

Concise Communication

Implementation of a hospital-wide EHR-integrated antibiotic challenge order set

Wesley Hoffmann PharmD¹ , Shivani Patel PharmD¹ , Shemual Tsai PharmD¹ , Natalie Finch PharmD¹  and Muhammad Yasser Alsafadi MD² 

¹Department of Pharmacy, Houston Methodist Hospital, Houston, TX, USA and ²Division of Infectious Diseases, Houston Methodist Hospital, Houston, TX, USA

Abstract

We implemented an electronic health record-integrated order set to standardize direct antibiotic challenges for patients with reported antibiotic allergies across nine healthcare facilities. In the first year, 104 patients were challenged (79% oral; 39% two-step). Embedded antibiotic selection, dosage, monitoring parameters, reaction guidance, and rescue medications facilitated uptake by hospitalists and subspecialists.

(Received 6 August 2025; accepted 10 October 2025)

Introduction

Antibiotic allergy labels affect approximately 10% of hospitalized patients, yet over 90% of these labels are inaccurate when formally evaluated.^{1–3} Inaccurate antibiotic allergy documentation leads to the unnecessary use of second-line or broader-spectrum antibiotics, higher healthcare costs, and worse clinical outcomes.^{3–5} Direct oral or intravenous antibiotic challenges in patients with low-risk allergy histories represent a safe and evidence-based strategy to clarify or remove inaccurate labels.^{6–8} However, real-world uptake has been limited due to operational and cultural barriers, including provider hesitation, inconsistent workflows, and time-consuming coordination with nursing and pharmacy staff.^{2,3,5,9}

As part of a multifaceted quality improvement initiative to enhance antibiotic allergy assessment and management, we developed and implemented an electronic health record (EHR)-integrated antibiotic challenge order set across a multi-hospital health system. The purpose of this order set is to make it easier, safer, and more consistent for clinicians to perform direct oral or IV antibiotic challenges in patients labeled as antibiotic-allergic, especially when they are determined to be low-risk based on their allergy history.

Here, we describe its development, key design features, and early utilization experience.

Methods

The quality improvement initiative was conducted across a nine-entity integrated healthcare system comprising an academic

tertiary medical center, seven community hospitals, and one long-term acute care facility, all of which utilized a shared Epic EHR platform. The antibiotic challenge order set was developed collaboratively by infectious diseases physicians, pharmacists, informatics specialists, and an allergy physician. Iterative feedback from these developers and the antimicrobial stewardship team was incorporated prior to formal release.

Figure 1 illustrates the structure and components of the EHR-integrated antibiotic challenge order set. The order set includes (1) selection of oral or IV antibiotic agents, (2) standardized test doses, (3) embedded nursing instructions and monitoring parameters, (4) definitions for mild, moderate, and severe reactions, and (5) preselected rescue medications. It is available to all credentialed prescribers and was promoted through committee newsletters, targeted provider e-mails, and real-time reinforcement by antimicrobial stewardship team members. Allergy risk assessments, patient selection, and order set use were at the discretion of the physician. Challenges may take place on any inpatient unit with bedside nursing monitoring per embedded instructions (vital signs prior to dosing and after each step; observation period specified in the order set). Rescue medications are preselected but not preadministered. Two-step challenges are administered 1 hour apart if the first dose was tolerated. The order set includes a prompt to update the EHR allergy list according to the outcome of the challenge; documentation is completed by the ordering team using an allergy activity update; a template is included with prespecified fields without direct stewardship oversight.

We conducted a retrospective descriptive analysis of the utilization of the order set for the initial 104 consecutive unique patients between June 28, 2024, and July 13, 2025. This project met criteria for quality improvement and did not require IRB oversight, consistent with institutional policy.

Corresponding author: Muhammad Yasser Alsafadi; Email: malsafadi@houstonmethodist.org

Cite this article: Hoffmann W, Patel S, Tsai S, Finch N, Alsafadi MY. Implementation of a hospital-wide EHR-integrated antibiotic challenge order set. *Antimicrob Steward Healthc Epidemiol* 2025. doi: 10.1017/ash.2025.10215

Antibiotic Challenge Orders

Instructions

- Communicate with patient's nurse that you will be performing the procedure
- Nursing to check/document vital signs (blood pressure, heart rate, respiratory rate, O₂ saturation) before dose
- Nursing to administer dose and observe for any signs of reaction at 15-minute time mark and 1 hour time mark after administering dose

Vital Signs

Vital Signs: Temperature, Pulse, Respiratory Rate and Blood Pressure Per Unit Protocol

- **Pre-antibiotic challenge** (routine, per unit protocol, until specified)
- **15 minutes post-antibiotic challenge** (routine, per unit protocol, until specified)
- **1 hour post-antibiotic challenge** (routine, per unit protocol, until specified)

Adverse Reactions Definitions

Mild Reaction:

- Identified as a localized reaction. Swelling (edema) of any body part that does not involve throat/laryngeal area, hives <50% body surface area, itching, flushing, eye redness/tearing, sneezing, runny nose, nasal congestion

Moderate Reaction:

- Identified by more systemic signs or symptoms. Swelling (edema) of any body part that does not involve throat/laryngeal area, hives >50% body surface area, cough/wheezing/dyspnea that responds to albuterol, O₂ sats at baseline, gastrointestinal symptoms including vomiting and diarrhea

Severe Reaction:

- Identified by life-threatening, more severe signs or symptoms. Swelling (edema) of throat/laryngeal area, hives >50% body surface area, respiratory compromise, hypotension with >20 point drop in systolic BP and/or mean arterial pressure <65,

Notify Physician

- Notify physician or advanced practice provider immediately if patient experiences adverse reaction during challenge
- Routine, until discontinued, until specified

Medications

Oral or IV (Intravenous) Test Dose Antibiotics

Oral Test Dose Medications

- Amoxicillin
- Cephalexin

IV Test Dose Medications

- Ampicillin IV
- Cefazolin IV
- Cefepime IV
- Cefoxitin IV
- Ceftazidime IV
- Ceftolozane-tazobactam IV
- Ceftriaxone IV
- Meropenem IV
- Nafcillin IV
- Penicillin G Potassium IV
- Piperacillin-tazobactam IV

If possible, hold the following medications the day of the test dose procedure:

- Beta blockers: inhibit the action of epinephrine
- ACE inhibitors: increase the risk of an allergic reaction

Example: Amoxicillin

- 250 mg/5 mL suspension 50 mg 50 mg, oral, once, 1 dose
- Indication: other
- Specify: oral challenge

Followed by:

- 250 mg/5 mL suspension 500 mg 500 mg, oral, once, 1 dose
- Indication: other
- Specify: oral challenge

Example: Ampicillin

- 200 mg in sodium chloride 0.9% 50 mL IVPB
- 200 mg, intravenous, at 100 mL/hr, administer over 30 minutes, once, 1 dose
- Indication: other
- Specify: IV challenge

Followed by:

- 1,800 mg in sodium chloride 0.9% 100 mL IVPB
- 1,800 mg, intravenous, at 200 mL/hr, administer over 30 minutes, once, 1 dose
- Indication: other
- Specify: IV challenge

Adverse Reaction Management

Epinephrine Injection

- 0.3 mg, intramuscular, once as needed, anaphylaxis, until discontinued, 1 dose
- Administer for moderate and severe adverse reaction

Albuterol Nebulizer Solution

- 2.5 mg, nebulization, once as needed, wheezing, until discontinued, 1 dose
- Administer for moderate and severe adverse reaction
- Aerosol delivery device: hand-held nebulizer

Diphenhydramine Injection

- 25 mg, intravenous, once as needed, anaphylaxis/allergic reaction, until discontinued, 1 dose
- Administer for mild, moderate, and severe adverse reaction

Methylprednisolone Sodium Succinate Injection

- 125 mg, intravenous, administer over 5 minutes, once as needed, anaphylaxis/angioedema, until discontinued, 1 dose
- Administer for moderate and severe adverse reaction

Note: If patient received a beta blocker in the last 24 hours, please order glucagon

Please document any appropriate changes in allergy status once test dose procedure is completed.

Figure 1. Structure of the EHR-integrated antibiotic challenge order set, including antibiotic agent selection, standardized single/two-step dosing options, nursing monitoring instructions, reaction definitions/next steps, as needed rescue medications, and allergy list update documentation prompt.

Table 1. Patient and challenge characteristics

Characteristic	n. of patients (%)
Total unique patients	104 (100%)
Two-step challenges	41 (39%)
Antibiotic challenged*	
• Amoxicillin (PO)	78
• Ampicillin (IV)	6
• Cephalexin (PO)	5
• Cefazolin (IV)	2
• Cefepime (IV)	2
• Ceftazidime (IV)	1
• Ceftriaxone (IV)	4
• Meropenem (IV)	3
• Nafcillin (IV)	1
• Penicillin G (IV)	1
• Piperacillin-Tazobactam (IV)	2
Hospital type	
• Tertiary academic medical center	60 (58%)
• Community hospitals	44 (42%)
• Long-term acute care	0 (0%)
Ordering provider specialty	
• Infectious diseases	85 (82%)
• Hospitalists	19 (18%)
Route of antibiotic challenge	
• Oral	82 (79%)
• Intravenous	22 (21%)

*One patient was challenged with two antibiotics on separate occasions. IV, intravenous; PO, by mouth.

Results

During the study period, the order set was utilized for 104 unique patients. A summary of patient and antibiotic challenge characteristics is provided in Table 1. Sixty patients were challenged at the academic tertiary medical center, and 44 at community hospitals. Of all the usages, 85 (82%) were ordered by infectious disease specialists, while the remaining were ordered by hospitalists.

The most frequently challenged agents were amoxicillin ($n = 78$), ampicillin ($n = 6$), cephalexin ($n = 5$), and ceftriaxone ($n = 4$). Challenges were administered orally in 82 patients and intravenously in 22 patients. Forty-one patients (39%) received two-step challenges. Data on partial completions were not captured in this early implementation review.

Discussion

This early implementation experience highlights the feasibility and practical utility of a standardized EHR-integrated order set for direct antibiotic challenges across a diverse hospital system. Uptake by both subspecialist and generalist providers suggests that the order set may help expand participation in antibiotic allergy

de-labeling initiatives. Key facilitators included embedded monitoring instructions, as needed rescue medications, and standardized workflows that reduced ambiguity and supported clinical decision-making.

We did not report on patient demographics or outcomes, as the focus of this analysis was on operational rollout, provider uptake, and usability. Systematic safety monitoring was not conducted, consistent with the prespecified scope of this quality improvement initiative.

Future directions

We plan to integrate the order set into our PEN-FAST-based allergy assessment workflow. This will involve linking low-risk scores to best practice alerts, prompting clinicians to use the antibiotic challenge order set and update allergy lists accordingly. We also aim to monitor process, balancing, and outcome metrics over time, including order set adoption, allergy list updates, and the change in antibiotic utilization trends.

Acknowledgments. The authors would like to thank the information technology, nursing, and allergy teams at Houston Methodist for their collaboration during the design and implementation of the antibiotic challenge order set.

Author contributions. Wesley Hoffmann, Shemual Tsai, Shivani Patel, Natalie Finch, and M. Yasser Alsafadi contributed to the conceptualization and implementation of the order set. Shemual Tsai extracted the data. M. Yasser Alsafadi conducted the analysis and drafted the manuscript. All authors reviewed and approved the final version.

Financial support. None.

Competing interests. None reported.

References

1. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin “allergy” in hospitalized patients: A cohort study. *J Allergy Clin Immunol* 2014;133:790–796.
2. Shenoy ES, Macy E, Rowe T, Blumenthal KG. Evaluation and management of penicillin allergy: a review. *JAMA* 2019;321:188–199.
3. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. *The Lancet* 2019;393:183–198.
4. Blumenthal KG, Lu N, Zhang Y, Li Y, Walensky RP, Choi HK. Risk of meticillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study. *BMJ* 2018;361:k2400.
5. Jeffres MN, Narayanan PP, Shuster JE, Schramm GE. Consequences of avoiding β -lactams in patients with β -lactam allergies. *J Allergy Clin Immunol* 2016;137:1148–1153.
6. Trubiano JA, Vogrin S, Chua KYL, et al. Development and validation of a penicillin allergy clinical decision rule. *JAMA Intern Med* 2020;180:745–752.
7. Kuruvilla M, Shih J, Patel K, Scanlon N. Direct oral amoxicillin challenge without preliminary skin testing in adult patients with allergy and at low risk with reported penicillin allergy. *Allergy Asthma Proc* 2019;40:57–61.
8. Maximos M, Pelletier R, Elsayed S, et al. Unpacking oral challenge protocols: a descriptive epidemiologic study of reactions, predictors, and practices for delabeling low-risk penicillin allergies leveraging data from a systematic review and meta-analysis. *Hosp Pharm*. 2025;60(5):423–431.
9. Sunagawa SW, Bergman SJ, Kreikemeier E, et al. Use of a beta-lactam graded challenge process for inpatients with self-reported penicillin allergies at an academic medical center. *Front Allergy*. 2023;4:1161683.