

PENICILLIN AND CEPHALOSPORIN ALLERGY, INPATIENT, ADULT AND PEDIATRIC

Updated: June 9, 2023

Clinical Pathway Summary

CLINICAL PATHWAY NAME: Penicillin and Cephalosporin Allergy, Inpatient, Adult and Pediatric

PATIENT POPULATION AND DIAGNOSIS:

1. Classifying and assessing risk in patients with a listed adverse reaction or allergy to penicillins and cephalosporins
2. Ordering antibiotics in a hospitalized patient with a history of adverse reaction or allergy to penicillins and cephalosporins

APPLICABLE TO: All Corewell Health Inpatient Hospitals

BRIEF DESCRIPTION: This guideline was developed to help guide providers in their antibiotic choices and consultation of specialty services when appropriate.

Approximately 95% of patients who report a penicillin allergy do not have a true Type I immediate-hypersensitivity (IgE-mediated) allergy to penicillin. Identifying these patients can improve patient care through use of more effective, less costly, and safer antibiotics. For the most part, there is very little cross-reactivity between cephalosporins and penicillins. Early data after cephalosporins were first developed cited a cross-reactivity of 10-20% in patients with penicillin allergy, but those drugs were contaminated with trace amounts of penicillin. The true rate of cross-reactivity is much lower and depends on common side chains (usually the “R1 side chain”) between the penicillin/aminopenicillin and cephalosporins rather than the common beta-lactam ring. Conversely, with Type I hypersensitivity reactions to penicillins, IgE is typically specific to the beta-lactam ring or a penicillin derivative and NOT the side-chains. Demonstration of amoxicillin tolerance enables future use of all penicillin antibiotics, including aminopenicillins. Patients with a penicillin allergy do not need to empirically avoid cephalosporins. Additionally, allergy to one cephalosporin does NOT mean that ALL cephalosporins need to be avoided. Rather, avoiding cephalosporins with similar or identical side chain structures is recommended.

OPTIMIZED EPIC ELEMENTS (if applicable):

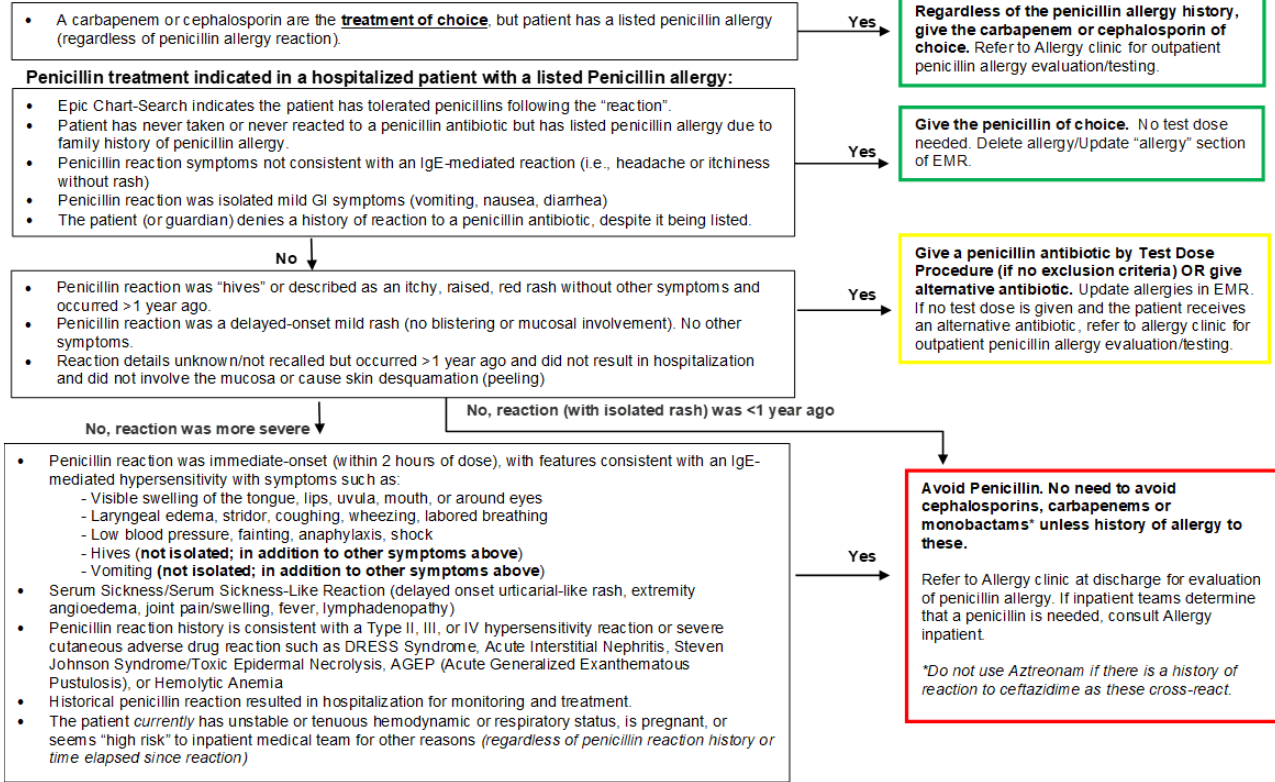
- Direct Amoxicillin Oral Challenge Orderset (Penicillin Allergy Oral Challenge)
- Direct Amoxicillin Oral Challenge ProcDoc ([CPT Coding Reference Sheet](#))

IMPLEMENTATION DATE: June 20, 2022

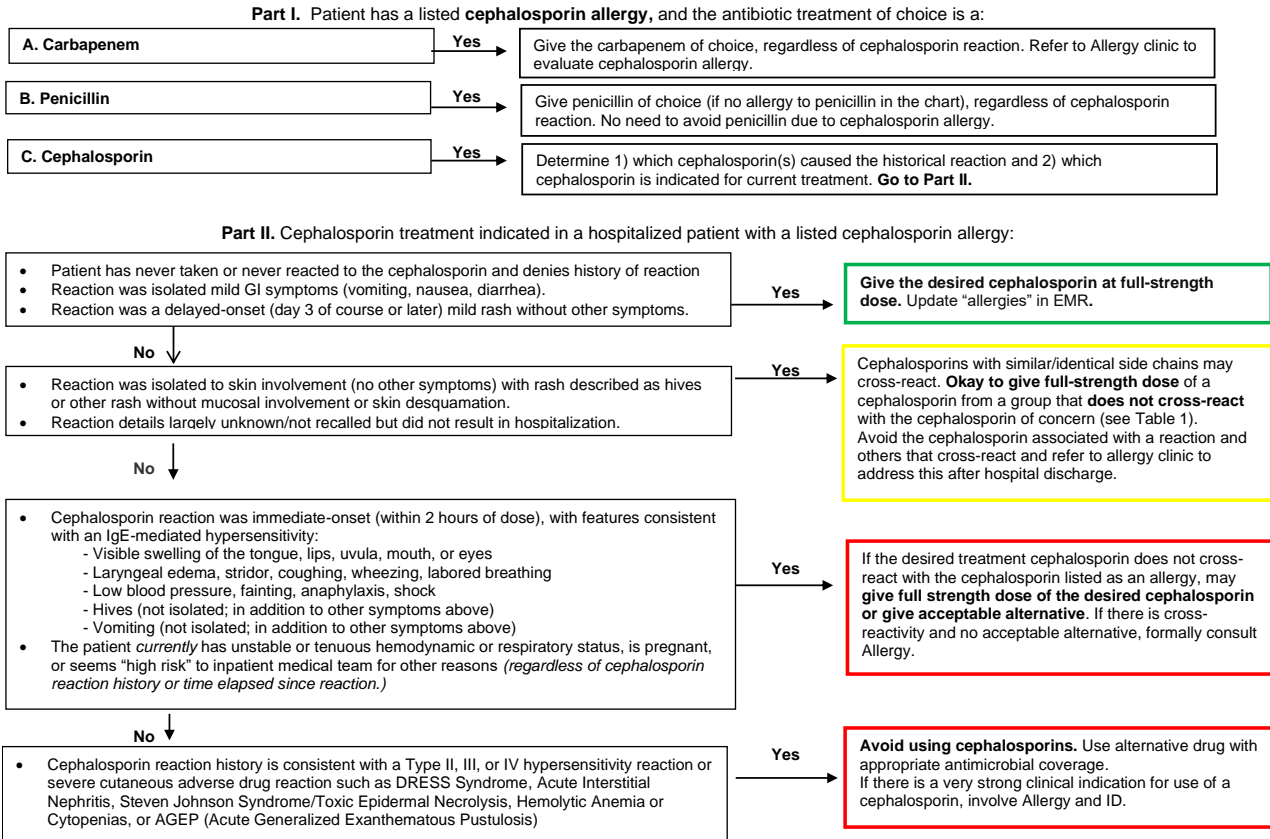
LAST REVISED: January 26, 2024

Clinical Algorithms:

Penicillin Allergy Inpatient Algorithm



Cephalosporin Allergy Inpatient Algorithm



Clinical Pathways Clinical Approach

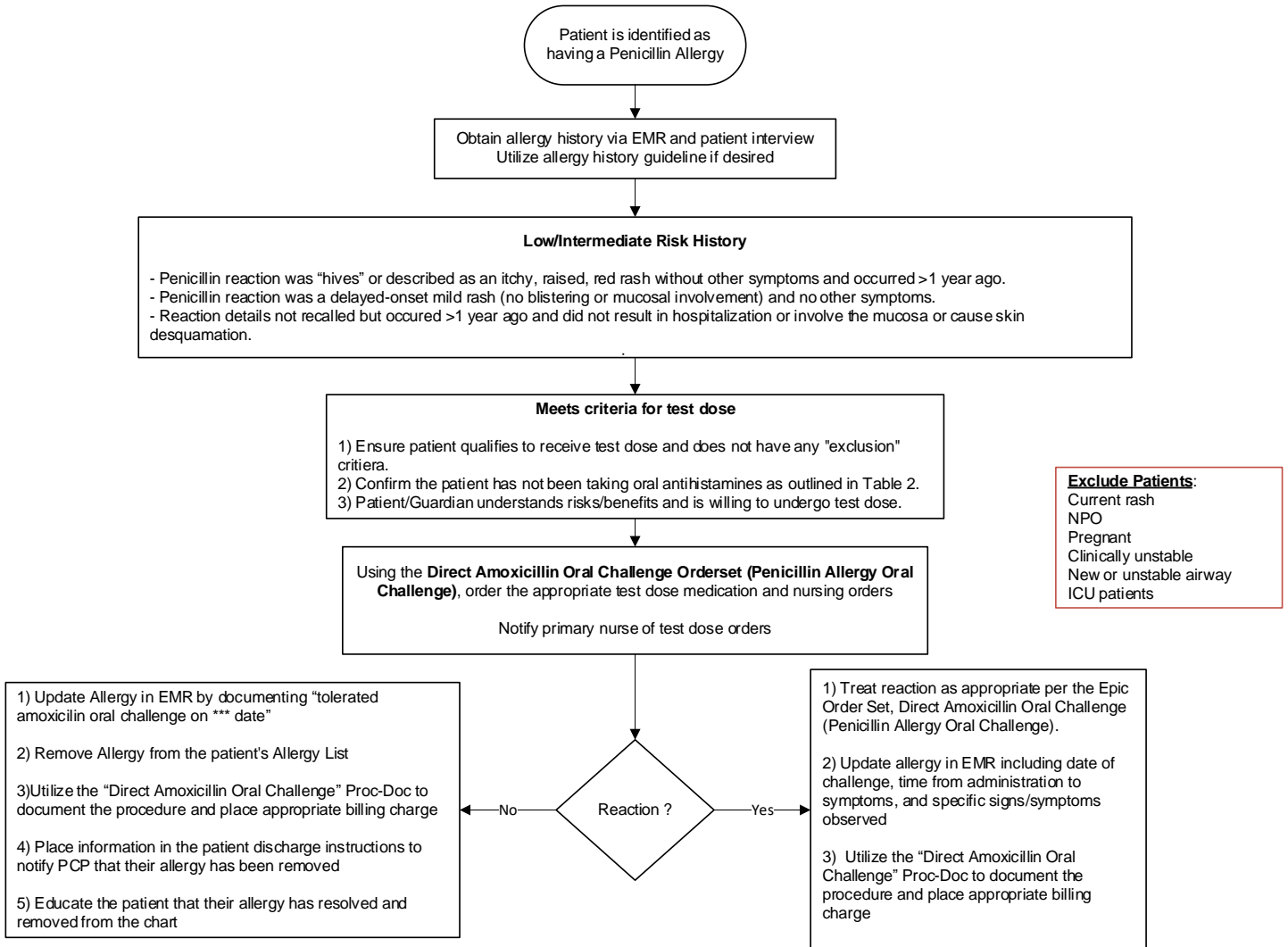
TREATMENT AND MANAGEMENT:

Table 1. Cephalosporin Drugs with Identical or Similar R1 Side-Chain Structures

1. Find the cephalosporin(s) the patient reacted to in the table below. Avoid this cephalosporin and any others in that same box.
2. Okay to give full strength dose of a cephalosporin in a different box (one that does not cross-react).

	Cephalosporin (generation)
Cephalosporins that have the same or similar R1 or R2 side chain and could cross-react	Cephalexin (1 st) Cefadroxil (1 st) Cefprozil (2 nd) Cefaclor (2 nd)
	Cefuroxime (2 nd)
	Cefdinir (3 rd) Cefixime (3 rd)
	Cefixime (3 rd) Cefditoren (3 rd) Cefpodoxime (3 rd) Cefotaxime (3 rd) Ceftriaxone (3 rd) Ceftazidime (3 rd) Cefepime (4 th)
Cephalosporins that do not cross-react with any other cephalosporins used in the United States (If reacted to one of these, only need to avoid the one associated with the reaction)	Cefazolin (1 st)
	Ceftibuten (3 rd)
	Ceftaroline (5 th)
	Ceftolozane (5 th)

Penicillin Test Dose Algorithm



Penicillin Test Dose Procedure:

1. Obtain consent. Discuss the risks, benefits, and alternative treatments with the patient.
2. Confirm no exclusion criteria are present.
3. Place orders using the "Pediatric/Adult Direct Amoxicillin Challenge (Penicillin Allergy Oral Challenge)"
 - a. Nursing:
 - i. Vital signs every 30 minutes starting before dose and every 30 minutes for 90 minutes following dose.
 - ii. Notify provider of hypersensitivity reaction per the order set (see signs/symptoms in order)
 - iii. Nursing to assess for allergic reaction every 30 minutes until 90 minutes after the dose.
 - b. Hypersensitivity Medications:
 - i. Ensure prn medications to treat a hypersensitivity reaction are checked: both diphenhydramine and epinephrine + IV fluid bolus
 - c. Amoxicillin Direct Oral Challenge Dose:
 - i. Order the amoxicillin single dose for the challenge (250 mg)
4. If no signs/symptoms of allergy/hypersensitivity reaction 90 minutes following the dose of amoxicillin, delete the allergy from "Allergy" section of the chart and from the problem list, if applicable. Inform the patient that the allergy will be removed from their chart, and they may take penicillin antibiotics going forward.
5. Document the procedure via the Penicillin Test Dose ProcDoc.

Table 2. Medications to avoid prior to amoxicillin test dose

These antihistamines should be stopped 5 days prior to test dose	Stop these antihistamines at least 3 days prior to test dose	Medications that should be CONTINUED (no need to stop if taking)
<ul style="list-style-type: none"> • Cetirizine (Zyrtec) • Fexofenadine (Allegra) • Loratadine (Claritin) • Desloratadine (Clarinex) • Levocetirizine (Xyzal) • Cyproheptadine (Periactin) 	<ul style="list-style-type: none"> • Diphenhydramine (Benadryl) • Chlorpheniramine (Chlortrimeton) • Promethazine (Phenergan) • Pyrilamine (Pyril/Midol) • Phenyltoloxamine (Tussionex) • Clemastine (Tavist) • Dimenhydrinate (Dramamine) • Dimetapp • Doxylamine (Nyquil, Unisom) • Dura-Tab • Meclizine (Antivert) • Azelastine nasal spray (Astelin/Dymista) • Olopatadine eye drops (Patanase/Patanol/Pataday) • Pheniramine eye drops (Visine-A/Opcon-A) • Other "allergy meds" not listed 	<ul style="list-style-type: none"> • Steroid nose sprays (Flonase/Nasonex/Rhinocort) • Oral corticosteroids (prednisone) • <u>All asthma inhalers</u> • Montelukast (Singulair) • Zafirlukast • Zileuton/Zyflo • Antidepressants

Beta-Lactam Allergy History Tool

Obtain a history about the reaction from the patient/family, supplementing with information from pharmacy records and chart review (notes) when applicable. Document a summary of the allergy history in the Patient Allergies section of EPIC. The following questions may be utilized as a tool to guide history-taking and documentation regarding the reaction.

1. Beta-lactam antibiotic associated with reaction: _____

2. Previous use of this antibiotic prior to the course that caused a reaction: Yes/No

3. Time since beta-lactam antibiotic reaction:
 - a. Less than 1 year
 - b. 1-10 years
 - c. ≥ 10 years
 - d. Unknown

4. Timing of reaction:
 - a. First day of treatment course, immediately after first dose (within ___ hours)
 - b. 1st or 2nd day but several hours after a dose
 - c. 3 or more days into the course
 - d. After treatment was complete
 - e. Unknown

5. Where was treatment provided for the historical beta-lactam antibiotic reaction?:
 - a. Caregiver/parent without medical attention
 - b. PCP
 - c. Urgent Care/Emergency Room
 - d. Hospitalization

- e. Other
 - f. Reaction occurred during a hospitalization
6. Treatment for historical reaction included:
- a. None/beta-lactam antibiotic was continued
 - b. Beta-lactam antibiotic discontinued
 - c. Antihistamines
 - d. Epinephrine
 - e. IV fluids
 - f. Systemic Steroids
 - g. Other or Unknown
7. What were the symptoms that provoked concern this was a reaction to the medication? _____
8. Are symptoms consistent with IgE-mediated/Type 1 hypersensitivity reaction?:
- a. Urticaria (hives): *Raised, red, itchy rash, with each individual skin lesion typically lasting <24 hours*
 - b. Angioedema (swelling): *laryngeal edema or visible swelling of the tongue, lips, mouth, face*
 - c. Bronchospasm: *wheezing, coughing, shortness of breath, labored breathing, low O2 sat*
 - d. Hemodynamic instability: *Low blood pressure, fainting, anaphylactic shock*
9. Did the reaction include any of the following (Type II, III, and IV hypersensitivity reactions)?
- a. Ulcers/sores/blisters of the mouth, lips, or eyes
 - b. Skin peeling/falling off
 - c. Abnormal kidney or liver function or significant eosinophilia
 - d. Swollen and/or painful joints
 - e. Low cell counts, bleeding, need for transfusion (cytopenias), hemolytic anemia (i.e., Zosyn)

Pathway Information

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EXPERT IMPROVEMENT TEAM (EIT): N/A

CLINICAL PRACTICE COUNCIL (CPC): Specialty Health

CPC APPROVAL DATE: June 20, 2022

OTHER TEAM(S) IMPACTED: Hospitalists, Infectious Disease, Nursing, Pharmacy, Allergy, Pediatrics

References

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