β-lactam Cross Reactivity Chart

Antimicrobial Stewardship Program

Children's Healthcare of Atlanta

Introduction:

Penicillin allergy is the most common drug allergy reported in children, with a prevalence rate of about 10%.[1] However, less than 5% of reported penicillin allergies are confirmed, acute-onset IgE-mediated allergy or delayed-onset T cell-mediated hypersensitivity. Nearly 75% of penicillin allergy labels are placed by the age of 3 years, and many of these are mislabeled.[2] Because of this, penicillin allergies are one of the main drivers of unnecessary broad-spectrum antibiotics use.

Cross-reactivity:

β-lactams include penicillins, cephalosporins, and carbapenems. These drugs all consist of a β-lactam ring but differ in their additional side chains. Traditionally, it was thought that cross-reactivity was attributed to the β-lactam ring. More recent evidence suggests cross-reactivity is due to side chain similarities.[3] Cephalosporins with similar or identical side chains to penicillins should be avoided in patients with a true penicillin allergy. β-lactams with dissimilar side chains carry a low risk of cross-reactivity.

Recommendations[4, 5]:

- Non-severe Allergies (rash, hives, urticaria, etc. without systemic symptoms):
  - For patients with non-severe allergies to penicillin, a cephalosporin may be used without additional testing or monitoring.
  - For patients with non-severe allergies to cephalosporins, a β-lactam with dissimilar side chain should be used in monitored settings.
- Severe Allergies (anaphylaxis, angioedema, hypotension, throat swelling, etc.):
  - For patients with severe, anaphylactic allergies to penicillin, a cephalosporin or carbapenem with dissimilar side chains may be administered in monitored settings. Avoid β-lactams with similar or identical side chains.
  - For patients with severe anaphylactic allergies to cephalosporins, a carbapenem should be used. Discussion with Allergy and Immunology is recommended prior to the administration of a penicillin or cephalosporin.

Antibiotic Allergy De-labeling:

- Proactive allergy de-labeling is recommended in patients with allergies that occurred >1 year ago and meet inclusion criteria
- See Antimicrobial Stewardship, Antibiotic Allergy Challenge (IP) BPR.pdf for de-labeling procedure
- See Antibiotic Allergy Challenge Consent.pdf for consent form
- Consult Antimicrobial Stewardship or Allergy and Immunology for further guidance

β-Lactams	Penicillin	Amoxicillin	Ampicillin	Oxacillin	Piperacillin	Cephalexin*	Cefazolin	Cefoxitin	Cefprozil	Cefuroxime	Cefdinir	Ceftazidime	Ceftriaxone	Cefepime	Meropenem
Penicillin		X	X	X	X	○		○							
Amoxicillin	X		X	X	X	○			X						
Ampicillin	X	X		X	X	○			X						
Oxacillin	X	X	X		X	○									
Piperacillin	X	X	X	X		○			○						
Cephalexin*	○	○	○	○	○				○						
Cefazolin															
Cefoxitin	○									○					
Cefprozil		X	X		○	○									
Cefuroxime								○				○	○	○	
Cefdinir															
Ceftazidime										○			○	○	
Ceftriaxone										○		○		X	
Cefepime										○		○	X		
Meropenem															

X= identical side chain. High risk of cross-reactivity. DO NOT ADMINISTER.

O= similar side chain. AVOID in patients with history of anaphylaxis. May be used in patients with non-severe allergies in monitored settings.

*= The risk of cross-reactivity between cephalexin and amoxicillin is 10 – 20%.[6] Cephalexin is an acceptable alternative to amoxicillin for patients without non-severe penicillin allergies. Consider administering a test dose with close monitoring for hypersensitivity reactions.[7]

References

1. Stukus, David R. “True penicillin allergy in children is rare; know how to delabel patients.” *American Academy of Pediatrics.* 2023.
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3. Patrick, David M, et al. “Beta-lactam allergy: Benefits of de-labeling can be achieved safely.” BC Centre for Disease Control. Vol 61. 2019. 350-351.
4. Khan DA, Banerji A, Blumenthal KG, et al. Drug allergy: A 2022 practice parameter update. *J Allergy Clin Immunol*. 2022;150(6):1333-1393.
5. Trubiano, Jason A et al. “The 3 Cs of Antibiotic Allergy-Classification, Cross-Reactivity, and Collaboration.” The Journal of Allergy and Clinical Immunology. Vol. 5,6. 2017. 1532-1542.
6. Exius R, Gabrielli S, Abrams EM, et al. Establishing Amoxicillin Allergy in Children Through Direct Graded Oral Challenge (GOC): Evaluating Risk Factors for Positive Challenges, Safety, and Risk of Cross-Reactivity to Cephalosporines. J Allergy Clin Immunol Pract. 2021.
7. “Amoxicillin Shortage: Antibiotic Options for Common Pediatric Conditions.” *American Academy of Pediatrics*. 2022.