β-lactam Allergy

Key points:

1. Approximately 10% of patients report a history of penicillin allergy. However, when completely evaluated, up to 90% of these patients are able to tolerate penicillins.
2. The widely cited figure of 10% cross-reactivity between penicillins and first-generation cephalosporins is now considered incorrect and an overestimate of the true cross-reactivity rate.
3. Immune response to cephalosporins is thought to be due to their side chains. In the case of IgE-mediated penicillin or cephalosporin allergy, cephalosporins with different 7- AND 3-position side chains can be used.
4. Cefazolin has dissimilar 7- and 3-position side chains and is not thought to cross-react with penicillins and cephalosporins.
5. Treatment of patients assumed to have penicillin allergy with alternate broad-spectrum agents may compromise patient care by promoting the development of drug-resistance, increased hospital costs, and increased adverse effects.

Figure 1: β-Lactam Allergy Algorithm

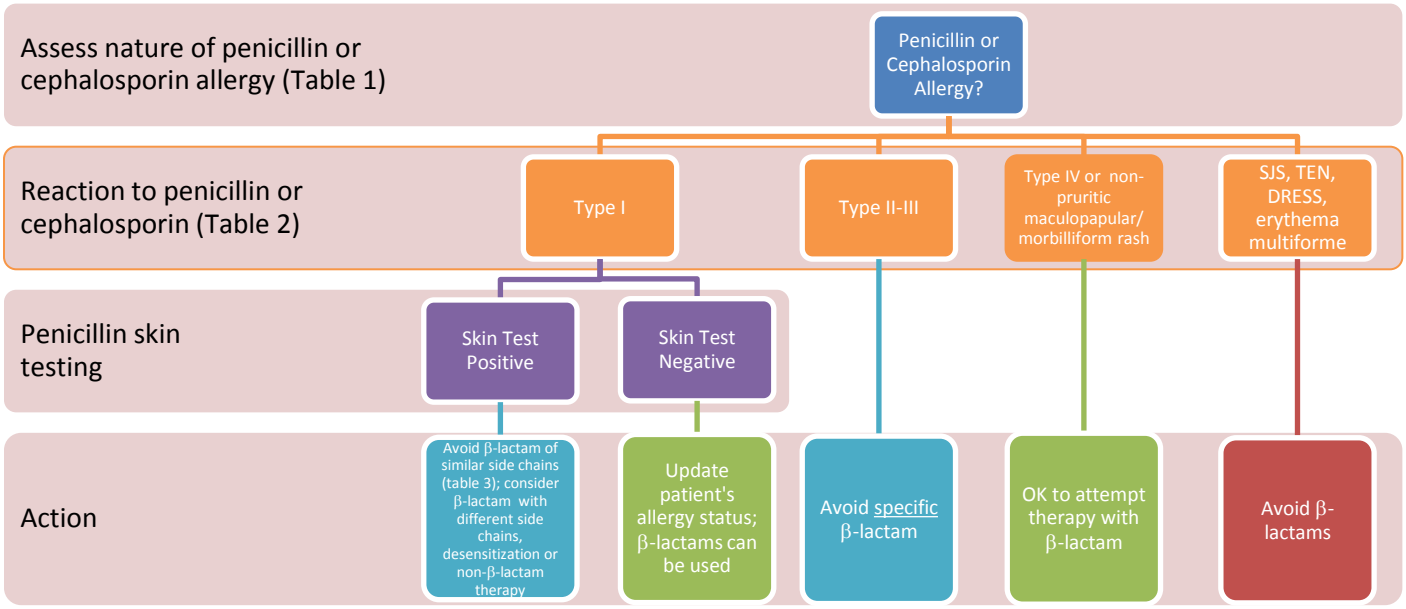

Table 1: Assessment of β-lactam Allergy

Questions to Ask Patients with a History of β-lactam Allergy	
Do you remember the details of the reaction?	• Drug involved • Route of administration of drug • Time from administration of drug to onset of symptoms of reaction • Symptoms of the reaction
How was the reaction managed? What was the outcome?	• Use and positive response to epinephrine and histamine-1 receptor antagonists suggest an IgE mediated reaction
How many years ago did the reaction occur?	• With IgE mediated reactions, ~80% or more will lose their sensitivity to the drug
Why did you receive β-lactam therapy?	• Many cutaneous reactions may be due to an underlying bacterial or viral infection (e.g. Epstein-Barr virus)
Have you tolerated other forms of penicillin since the reaction?	

Table 2: Classification of Hypersensitivity Reactions

Coombs and Gell Classification of Hypersensitivity Reactions				
Type	**Mediator**	**Onset**	**Clinical Reaction**	**Comments**
I	IgE	<1 hour (rarely up to 72 hours)	Anaphylaxis, angioedema, hypotension, laryngeal edema, urticarial, wheezing	
II	IgG, complement	>72 hours	Hemolytic anemia, neutropenia, thrombocytopenia	Drug specific; cross-reactivity does not appear to occur
III	IgG, IgM, immune complex	>72 hours	Drug fever, glomerulonephritis, serum sickness, small vessel vasculitis	Drug specific; cross-reactivity does not appear to occur
IV	T cell	>72 hours	Contact dermatitis, pustulosis	
Other				
Idiopathic	Unknown	>72 hours	Non-pruritic maculopapular or morbilliform rash	Not a contraindication to β-lactam therapy
			Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), erythema multiforme	β-lactams should be avoided

Table 3: Penicillins and Cephalosporins with Similar Side Chains

Similar 7-Position Side Chain – Cross Reactivity Possible Within Group			**Similar 3-Position Side Chain – Cross Reactivity Possible Within Group**		
Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
Penicillin G Cefoxitin Cephalothin	Amoxicillin Ampicillin Cefaclor Cefadroxil Cefprozil Cephalexin	Cefotaxime Ceftizoxime Ceftriaxone Cefepime	Cefadroxil Cephalexin	Cefotaxime Cephalothin	Cefuroxime Cefoxitin

NOTE: If patient has a type I reaction to a cephalosporin, can use another cephalosporin that does not have similar 7 AND 3-position side chain. Cephalosporins not included in above groups (i.e. cefazolin) have dissimilar structure to the above and cross-reactivity is unlikely.

References:

1. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol 2010;105(4):259-73.
2. Pichichero ME. A review of evidence supporting the American Academy of Pediatrics recommendation for prescribing cephalosporin antibiotics for penicillin-allergic patients. Pediatr 2005;115:1048-57.
3. Gonzalez-Estrada A, Radojicic C. Penicillin allergy: a practical guide for clinicians. Cleveland Clinic J Med 2015;82(5):295-300.
4. Lagace-Wiens P, Rubinstein E. Adverse reactions to β-lactam antimicrobials. Expert Opin Drug Saf 2012;11(3):381-99.