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Penicillin Allergy Assessment and Medical Referral to Promote Antibiotic Stewardship

By Elaine Bailey, PharmD, Mackenzie Connell, Marie Fluent, DDS, and Erinne Kennedy, DDS, MPH, MMSC

Abstract

Antibiotic stewardship is an integral practice for the dental team to ensure a safe dental visit for patients. Now, with clinical practice guidelines and state toolkits, more dentists are aware of and actively practicing antibiotic stewardship. With the application of antibiotic stewardship practices, dentists are identifying the need for additional tools to enhance practice. For example, one need that has been identified is a tool for screening patients for true penicillin allergies.

The Penicillin Allergy Assessment Tool (PAAT) is a decision-making tool that can be used chairside to screen patients who report an allergy to penicillin. After screening, dentists can refer and collaborate alongside the health care team to recommend testing, and confirm the information in the medical record. If the allergy is confirmed, the health care team may recommend the use of alternate antibiotics, and/or desensitization therapy if indicated. For patients who find that they do not have an allergy, the health care team can update the documentation in the medical and dental record(s), and suggest the return to use of first line antibiotics, including beta lactams, when indicated.

Drug-resistant bacteria are a growing threat to public health, causing 2.8 million infections that result in upwards of 35,000 mortalities in the United States each year.¹ Dentists rank in the top three prescribers of antibiotics among health care professionals, and are responsible for approximately 25 million prescriptions yearly.^{2,3} All antibiotics come with benefits and risks to the patients; however, some antibiotics are more likely to result in a serious adverse reaction compared to others.

For example, a seven-day course of clindamycin has 164% higher risk of resulting in an opportunistic diarrheal infection from *Clostridioides difficile*, an infection with a higher incidence of morbidity and mortality, compared to a seven-day course of amoxicillin.⁴ Reports of *Clostridioides difficile* infections (CDI) occurring in dental patients are increasing in frequency, often in patients who have minimal or no additional risk factors for developing CDI.^{5,6} Often, when dental patients share their allergy to penicillin with their dentist, clindamycin is frequently prescribed as an alternative antibiotic.

Because of the additional risks associated with second-line antibiotics, the Centers for Disease Control and Prevention encourages all health care professionals to verify penicillin allergies, with an emphasis on “de-labeling” patients, if appropriate, in an effort to increase the use of first-line antibiotics.⁷ The American Academy of Allergy, Asthma & Immunology published updated guidance for the evaluation and management of drug hypersensitivity, including penicillin allergy, in 2020.⁸ The evaluation of a penicillin allergy is increasingly being performed by allergists and other health professionals.

In 2019, the American Dental Association developed evidence-based clinical practice guidelines for the management of pulpal- and periapical-related dental pain and intraoral swelling.⁹ The guidelines introduced broad general principles that apply to the prescribing of antibiotics, and specific prescribing recommendations based on the diagnosed condition and availability of dental care. Broadly, antibiotic stewardship practices include:

- Only using antibiotics when they are absolutely necessary.

■ If antibiotics are indicated, prescribe a first line antibiotic when applicable.

■ Screening for and confirming true penicillin allergies.

■ Referral for definitive conservative dental treatment (DCDT)

■ Recommending the use of over-the-counter (OTC) products for pain management.

■ Discontinuing use of antibiotics 24 hours after the symptoms resolve.

In order to use first-line antibiotics when indicated, the dental clinic needs to screen and confirm for true penicillin allergies. Less than 1% of the U.S. population has a true IgE mediated allergy that would prevent them from taking penicillin. While many adults recount an allergy to penicillin as a child, that does not confirm a true allergy at the present time. Due to waning immunity, it is estimated that approximately 20% of adults with penicillin allergies will remain allergic after 10 years, and after 20 years fewer than 1% will maintain their sensitivity.⁸ Since patients labeled “penicillin allergic” are more likely to receive second-line antibiotic therapy, the ADA guidelines encourage confirmation or disproof of a true penicillin allergy. Alternative antibiotics for patients with penicillin allergy are included in the guidelines and are summarized in the two chair-side guides developed by the ADA.⁹

The Penicillin Allergy Assessment Tool (PAAT) is a decision-making tool developed by the Michigan Antibiotic Resistance Reduction Coalition (MARR) and the Organization for Safety and Asepsis Procedures (OSAP). The tool is intended to be used by the dental team to evaluate whether a patient may benefit from safer antibiotic use by having their penicillin allergy evaluated by a health care professional. The tool is not intended to guide antibiotic choice, but rather to identify patients who may benefit by having their penicillin allergy evaluated by a health

care professional, with possible referral to an allergist for penicillin skin testing. This patient-provider collaborative effort provides a framework for conversation and opens a gateway for more effective treatment with fewer adverse effects, including antibiotic resistance.

Dentists can use the MARR/OSAP Penicillin Allergy Assessment Tool for patients who present to their dental clinic requiring prophylactic and/or therapeutic antibiotics who report a penicillin allergy. The dental team will review a full medical history, and a detailed account of the reported allergy signs and symptoms, including the 4 W's:

Who — Who reported the allergy? Was the patient old enough to generate a firsthand account of the allergy? Did the patient learn this information from a parent or care-giver if they

were too young?

What — What happened? Record the signs, symptoms, and response. How long did the signs and symptoms last? How severe were they? What medications or treatments were provided to resolve the symptoms?

When — When did this happen? What age? Has it happened since? If so, how frequently has it happened?

Who — Who confirmed the allergy signs and symptoms? If so, when?

Based upon medical history review, the dental provider may suggest follow-up with a health care professional. The PAAT tool uses four categories of signs and symptoms to help categorize patients during screening: non-allergy drug side effects (green box); mild to moderate (yellow box); severe IgE mediated (or

(Continued on Page 48)



Penicillin Allergy Assessment

(Continued from Page 47)

ange box); and severe Type II-IV (red box). These are explained below.

Green Box: In a scenario where symptoms are categorized as side effects rather than an allergic reaction, yet the electronic health record (EHR) indicates a penicillin allergy or unknown allergic status (green box), a referral to a health care provider for evaluation is recommended. Further assessment and an accurate diagnosis would confirm allergic vs. non-allergic symptoms, and may validate or remove the “penicillin-allergic” label from the patients’ medical record.

Yellow Box: Mild-to-moderate rashes that are delayed in onset are generally not IgE-mediated and often can be managed by administering OTC antihistamines. In many cases, the allergy may have been eliminated due to waning immunity, especially if the reaction occurred when the patient was a child and he or she is now an adult. Follow-up with a health care professional is advised for accurate assessment of the reaction, accurate and current documentation in the medical record, and recommendation for antibiotic therapy.

Orange Box: IgE-mediated reactions occur immediately or usually within one hour. Signs and symptoms may include:

- Hives, which are multiple pink/red raised areas of skin that are itchy.

- Angioedema or localized edema without hives affecting the abdomen, face, extremities, genitalia, oropharynx, or larynx.

- Wheezing and/or shortness of breath.

- Anaphylaxis, which is a condition diagnosed when the patient experiences signs and symptoms caused by two or more organ systems (skin, respiratory, cardiovascular, GI).⁷

Patients who have a history of IgE-mediated reactions have the potential to receive the most benefit by a complete evaluation by an allergist, since they are most likely to not receive a first-line antibiotic. As mentioned previously, many of these allergies will have waned, making these patients candidates for removal of the drug allergy from the patient medical record.

Red Box: Severe symptoms occur-

ring more than 72 hours after antibiotic exposure are more accurately labeled “hypersensitivity reactions.” These include Type II (cytotoxic), Type III (immune complex), and Type IV (cell-mediated) reactions. Patients experiencing these reactions are not candidates for skin testing since these reactions are not IgE-mediated. It is difficult to predict whether patients with a history of delayed hy-

(Continued on Page 50)

A Chairside Tool Supporting Clinical Antibiotic Stewardship ►

The June 2021 issue of the *MDA Journal* published a “10-Minute EBD” feature detailing the critical role that the dental office can play in evaluating purported penicillin allergies. The author pointed out that many patients labeled “penicillin allergic” do not have a true allergy. These patients may needlessly receive an alternative antibiotic therapy that may not be as effective and pose an increased risk of harm.

A simple penicillin skin test, generally performed by an allergist, will diagnose the presence or absence of the allergy. If the allergy is no longer present, the patient’s health record is updated to reflect the lack of the allergy. This antibiotic stewardship practice promotes patient safety and informed decision-making for the consideration of optimal antibiotic therapy if future infections arise.

In this issue of the *Journal*, the Michigan Antibiotic Resistance Reduction (MARR) Coalition, in collaboration with the Organization for Safety and Asepsis Procedures (OSAP), provides a tool to support the dental office in referring appropriate patients for penicillin allergy assessment (see facing page). Dr. Erinne Kennedy, a member of the expert panel that developed the ADA guidelines for the use of antibiotics, co-authored the article on these pages describing how the entire dental team can effectively utilize this tool to ensure a safer dental visit.

SHOULD YOUR PATIENT BE REFERRED FOR PENICILLIN-ALLERGY ASSESSMENT?

USE THIS TOOL TO IDENTIFY PATIENTS WHO MAY BENEFIT FROM HAVING THEIR PENICILLIN ALLERGY EVALUATED BY A HEALTHCARE PROFESSIONAL.

Who?

The "Penicillin Allergy Assessment Algorithm" is designed for use by the dental team.

What?

The "Penicillin Allergy Assessment Algorithm" is a decision-making tool to guide the dental team to identify patients who may benefit from having their penicillin allergy evaluated by a healthcare professional with the ultimate goal being to "de-label" the patient as penicillin allergic--if appropriate.

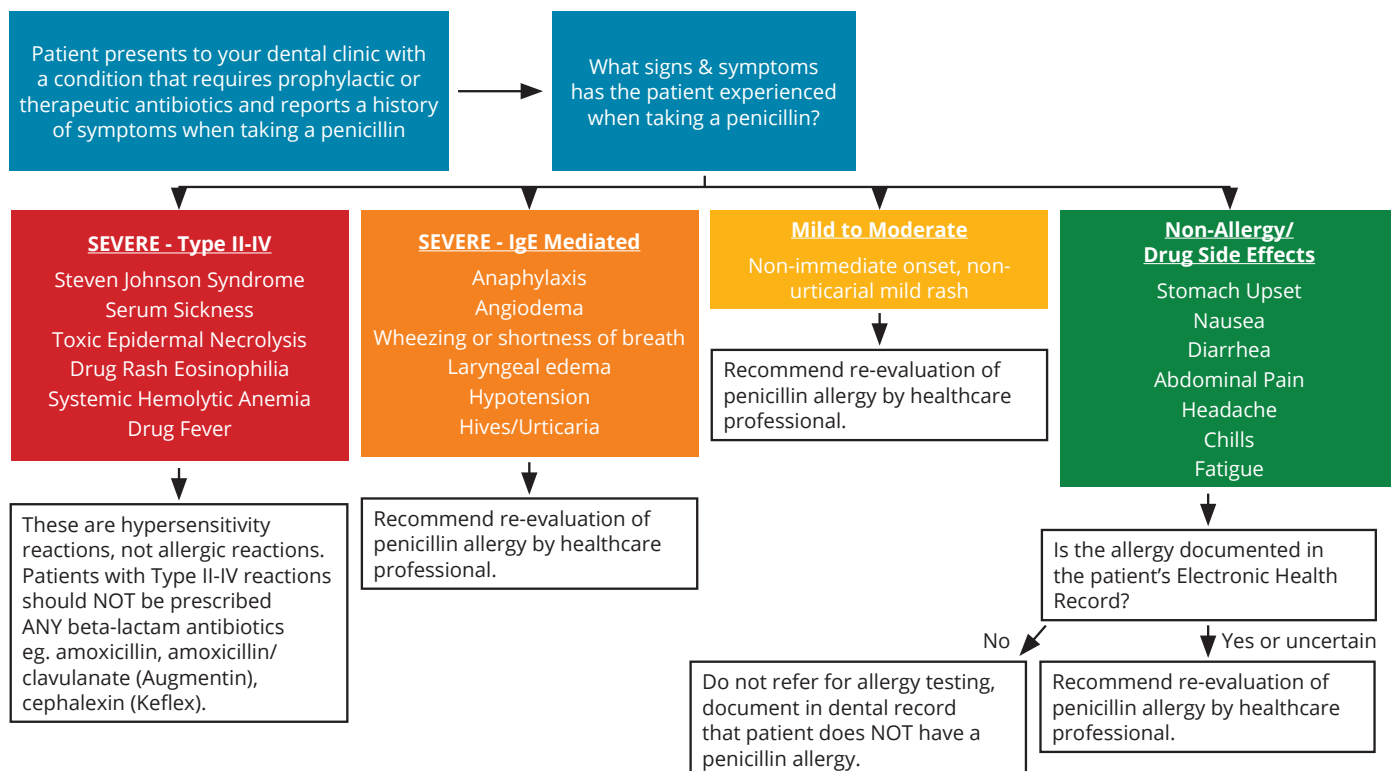
When not?

The framework is NOT intended to provide precise prescribing recommendations* for individual clinical situations, but rather assist the clinician and the patient to collaborate and determine if there is evidence from the patient's allergy history to recommend an evaluation.

Why?

- Patients who state that they are allergic to penicillin often do not have a true allergy, or their allergy may have waned over time.¹
- Patients labelled as penicillin-allergic are more likely to receive antibiotics that are NOT recommended as first-line therapy that have been associated with:
 - Reduced efficacy
 - More adverse reactions, including C. diff diarrhea which has been frequently observed in dental patients
 - Increased risk for antibiotic resistance
 - Higher healthcare costs

1. *J Allergy Clin Immunol Pract.* 2020 Oct;8(9S):S16-S116



*References for antibiotic choices and dosing:

For management of oral pain and swelling: <https://ebd.ada.org/en/evidence/guidelines/antibiotics-for-dental-pain-and-swelling>

For prophylaxis: https://aaos.webauthor.com/go/auc/terms.cfm?actionxm=Terms&auc_id=224965



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Penicillin Allergy Assessment

(Continued from Page 48)

persensitivity reactions will experience similar reactions to penicillin or other beta-lactams (e.g., cephalosporins, including Keflex) in the future. Due to this ambiguity and the severity of the reaction, their dental and medical records should indicate that they have a delayed hypersensitivity/allergic reaction, and alternative antibiotics should be considered.

The Penicillin Allergy Assessment Tool does not include antibiotic recommendations in patients who claim to have a penicillin allergy; the Chairside Guides included in the ADA Guidelines are an excellent reference for antibiotic recommendations.⁸ In publishing these guidelines, the guideline panel members recognized the need for dentists to consider alternative antibiotic choices in patients who report having a penicillin allergy, as the evidence around the adverse outcomes associated with clindamycin has emerged, and the presence of true allergies remains rare.⁸

According to these Guidelines, for patients who have not experienced anaphylaxis, angioedema, or hives with penicillin or a related beta-lactam (amoxicillin, ampicillin), the recommended antibiotic is cephalexin (Keflex). Patients who have experienced the aforementioned symptoms are candidates for treatment with azithromycin. The ADA Guidelines include clindamycin as another alternative but caution against its use due to the associated risk of CDI. Of note, the American Association of Orthopedic Surgeons has removed clindamycin entirely as an alternative treatment in penicillin-allergic patients.¹⁰

If the patient decides to have a suspected penicillin allergy evaluated, his or her primary care provider will ask a series of questions about

symptoms and possibly refer the patient to an allergist to perform penicillin skin testing. Penicillin skin testing is a standardized and relatively simple procedure that is frequently performed in hospitalized patients and is becoming more common in ambulatory settings. There is a nationally-recognized Penicillin Allergy Assessment and Skin Testing (PAAST) Certificate program offered by the University of South Carolina that supports further expansion of the service. (See: https://sc.edu/study/colleges_schools/pharmacy/centers/penicillin_allergy_skin_testing_certificate_program/index.php).

**The collaboration
between the patient
and dental team to
practice antibiotic
stewardship is crucial
to provide safe
dental visits.**

Ambulatory locations throughout Michigan can provide this service. For example, the Allergy and Asthma Center of Rochester (aaacr.com) will evaluate patients for penicillin allergy without a referral. The testing takes about three hours and the patient will be provided with a letter containing the results to be shared with other medical providers. The testing costs between \$500 — \$700, with many insurance companies covering some or all of the expenses.

Healthier, safer care

The goal of penicillin allergy reassessment in the dental office is for clinicians to work collaboratively with the patient to provide healthier and safer dental care for the individual and to improve public health. Safer antibiotic options would be selected

in the dental clinic and, more importantly, overall prescribing of broad-spectrum antibiotics that have been associated with the public health threat of antibiotic resistance would be decreased. Individuals who may most benefit from a penicillin allergy assessment include people with risk factors for CDI, such as prior CDI infection, older age, recent hospitalization, frequent antibiotic use, and/or other co-morbidities.

The Penicillin Allergy Assessment Tool is available on the MARR website (mi-marr.org); laminated copies may be obtained by emailing info@mi-marr.org. A copy is also included along with this article.

Summary

The Penicillin Allergy Assessment Tool presented in this article is one tool that may effectively reduce unnecessary or sub-optimal antibiotic use, decrease adverse health effects, and reduce the potential for infections caused by drug-resistant bacteria. The PAAT can be used to screen patients who report penicillin allergies and recommend follow-up assessment by a qualified health care professional.

The collaboration between the patient and dental team to practice antibiotic stewardship is crucial to provide safe dental visits. Utilization of the outlined tool will provide evidence-based guidance to identify and guide eligible patients to confirm the penicillin allergy diagnosis reported in their medical history so that the optimal antibiotics can safely be prescribed when needed. ●

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About the Authors

Elaine Bailey, PharmD, is the executive director of the Michigan Antibiotic Resistance Reduction Coalition and has served on the MARR Advisory Council since 2000. Through her work with the MARR Coalition, her goal is to educate the wider community to be stewards of antibiotics in an effort to curb the public health crisis of antibiotic resistance.

Mackenzie Connell is a graduate student at Wayne State University earning a master of public health degree. She has a background in environmental and public health research as well as a bachelor of science degree in public health. Her graduate education has a focus on urban public health practice.

Marie Fluent, DDS, has extensive experience and expertise as a dental infection control clinical instructor, educator, speaker, author, and consultant. Her dental career spans 35 years and includes roles as dentist, both as an associate and practice owner, infection control coordinator, office manager and dental assistant. She serves as education consultant for the Organization for Safety, Asepsis, and Prevention.

Erinne Kennedy, DDS, MPH, MMSc, is a graduate of Nova Southeastern College of Dental Medicine. She created and released a state toolkit, website, and training specifically for oral health clinicians on antibiotic stewardship clinical practice in Massachusetts. Kennedy is the director of pre-doctoral education at Kansas City University College of Dental Medicine.



Bailey



Connell



Fluent



Kennedy