amoxicillin	◆	◆	◆	◆	◆	◆	◆		◆		◆	◆											
Ampicillin	◆	◆	◆	◆	◆	◆	◆		◆		◆	◆											
Cloxacillin	◆	◆	◆	◆	◆	◆	◆																
Piperacillin	◆	◆	◆	◆	◆	◆	◆																
Ticarcillin	◆	◆	◆	◆	◆	◆	◆																

Legend: ◆ Risk of type-1 hypersensitivity cross-reactivity; ■ Alerted upon prescribing as per new alerting rules

## Results

Table 1: Prescribing of Alerted versus Non-Alerted β-Lactam Antibiotics

	Sample Population (n=325)	Total Population (n=1292)
<b>Alerted β-lactam Antibiotics</b>	25 (7.7%)	167 (12.9%)
<b>Non-Alerted β-lactam Antibiotics</b>	300 (92.3%)	1125 (87.1%)

Table 2: Patient Demographics

	n (%)
<b>Sex</b>	
Female	214 (65.8)
Male	111 (34.2)
Total	325
<b>Age (in years)</b>	
Mean (range)	63 (7-103)
Median	66
<b>Allergy</b>	
Penicillin	173 (49.0)
Penicillins (drug class)	110 (31.2)
Other penicillin derivatives	70 (19.8)
Total <sup>1</sup>	353
<b>Allergic Reaction</b>	
Not Documented	175 (45.3)
Rash	72 (18.7)
Hives/urticaria	34 (8.8)
Anaphylaxis	25 (6.5)
Other	80 (20.7)
Total <sup>1</sup>	386

<sup>1</sup> Not equal to sample size as some patients had documented allergies to multiple penicillin derivatives and multiple allergic reactions per allergy.

Table 3: Characteristics of β-Lactam Antibiotics Prescribed

	n (%)
<b>Alerted β-Lactam Antibiotics</b>	
Cephalixin	15 (4.6)
Piperacillin-Tazobactam	7 (2.2)
Amoxicillin	3 (0.9)
Total	25 (7.7)
<b>Non-Alerted β-Lactam Antibiotics</b>	
Cefazolin	201 (61.8)
Ceftriaxone	93 (28.6)
Meropenem	4 (1.2)
Cefixime	1 (0.3)
Cefuroxime	1 (0.3)
Total	300 (92.3)
<b>Most Common Indications</b>	
Surgical Prophylaxis	181 (55.7)
Pneumonia	26 (8.0)
Cellulitis	24 (7.4)
Other	94 (28.9)
<b>Duration of Exposure (in days)</b>	
Mean (range)	2 (1-14)
<b>Duration of Chart Review Post-Exposure (in days)</b>	
Mean (range)	9 (1-30)

Table 4: Primary and Secondary Outcomes

	n (%)
<b>Primary Outcome</b>	
Anaphylaxis	0 (0)
<b>Secondary Outcome</b>	
Non-Anaphylactic Adverse Reactions	5 (1.5)
Immediate Reactions	1 (0.3)
Delayed Reactions	3 (0.9)
Indeterminate	1 (0.3)

Table 5: Non-Anaphylactic Adverse Reactions

Type of Reaction	Antibiotic	Adverse Reaction
Immediate	Piperacillin	Hives, pruritus
Delayed	Piperacillin	Eosinophilia
	Piperacillin	Eosinophilia, acute kidney injury
	Ceftriaxone	Rash
Indeterminate	Multiple antibiotic exposure including cefazolin and cephalixin	Query delayed rash

## Limitations

- Results were based upon chart review of a 25% sample and not the total population. Nonetheless, comparable prescribing patterns were observed between the sample and total population (Table 1).
- More than 50% of patients were prescribed cefazolin for surgical prophylaxis. While this reflects real life practice, the results of this study are most applicable to validate safety in surgical prophylaxis.

## Conclusions

- The new alerting rules are considered safe given that no anaphylaxis was reported.
- Despite the alerting rules not prompting for delayed (type 2-4) hypersensitivity reactions and a low documentation of allergic reaction history in patient charts, at most, 2 patients (0.6%) experienced non-anaphylactic reactions (delayed rash) secondary to exposure to a non-alerted β-lactam antibiotic.