



GUIDANCE IN EVALUATING PENICILLIN ALLERGY AND RECOMMENDATIONS FOR TREATMENT AND PROPHYLAXIS OF HEAD AND NECK PATIENTS WITH SEVERE PENICILLIN ALLERGIES

What is the problem?

Up to 15% of hospitalized patients report that they are allergic to penicillin. However, it is estimated that this label is either inaccurate or not indicative of a true IgE-mediated reaction in up to 90% of cases. Often, penicillin “allergies” consist of family history, non-allergic adverse reactions or confounders related to the patient’s underlying illness, or historical childhood events.¹ Being labelled as penicillin allergic results in dramatic shifts in antibiotic use, with more frequent use of vancomycin, fluoroquinolones, and clindamycin, primarily.²⁻⁴ These alternative agents, as compared to beta-lactam therapy, may be associated with increased toxicity (kidney injury with vancomycin), collateral damage (*C difficile* infection with fluoroquinolones and clindamycin), and clinical failure⁵ which may result in increased length of stay and mortality.⁶ For example, patients with *Enterococcus faecalis* bacteremia and methicillin-susceptible *Staphylococcus aureus* bacteremia and endocarditis have been demonstrated to experience higher mortality when treated with vancomycin than when treated with beta-lactams.^{7,8} **In patients undergoing head and neck free flap reconstruction, use of clindamycin (instead of ampicillin/sulbactam) as surgical prophylaxis is associated with a nearly 7-fold higher risk of postoperative flap or neck infection by multivariate analysis.¹¹ This discrepancy is likely due to superior activity of beta-lactams compared to clindamycin for oral flora, especially regarding oral streptococci. At UMHS, 23% of *S. anginosus* are clindamycin resistant, compared to 0-1% resistance with penicillin.** Clearly, the consequences of such a sizable proportion of patients being incorrectly labelled penicillin allergic are significant.

What can we do to identify patients who can receive beta-lactams despite a history of allergy?

In summary, beta lactam treatment such as penicillin, ampicillin and cephalosporins are the best choices for the treatment of odontogenic infection. Therefore, when a patient tells you they have a PCN allergy, you should ...

1. Ask for a description of the reaction.
 - a. To clarify if this may be labeled on non-severe allergy, and therefore using a cephalosporin is still an option.
2. Ask them if they’ve ever received a penicillin or a cephalosporin previously.
 - a. It is often helpful to name some specifically (i.e., amoxicillin, Keflex, Augmentin, cefdinir)
3. Consider referring them to Michigan Medicine Allergy and Immunology clinic for penicillin skin testing prior to the surgery if there is some doubt about the allergy.
 - a. In the setting of planning a non-emergent procedure.
4. Use all of this information to decide the best antibiotic choice for your patient.
 - a. Refer to the Odontogenic Infections Guideline.

It is crucial to accurately characterize (and correct) penicillin allergy records. **A detailed medication history by itself may identify erroneous “allergies”, by either clarifying the reaction or identifying that the patient has safely received penicillins or cephalosporins previously.**⁹ In addition, outpatients may be referred to the Michigan Medicine Allergy and Immunology clinic for penicillin skin testing (PST). Penicillin skin testing using the PRE-PEN® skin test antigen is FDA indicated for the assessment of penicillin allergy and has a 97-99% negative predictive value. ~95% of patients with a reported penicillin allergy have a negative PST and can thus be safely prescribed penicillins.¹⁰

If clindamycin may be a suboptimal agent for both treatment of suppurative odontogenic infections and prophylaxis for clean/contaminated odontogenic procedures, what other options are available in patients who cannot receive a beta-lactam?

Antibiotic choice for both treatment of suppurative odontogenic infections and prophylaxis for clean/contaminated odontogenic procedures are similar. **Ampicillin/sulbactam is preferred** due to superior susceptibilities and minimal collateral damage. **In patients with a non-severe allergy to ampicillin or penicillin (no record of anaphylaxis, angioedema, or urticaria, for example), cefazolin plus metronidazole can be safely prescribed. In patients with a severe allergy to penicillins, the combination of levofloxacin and metronidazole provides superior activity to clindamycin** (see below).

*There is a dearth of literature exploring non-clindamycin prophylactic regimens in patients who cannot receive beta-lactams. We did find that the Nebraska Medical Center utilizes levofloxacin + metronidazole for clean-contaminated head and neck procedures in patients with severe beta-lactam allergy. Regarding treatment of odontogenic infections, moxifloxacin has been shown to be potentially more efficacious than clindamycin, with superior susceptibilities, in patients with odontogenic abscesses and inflammatory infiltrates.^{12,13} Susceptibilities are similar with levofloxacin as moxifloxacin for aerobic bacteria.¹³ While moxifloxacin possesses superior anaerobic activity compared to levofloxacin, that advantage can be negated with the addition of metronidazole to levofloxacin.¹⁴ At Michigan Medicine, 99% of *S. anginosus* are levofloxacin susceptible.

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The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider’s professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

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