

Penicillin Allergy: Improving Patient Care and the Medical Record

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Penicillins remain extremely useful, cost-effective, and important antibiotic agents, yet the patient's "allergy to penicillin" makes antibiotic ordering more complicated. Surprisingly, in a study of 1893 patients who had an order written for an anti-microbial agent at Northwestern Memorial Hospital, a tertiary care center, a concurrent notation of an antimicrobial allergy was recorded in 470 (25%) patients.¹ Penicillin was cited in 295 (15.6%) patients, and 85 (18.1%) patients had two or more antimicrobial agents listed. These findings emerged in a study investigating reasons for selection of alternative agents that may have less desirable microbiocidal activities and greater cost.

IgE-mediated penicillin allergy is often lost over time. For example, when a convincing allergic reaction has occurred at least 10 years previously, just 22% of subjects have been found to have immediate skin test reactivity to major or minor determinants.² In contrast, in the same study, of patients who had reported an immediate reaction within the previous 7–12 months, 93% were found to be skin test positive.² When just the major determinant, penicilloyl-polylysine, and penicillin G (freshly prepared at

10,000 u/mL) were used for skin testing, 36.2% of patients whose anaphylactic reaction occurred 4–12 months previously were found to be skin test positive compared to 19.4% of patients whose penicillin allergic reaction had occurred at least 60 months previously.³ Although these incidences of skin test positivity are greater than in some other cross-sectional studies,^{4–7} the loss of IgE antibodies to penicillin major and minor determinants provides the opportunity to test and exclude penicillin allergy in patients considered penicillin-allergic. In addition, negative skin tests to major and minor penicillin determinants help clarify the status of patients who have false diagnoses of penicillin allergy.

Skin testing is feasible to assess the immunologic status of penicillin-allergic patients, but there still are no FDA-approved minor determinants. Approximately 16–20% of penicillin skin test positive patients will react to minor determinants and not the major determinant.^{6–8} Having reactive minor determinants to use along with benzylpenicilloyl-polylysine (Pre-Pen, Schwarz Pharma, Milwaukee, WI) provides a high degree of precision in excluding IgE antibodies to penicillins in that the predictive value of negative immediate skin tests is 99% for not having anaphylaxis.⁷ Thus, many patients can have their current penicillin allergy status clarified, which is extremely important in patients about to undergo chemotherapy where neutropenic fever and need for penicillin treatment can be anticipated.

Warrington et al.⁹ report in this issue their review of the medical records of penicillin-allergic patients who had been found to be negative to major and minor penicillin determinants. Seventeen of 34 patients who had received a full course of beta-lactam antibiotics still had the designation of

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"penicillin-allergic" on the medical record at the time of discharge from the hospital. On future hospitalizations, the retained but inaccurate "penicillin-allergic" information would be carried forward, especially if the old chart were not available for review and correction. Improved information technology systems for medical records should help us store and retrieve information, but clearly not "think" for us (or at least not this year).

The incidence of adverse drug reactions in hospitalized patients has been estimated to be 6.7% with ~2,200,000 patients experiencing severe reactions.¹⁰ This high number has led to the suggestion for systems approaches as to how medications are "ordered, dispensed, and administered."^{11,12} Much work will be required in different ways to make meaningful improvements, and even documentation of allergic reactions seemingly is not precise. For example, in an analysis of how adverse drug reactions were identified, voluntary reporting was compared with chart reviews and a computer monitoring system.¹³ Of 101 allergic reactions, 4 (4%) were identified by voluntary reporting compared with 50 (50%) by computer monitoring, and 74 (73%) by deliberate chart reviews. In management of patients who have experienced a previous cutaneous reaction to a beta-lactam antibiotic, such information may not have been entered in the medical record, creating a potentially dangerous situation for patient, physician, and hospital or ambulatory facility. For example, as many as 15% of patients who have experienced a delayed maculopapular skin rash subsequently may be found to have immediate skin test reactivity to penicillin determinants.⁵ Alternatively, safeguards need to be in place so that when a patient's profile notes antibiotic allergies, the pharmacist can withhold the incriminated medication unless there is an allergy-immunology consultation or attending physician notation that the allergy no longer exists. In addition, physicians need to recognize that minimizing the importance of a history of penicillin allergy may result in anaphylactic shock, especially when beta-lactam antibiotics are administered to patients who have anti-penicillin IgE antibodies. What are the challenges? We need improvements in our information technology systems, systems operations, physician ordering, and pharmacist practices accompanied by examination of the patient and improved information entry into the medical record. Hopefully, these combined advances can lead to meaningful reductions in the number of

serious and fatal adverse drug reactions. The Warrington⁹ study and the Northwestern Memorial Hospital¹ experience of hospitalized patients are based on the availability of the penicillin minor determinants made in the respective programs. Hopefully, these valuable diagnostic aids will be available to physicians in the future.

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