Clinical Pathway: PENICILLIN AND CEPHALOSPORIN ALLERGY, INPATIENT

Updated: March 21, 2022

Clinical algorithm:

**Cephalosporin Allergy Inpatient Algorithm**

**Part I.** Patient has a listed cephalosporin allergy and the antibiotic treatment of choice is a:

- A. Carbapenem (i.e. imipenem, ertapenem)
- B. Penicillin (i.e. ampicillin, amoxicillin, Unasyn, Zosyn)
- C. Cephalosporin

**Give the carbapenem of choice.** Refer to Allergy clinic to evaluate cephalosporin allergy.

**Give full-strength dose of** a cephalosporin from a group that **does not cross-react** with the cephalosporin of concern (see table).

**Give acceptable alternative antimicrobial drug OR**

If patient does NOT have a penicillin allergy, give the cephalosporin of choice. (If the patient has a penicillin allergy, follow penicillin algorithm.)

**Part II.** Cephalosporin treatment indicated in a hospitalized patient with a listed cephalosporin allergy:

- Patient has never taken or never reacted to a cephalosporin. The allergy is listed due to family history of cephalosporin allergy.
- Cephalosporin reaction symptoms not consistent with an IgE-mediated reaction (i.e. headache, diaper rash, “tingling”, itchiness but no rash, etc.)
- Reaction was isolated mild GI symptoms (vomiting, nausea, diarrhea).
- Reaction was a delayed-onset (day 3 of course or later) mild rash without other symptoms.

**Give the desired cephalosporin.** No test dose needed. Update “allergies” in EMR.

Cephalosporins with similar/identical side chains may cross-react.

**Give full-strength dose of** a cephalosporin from a group that **does not cross-react** with the cephalosporin of concern (see table).

Avoid using cephalosporins. Use alternative drug with appropriate antimicrobial coverage. If there is a very strong clinical indication for use of a cephalosporin, involve Allergy and ID.

Give acceptable alternative antimicrobial drug.

If a cephalosporin is the ideal treatment and the desired cephalosporin does not cross-react with the cephalosporin listed as an allergy, give full dose. If there is cross-reactivity and no acceptable alternative, formally consult Allergy.
A carbapenem (imipenem, ertapenem, meropenem) is the treatment of choice, but patient has a listed penicillin allergy.

Penicillin treatment indicated in a hospitalized patient with a listed Penicillin allergy:

- Epic Chart Search indicates the patient has previously tolerated the penicillin of choice.
- Patient has never taken or never reacted to a penicillin antibiotic. Family member history of penicillin allergy is the reason for the listed penicillin allergy for the patient.
- Patient has a history of reaction to penicillin antibiotic. Family member history of penicillin allergy is the reason for the listed penicillin allergy for the patient.
- Penicillin reaction symptoms not consistent with an IgE-mediated reaction (i.e., headache or itchiness without rash)
- Penicillin reaction was isolated mild GI symptoms (vomiting, nausea, diarrhea)
- Penicillin reaction was a delayed-onset (day 3 of course or later) mild rash without other symptoms

1) Update Allergy in EMR by documenting reaction history or time elapsed since reaction.
2) Remove Allergy from the patient’s Allergy List
3) Patient/Guardian understands risks/benefits and is willing to undergo test dose.
4) Place information in the patient discharge instructions to notify PCP that their allergy has been removed.
5) Educate the patient that their allergy has been removed.

**Penicillin Allergy Inpatient Algorithm**

**Test Dose Algorithm**

Patient identified as having a Penicillin Allergy

Obtain allergy history via EMR and patient interview

Utilize allergy history guideline (page 2)

Low/Intermediate Risk History

- Penicillin reaction was “hives” or itchy, raised, red rash without other symptoms.
- The patient (or guardian) denies a history of reaction to a penicillin antibiotic, despite it being listed in his/her allergies. Using the search function in the chart is consistent with the patient/guardian’s report.

Meets criteria for test dose

- 1) Ensure patient is medically stable to receive test dose
- 2) Confirm the patient has not been taking oral antihistamines as outlined in Table 1.
- 3) Patient/Guardian understands risks/benefits and is willing to undergo test dose.

Using the Direct Amoxicillin Oral Challenge Orderset (Penicillin Allergy Oral Challenge), order the appropriate test dose medication and nursing orders

Notify primary nurse of test dose orders

1) Update Allergy in EMR by documenting tolerated amoxicillin oral challenge on *** date
2) Remove Allergy from the patients Allergy List
3) Utilize the “Direct Amoxicillin Oral Challenge” Proc Doc to document the procedure and place appropriate billing charge
4) Place information in the patient discharge instructions to notify PCP that their allergy has been removed
5) Educate the patient that their allergy has been removed

Exclude Patients
- NPO
- Clinically unstable
- Unstable or new airway
- ICU patients

Yes

- Give the carbapenem of choice. Refer to Allergy clinic for outpatient penicillin allergy evaluation/testing.
- Give the penicillin of choice. No test dose needed. Update allergies in EMR.
- Avoid penicillins. Use alternative drug with appropriate antimicrobial coverage.

Yes

- Give a penicillin antibiotic by test dose procedure OR give alternative antibiotic.
- Update allergies in EMR. If no test dose is given and the patient receives an alternative antibiotic, refer to allergy clinic for outpatient penicillin allergy evaluation/testing.
- Use a 3rd or 4th generation cephalosporin, a carbapenem, or a monobactam (Aztreonam*). OR use an alternative antibiotic. Refer to Allergy clinic for discharge evaluation for penicillin allergy. If ID consult determines that a penicillin is needed and there are no alternative therapies, consult Allergy.

Yes

- "Do not use Aztreonam if there is a history of reaction to cefazidime as these cross react.

Yes

- Avoid penicillins. Use alternative drug with appropriate antimicrobial coverage. If there is a very strong clinical indication for use of a penicillin, involve Allergy and Infectious Disease.

Yes

- Avoid penicillins. Use alternative drug with appropriate antimicrobial coverage. If there is a strong clinical indication for use of a penicillin, involve Allergy & ID teams.
### Clinical pathway summary

**CLINICAL PATHWAY NAME:** Penicillin and Cephalosporin Allergy, Inpatient

**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 Spectrum Health Hospitals

**BRIEF DESCRIPTION:**
This guideline was developed by the Spectrum Health Allergy & Immunology, Infectious Disease, and Pharmacy clinicians 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.

OVERSIGHT TEAM LEADER(S): Dr. Stephanie Burdick, Dr. Nicholas Hartog, Dr. Amanda Holsworth, Dr. Liam Sullivan, Derek VanderHorst, PharmD

OWNING EXPERT IMPROVEMENT TEAM (EIT): N/A

MANAGING CLINICAL PRACTICE COUNCIL (CPC): Specialty Health

CPC APPROVAL DATE: June 20, 2022

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

OPTIMIZED EPIC ENHANCEMENTS:
- 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: 3/21/22

FOR MORE INFORMATION, CONTACT: Stephanie Burdick

Clinical pathways clinical approach

TREATMENT AND MANAGEMENT:

Allergy History Guideline:

Obtain an accurate history about the reaction from the patient/family, chart review, pharmacy, PCP, etc. Document allergy history in the Patient Allergies section of EPIC.

1. Beta-lactam antibiotic that the patient reacted to:__________

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. Less than 1 year
   c. 1-10 years
   d. >10 years
   e. Unknown

4. Timing of reaction:
   a. First day of treatment course, immediately after first dose (***hours)
b. 1st or 2nd day but 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:
   a. None/beta-lactam antibiotic was continued
   b. Beta-lactam antibiotic discontinued
   c. Antihistamines
   d. Epinephrine
   e. IV fluids
   f. Steroids
   g. Other or Unknown

7. Did the reaction include any of the following?
   a. Rash that does NOT sound consistent with hives, such as a delayed-onset maculopapular rash
   b. Upset stomach, abdominal pain, nausea, vomiting, diarrhea
   c. Minor lab abnormalities
   d. Other minor reaction:

8. Symptoms of adverse reaction included (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*
   c. Bronchospasm: *wheezing, coughing, shortness of breath, labored breathing*
   d. Hemodynamic instability: *Low blood pressure, fainting, 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
   d. Swollen and/or painful joints
   e. Low cell counts, bleeding, need for transfusion (cytopenias), hemolytic anemia (Zosyn)
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.

Table 2: Cephalosporin Drugs with Identical or Similar R1 Side-Chain Structures

1. Find the cephalosporin(s) the patient reacted to and avoid all cephalosporins in that same group.
2. Give full strength dose of a cephalosporin from a different group

<table>
<thead>
<tr>
<th>R1 Side Chain Group</th>
<th>Cephalosporin (generation) *denotes HDVCH/SH formulary</th>
<th>Oral/Enteral</th>
<th>IV/Parenteral</th>
</tr>
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<tbody>
<tr>
<td>Group 1</td>
<td>Cephalexin (1st)</td>
<td></td>
<td>Cefaclor (2nd)</td>
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<tr>
<td>Group 2</td>
<td>Cefprozil (2nd)</td>
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<td>Cefpodoxime (3rd)</td>
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<td>Cefiderocol (5th)</td>
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<td>Group 5</td>
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<td>Cefoxitin (2nd)</td>
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<td>Cefuroxime (2nd)</td>
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<td>Group 9</td>
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<td></td>
<td>Ceftolozane (5th)</td>
</tr>
</tbody>
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References:


Macy E. Why was there ever a warning not to use cephalosporins in the setting of a penicillin “allergy”? *The Journal of Allergy and Clinical Immunology: In Practice*. 2021;9(11):3929-3933. doi:10.1016/j.jaip.2021.06.059
