



Conquering the Fear of Penicillin Allergy: The Boogeyman of Urgent Care



I had time to see one more patient as my shift was winding down. “Wound check. That should be a quick one,” I said to myself.

Famous last words. I soon learned that the young woman with the dog bite on her hand was returning for her fourth visit in as many days for the same issue.

She sat fidgeting on the exam table and was visibly irritated when I walked in the room. “It’s getting worse,” she said, holding her hand to my face before I had the chance to introduce myself. I hadn’t seen her before, but suddenly I felt responsible for her frustration.

Upon first glance, her hand was admittedly quite swollen. I asked her about how she’d been taking the antibiotics as I waited for her chart to load on my computer screen.

“Which ones?” she asked as she upended her purse, allowing a pile of pill bottles to spill onto her lap. Clearly, this wasn’t the “in and out” wound check case I’d planned for.

She went on to explain how her antibiotics had been changed at each visit. I nodded and tried to follow her narrative of the reasoning behind each change in prescription while stealing glances at the notes from her prior visits: doxycycline, clindamycin, ciprofloxacin, metronidazole, trimethoprim/sulfamethoxazole. She also mentioned she’d had “a little diarrhea.” I was surprised it wasn’t more.

As she continued to recount the saga, in the back of my mind I wondered why she wasn’t started on amoxicillin-clavulanate at the first visit. Then the obvious hit me as my eyes moved to the top of her chart. “Allergies: Penicillin,” appeared in glaring red and foreboding font. Of course.

The simplest and most effective treatment for dog bite prophylaxis, as is the case for so many other conditions, involves the use of one of penicillin’s many cousins.¹ And, as is also frequently the situation, my colleagues had been discouraged from prescribing the first-line antibiotic because of an allergy alert.

The modern EMR can feel like an overprotective parent at times—always hovering and ready to swoop in at the first sign of roughhousing on the playground. These alerts were created under the auspices of patient safety, but



often have unintended consequences like those I bore witness to that evening. And nowhere is this more commonly problematic than when a patient reports an allergy to penicillin.

If you feel like you’ve lived some variation of this scenario in the last week, there’s a reason: penicillin allergy is by far the most common drug allergy patients cite. In fact, over 10% of Americans carry a label for this sensitivity.² However, this is a vast overestimation of the reality of the situation. In fact, studies using skin testing have found that less than 1 in 10 patients who reported a penicillin allergy actually had a true IgE-mediated hypersensitivity reaction on formal challenge.³

This is where the problem begins. What other condition do we allow to propagate inaccurately in patient’s records 90% of the time?

The circumstances that allow this to occur so frequently are worth examining. When we enter an allergy in the medical record, we are, in effect, assigning a diagnosis. When we “verify allergies,” as most EMRs compel us to with each visit, we are affirming these allergic diagnoses.

This process is most commonly initiated by a nonprovider staff member who reviews the patient-reported allergies and list of medications at check-in. This verification process relies on historic entries and patient reports en-

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tirely. It is then incumbent on the clinician evaluating the patient to confirm the accuracy of the information with the patient.

Some of you may object at this point as to our culpability, citing that this responsibility should fall on the shoulders of patients' primary care providers. A reasonable argument. Given the pace of UC evaluations, certainly a complete review of allergies, medications, and the problem list is often impractical. Moreover, based on the scope of the issues we are addressing in UC, this is generally acceptable. For example, in a patient presenting with a laceration, there is scarcely a cogent argument supporting the necessity of verifying their dose of levothyroxine or ensuring that they're still taking a statin. That's because these details of their history shouldn't conceivably affect management.

However, many cases are different, especially when it comes to the common UC decision-point of antibiotic selection.

We practice in a fortunate era where evidenced-based guidelines exist for the treatment of most bacterial infections. This is coupled with the added benefit of EMR verifications which reduce the risk of errors in dosing and ensure that patients haven't had adverse reactions to the medications we prescribe.

Unfortunately, these alerts have led to the lamentable, unintended consequence of prescription paranoia. Many EMR alerts resemble the one I experienced while caring for the woman with the infected dog bite: bright red, large font, multiple exclamation points.

Occasionally, these alerts prevent a dangerous prescription. However, more often the alerts occur with low-probability, minor, or even theoretical interactions. For example, when prescribing a product with dextromethorphan for several days to a patient taking an SSRI, a cautionary message may appear to warn clinicians about the possibility of serotonin syndrome. This would be highly improbable if taking these medications at appropriate doses⁴; however, the alert will typically appear foreboding enough so as to dissuade most providers from prescribing.

Concerning antibiotic choice, such advisories commonly appear when prescribing cephalosporins to patients who

have a reported penicillin allergy and vice versa, despite abundant evidence that cross-reactivity between these classes has been drastically overestimated.^{3,5} This level of caution is even more clearly excessive given what we reviewed earlier about the frequency with which penicillin allergies are spurious.

Prescription paranoia extends to the other end of the bedside, as well. Patients tend to remember that they have a "penicillin allergy" above almost anything else in their health history, including things like organ transplants and open-heart surgery.

This is likely because the label of penicillin-allergic is frequently assigned in childhood. Kids receive amoxicillin for ear infections and strep throat, and adverse reactions ranging from rash, to vomiting, to diarrhea commonly occur. This occasion often serves as the genesis of the initial diagnosis of "allergy" to the drug. Understandably, well-meaning parents then attempt to ingrain a fear of penicillin in their children in the same way they repeatedly caution them about strangers with candy and crossing the road without looking. Having been conditioned as to the dangers of penicillin from a young age, many patients labeled as such cling tightly to this belief.

This creates a bidirectional boogeyman phenomenon whereby both the patient and clinician share an exaggerated and irrational fear of this highly useful class of antibiotics. This paranoia would not be problematic if situations calling for the use of penicillins were rare or if there were usually equally effective and well-tolerated alternatives. But that's not the case.

Inaccurate penicillin allergy can be quite consequential; I witnessed this firsthand while caring for the frustrated woman with the infected hand. In fact, a number of studies have shown that a penicillin allergy label increases patient's overall healthcare costs and the likelihood of adverse medication reactions.⁶⁻⁸ This is because alternative antibiotic regimens often have lower efficacy and have a broader spectrum of activity when used in the treatment of conditions for which a penicillin antibiotic is the recommended first-line therapy. More diarrhea, more money, and fewer cures.

So, how can we combat this epidemic of inappropriate medication allergy diagnoses? Well, we must first disarm the penicillin allergy boogeyman in our own minds. This is best achieved by familiarizing ourselves with the robust findings within the allergy and immunology literature on this topic.

In addition to the rarity of true penicillin hypersensitivity (again, present in fewer than 10% of patients reporting an allergy), it's also worth noting that 80% of patients will outgrow even a real penicillin immune-mediated reaction

after 10 years.² Moreover, life-threatening allergic reactions (ie, anaphylaxis) are exceedingly rare even in patients with bona-fide penicillin allergies when the antibiotic is administered orally. In fact, a UK database revealed only one confirmed report of fatal allergic reaction in over 100 million doses of orally administered amoxicillin.⁹

Secondly, we must be more precise with our language. It's an unfortunate but ubiquitous practice to categorize any unpleasant medication reaction ranging from minor expected side effects (eg, drowsiness with diphenhydramine) to life-threatening idiosyncratic reactions (eg, Stevens-Johnson syndrome) as an "allergy." One of the foundational practices of good medicine is using precise language, yet we conflate these adverse reactions in the chart and in patient's minds. This is an odd practice indeed.

When discussing our diet, for example, it's universal to make distinctions between a peanut allergy and feeling bloated after eating pasta or dizzy after drinking four martinis. These are all unpleasant reactions to what we've consumed, but the mechanism and consequence of the reactions are quite different.

When we use imprecise language to describe medication intolerances, patients become understandably confused about which medications they must avoid vs medications that can be taken occasionally and with caution.

Finally, we need to analyze each "penicillin allergy" for veracity when the opportunity arises.

As previously mentioned, patients who carry this label face higher healthcare expenses and worse outcomes than patients without a documented intolerance to penicillin. Given that 90% of patients labeled as penicillin-allergic actually are not, it would be a net win for patient safety if we asked every patient with an alleged penicillin allergy to determine its veracity.

This would be impractical during most UC shifts. What we can do instead, however, is question penicillin allergies each time we find ourselves compelled to reach for a second-line antibiotic. For example, when treating otitis media, it may be slightly faster to simply write for a Z-Pak, but this option has become increasingly ineffective with rising rates of *Streptococcus pneumoniae* resistance. Instead, it's better for the patient both in that moment and also for future encounters to examine their penicillin allergy.

Thankfully, in recent years, several validated decision aids have been developed to categorize a patient's risk of a dangerous reaction to a penicillin antibiotic based on their answers to several simple questions.

The easiest tool to use among these is the PEN-FAST rule, which is available on MDCalc.com. Based on a patient's answers to three questions, risk of serious reaction can be categorized from very low (<1%) to high (50%).^{10,11}

Patients with very low or low risk of adverse reactions can be reassured and prescribed a penicillin safely. For clinicians and/or patients who are still skittish, administering a test dose of oral amoxicillin, for example, while the patient is in UC can offer a more palatable option. For patient categorized as medium- to high-risk based on the PEN-FAST tool, referral to an allergist for formal assessment (usually with skin testing) will result in the majority of patients being cleared for safe use of beta-lactam antibiotics when indicated.¹²

I'm not unique in my concern for this problem. The Centers for Disease Control and Prevention and the Infectious Diseases Society of America have identified de-labeling inappropriate penicillin allergies as an important patient and public health issue. They've even created a Penicillin Allergy Awareness Day to highlight the issue (September 28, if you'd like to mark your calendar). This is because penicillins remain highly useful and, often, reasonably narrow-spectrum antibiotics for a wide range of infections. We owe it to our patients to minimize potential harms and maximize benefits for the treatments we prescribe.

It's time to call out inappropriate penicillin allergy labels for what they are in the vast majority of cases and disarm and demystify the boogeyman. Using the PEN-FAST tool, it doesn't take very much time either. When we fail to do this, we perpetuate an irrational fear in the minds of our patients. We'll also be serving our colleagues by sparing them the frustration of having to see our bounceback cases for treatment failure and/or adverse reactions to whatever alternative antibiotics they may have received under the incompletely informed auspices of patient safety. ■

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