



Cephalosporin Side Chain Cross-reactivity

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Each month we present highlights from the Ask the Expert section of the American Academy of Allergy, Asthma & Immunology (AAAAI) Web site written by Dennis K. Ledford, MD. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Question:

I have a 4-year-old boy with a history of urticaria and angioedema to both penicillin and Suprax (cefixime). A skin test is negative to Pre-Pen and penicillin G. He is scheduled for a cautious oral challenge to penicillin. My question is: what are the other cephalosporins to which I can challenge him that have nonidentical R-group side chains to those of Suprax?

Answer:

Thank you for your question. Most of the cross-reactivity information related to side chains is related to amoxicillin and ampicillin. The R-group side chains are identical in amoxicillin and cefadroxil, cefprozil, and cefatrizine. Ampicillin shares side chains with cephalexin, cefaclor, cephradine, cephaloglycin, and loracarbef. Benzyl penicillin has similar side chains as cephalothin and cephaloridine. Ceftriaxone, cefuroxime, cefepime, cefotaxime, and cefodizime share a methoxymino side chain. Thus, I cannot find any sharing of side chains with cefixime and other cephalosporins (see Table I and statements from Practice Parameters below).¹

Summary Statement 93: Most hypersensitivity reactions to cephalosporins are probably directed at the R-group side chains rather than the core β -lactam portion of the molecule. (D)

Summary Statement 104: Patients allergic to amoxicillin should avoid cephalosporins with identical R-group side chains (cefadroxil, cefprozil, and cefatrizine) or receive them via rapid induction of drug tolerance. (C) Similarly, patients allergic to

ampicillin should avoid cephalosporins and/or carbacephems with identical R-group side chains (cephalexin, cefaclor, cephradine, cephaloglycin, loracarbef) or receive them via rapid induction of drug tolerance. (C)

Summary Statement 105: Patients with a history of an immediate-type reaction to a cephalosporin should undergo penicillin skin testing, if available, before treatment with penicillin. (E) If test results are negative, they may safely receive penicillins. (B) If test results are positive, an alternate drug should be used or they should undergo rapid penicillin induction of drug tolerance. (B) If penicillin skin testing is unavailable, penicillin may be administered via cautious graded challenge. (C) Patients with a history of an immediate-type allergic reaction to a cephalosporin who require penicillin should undergo penicillin skin testing. If results are negative, they can receive penicillin; if results are positive, they should receive an alternate drug or undergo penicillin induction of drug tolerance.”

Because your patient had a mild reaction to both penicillin and cefixime and these do not share side chain similarities, it is possible that the reactivity is to the β -lactam nucleus, despite the fact that cephalosporin reactions are often side chain dependent (see above from Practice Parameters). Because testing is now negative to penicillin and penicilloyl-polylysine, I think your patient is at very low risk of reacting to an oral challenge. I would suggest cefpodoxime as it is available in a liquid formulation and has a unique side chain. For additional reassurance, skin testing could be considered using 2-3 mg/mL

TABLE I. Groups of β -lactam antibiotics that share identical R1-group side chains^{*,1}

Amoxicillin	Ampicillin	Ceftriaxone	Cefoxitin	Cefamandole	Ceftazidime
Cefadroxil	Cefaclor	Cefotaxime	Cephaloridine	Cefonicid	Aztreonam
Cefprozil	Cephalexin	Cefpodoxime	Cephalothin		
Cefatrizine	Cephradine	Cefditoren			
	Cephaloglycin	Ceftizoxime			
	Loracarbef	Cefmenoxime			

*Each column represents a group with identical R1 side chain.

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of the cephalosporin.² The predictive value of cephalosporin skin testing is not proven. Cefdinir does share some vague similarities with cefixime, but I am not aware of any data demonstrating cross-reactivity.

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