Original Article

# A Proactive Approach to Penicillin Allergy Testing in Hospitalized Patients

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***What is already known about this topic?*** Penicillin allergy is often misdiagnosed and leads to overuse of broad-spectrum alternatives. Although well validated, testing is rarely performed in the hospital despite its potential benefits toward antibiotic use in the acute care setting.

***What does this article add to our knowledge?*** A multidisciplinary approach to penicillin allergy testing incorporating computerized protocols and pharmacist education effectively locates and removes reported allergies in hospitalized patients. Proactive screening addresses an overlooked opportunity to reduce unnecessary antibiotic use.

***How does this study impact current management guidelines?*** We offer practical guidance for large-scale penicillin allergy testing in a modern health care environment. Our model stratifies testing candidates via multiple criteria and is easily adaptable to the needs of varying institutions.

**BACKGROUND: Penicillin allergy testing is underutilized in inpatients despite its potential to immediately impact antibiotic treatment. Although most tested patients are able to tolerate penicillin, limited availability and awareness of this tool leads to the use of costly and harmful substitutes.**

**OBJECTIVE: We established an inpatient service at a large academic hospital to identify and test patients with a history of penicillin allergy with the goals of removing inaccurate diagnoses, reducing the use of beta-lactam alternatives, and educating patients and clinicians about the procedure.**

**METHODS: Eligible inpatients were flagged daily through the electronic medical record and prioritized via a specialized algorithm. A trained clinical pharmacist performed penicillin skin tests and challenges preemptively or by provider request. Clinical characteristics and antibiotic use were analyzed in tested patients.**

**RESULTS: A total of 1203 applicable charts were detected by our system leading to 252 direct evaluations over 18 months. Overall, 228 subjects (90.5%) had their penicillin allergy removed. Of these, 223 were cleared via testing and 5 by discovery of prior penicillin tolerance. Among patients testing negative, 85 (38%) subsequently received beta-lactams, preventing 504 inpatient days and 648 outpatient days on alternative agents.**

**CONCLUSIONS: Penicillin allergy testing using a physician-pharmacist team model effectively removes reported allergies in hospitalized patients. The electronic medical record is a valuable asset for locating and stratifying individuals who benefit most from intervention. Proactive testing substantially reduces unnecessary inpatient and outpatient use of beta-lactam alternatives that may otherwise go unaddressed.** © **2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2016;■:■-■)**

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Penicillin allergy is the most reported drug allergy in the United States, with a prevalence of 8% to 12% in various studies. However, approximately 90% of history-positive patients actually tolerate penicillins.[1-3] The reasons for this discrepancy are varied—reaction histories are often remote and poorly characterized, or the symptoms may represent non−IgE-mediated consequences of an underlying illness wrongly attributed to the medication.[4] Furthermore, true hypersensitivity to penicillin wanes with time, with more than half of skin test positive patients losing sensitivity by 5 years, and 80% by 10 years.[5,6]

Penicillin allergy is not a trivial diagnosis. A cohort study of hospitalized patients by Macy et al found that a documented penicillin allergy, authentic or not, increased hospital time versus

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*Abbreviations used*
*EMR- Electronic medical record*
*MRSA- Methicillin-resistant* Staphylococcus aureus
*PRE-PEN- Penicilloyl-polylysine*

matched controls. Unsurprisingly, these patients received considerably greater doses of vancomycin, fluoroquinolones, and clindamycin over time. Most significantly, the prevalence of *Clostridium difficile*, vancomycin-resistant *Enterococcus*, and methicillin-resistant *Staphylococcus aureus* (MRSA) infections increased in the penicillin allergic population.[7] These nosocomial infections may be attributed to the usage of these alternative agents, or in the case of MRSA to increased hospitalizations.[8-10]

The Centers for Disease Control and Prevention in its most recent Threat Report published in 2014 calls to attention the hazard posed by antibiotic resistance, surmising that more than 2 million infections and 23,000 deaths occur annually because of antibiotic-resistant organisms.[11] Even today, penicillin and its derivatives remain among the cheapest, most effective, and least toxic antimicrobials. With few new antibiotics on the horizon, treatment options are further reduced when patients report drug allergies. The frequency of anaphylaxis to penicillin is extremely rare and estimated at 1 to 5 per 10,000 courses.[12] Unfortunately, many clinicians still forgo using penicillin and by extension other first- and second-generation beta-lactam antibiotics in these patients because of fear of a severe reaction, leading to substitution with agents that are often limited to intravenous administration, costlier, and potentially more toxic.[13-15]

Penicillin allergy testing is well validated for diagnosing IgE-mediated penicillin allergy. Skin testing using the major determinant penicilloyl-polylysine (PRE-PEN) and minor determinants penicillin G, penicilloate, and penilloate has a negative predictive value of 97% to 99%.[16-18] Although penicilloate and penilloate are not commercially available in the United States, a protocol utilizing PRE-PEN and penicillin G for skin testing followed by oral amoxicillin challenge appears to make the diagnosis with similar accuracy.[19] Routine testing of inpatients has been proposed as a tool for reducing expenses and broad-spectrum antibiotic use, but existing efforts have been limited to small programs at a handful of institutions.[20-25]

Penicillin allergy testing in admitted patients is underutilized and underpublicized by both allergists and inpatient providers. To address this, we established an enduring multidisciplinary inpatient service dedicated to the active identification, testing, and education of penicillin allergy. The service partners the Division of Allergy and Immunology at the University of Texas Southwestern Medical Center (UT Southwestern) with the Department of Pharmacy Services at Parkland Health and Hospital System. Parkland is an 870-bed public hospital serving Dallas County, Texas, and a primary teaching affiliate of UT Southwestern. In 2015, Parkland recorded 65,585 inpatient admissions and 250,550 emergency visits and is one of the largest providers of uncompensated care in the state. Internal audits have demonstrated an approximately 8% incidence of documented penicillin allergy in admitted patients, yet in a 20-month span from October 2012 to May 2014, penicillin allergy testing was ordered in only 17 patients. We present the impact of this intervention and offer a framework for implementing such a program at other institutions.

## METHODS

The service utilizes a trained clinical pharmacist to evaluate patients for penicillin hypersensitivity. Previously, Wall et al described a protocol in which pharmacists under allergist oversight conducted skin tests in patients with positive histories. This service was offered on a limited basis to consulting physicians and safely removed the majority of penicillin allergy labels in those enrolled.[26] Our program expands this concept by utilizing electronic medical record (EMR)-assisted algorithms in the selection and prioritization of subjects who may benefit from testing. In addition, once testing candidates are identified, the service initiates discussion with the patient and the current inpatient provider regarding the allergy.

In September 2014, the protocol for pharmacist administered testing was approved through the Pharmacy and Therapeutics Committee at Parkland. This protocol may be ordered by the primary team or allergy faculty and fellows, and allows the specialty pharmacist to screen the patient, order the necessary drugs to perform allergy testing, administer the test, and use rescue medications if needed. A new procedure was developed with the central pharmacy to streamline preparation of testing materials ensuring that the majority of the pharmacist's time is spent with the patient. An emergency reaction kit carried by the pharmacist avoids reliance on items sent from the pharmacy or stored in a medication dispensing system. After approval by the Institutional Review Board at Parkland and UT Southwestern, screening began on all hospitalized patients who reported an allergy to penicillin. The population detailed in this study encompasses patients screened from November 2014 through April 2016.

Our institution uses Hyperspace (Epic Systems Corporation, Verona, Wis) as its EMR. At the beginning of the day, a report is generated of all admitted patients carrying an active penicillin allergy, which begins the screening. A series of automated filters help prioritize patients within this pool for testing (Figure 1). All patients receiving antihistamines are excluded as their use can affect interpretation of skin testing. Patients with discharge orders are filtered next, as they are unlikely to remain for testing and yield minimal impact on inpatient pharmacotherapy. The remainder are stratified based on current antibiotic orders with preference given to patients on high value broad-spectrum agents such as carbapenems or aztreonam, and those with immunocompromising conditions increasing risk for subsequent infection (defined as diabetes mellitus, human immunodeficiency virus infection, active malignancy, or use of immunosuppressant medication including chemotherapy). Inpatients meeting the most criteria are deemed likeliest to benefit from allergy testing. Their primary provider is contacted by pager or phone to obtain a verbal order for formal evaluation. The service also sees consultations by provider request and these patients are addressed preferentially as the intention is often to immediately change antibiotic therapy based on test results. Final suitability is determined by the pharmacist via a manual chart review and personal interview. The interview characterizes the nature of the reaction through a standardized series of questions (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). Any query on whether to proceed is discussed with the allergist on-call.

The exclusion criteria include the following:

(1) History of a severe cutaneous adverse reaction such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug-induced exfoliative dermatitis, drug rash with eosinophilia and systemic symptoms, or acute generalized exanthematous pustulosis.
(2) Non–IgE-mediated reaction such as vasculitis, interstitial nephritis, or hemolysis.

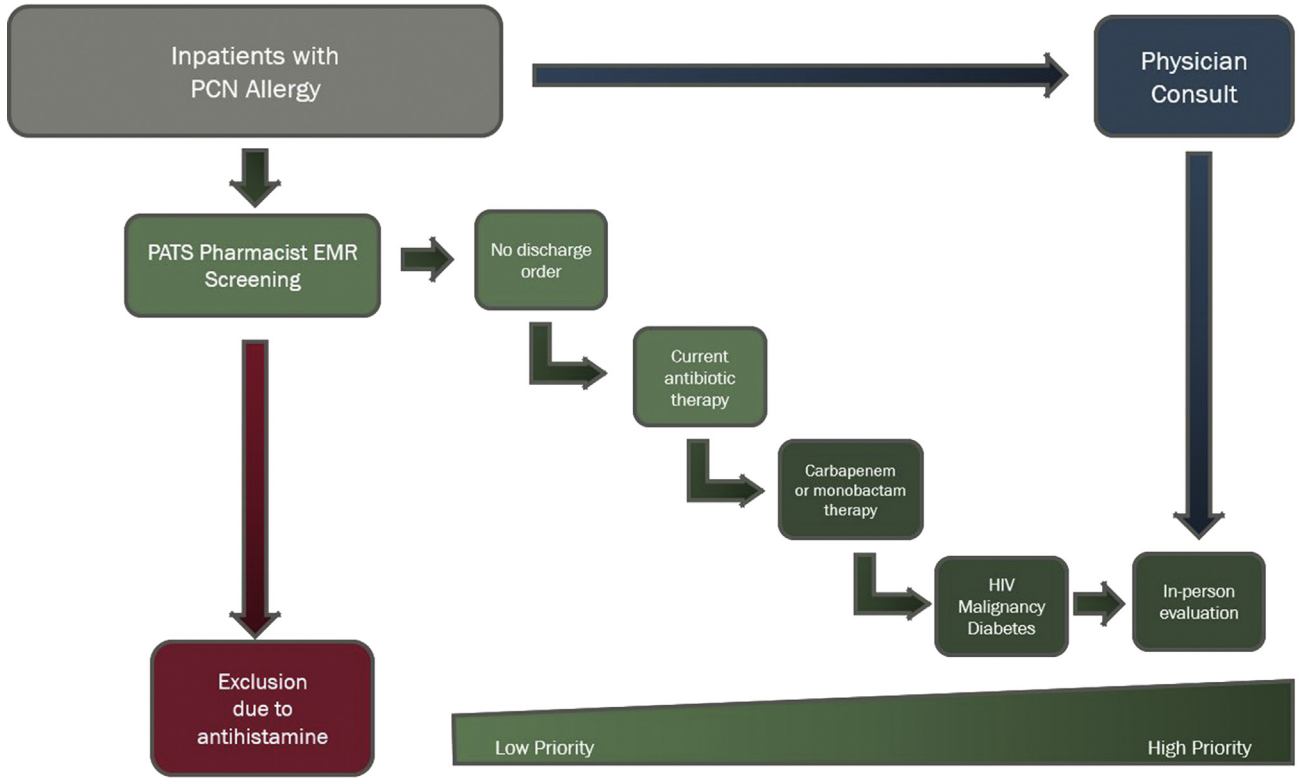


**FIGURE 1.** Prioritization algorithm for inpatients receiving penicillin allergy testing. *EMR*, Electronic medical record; *PATS*, penicillin allergy testing service; *PCN*, penicillin.

(3) Recent anaphylaxis within 4 weeks.
(4) Use of medications with antihistaminergic properties within 48 hours or 7 days (depending on agent).
(5) Insufficient skin amenable for interpretation of the test.
(6) Pregnancy—with the exception of patients with confirmed syphilis or other condition where the benefit of penicillin treatment outweighs the risk of testing.

## Penicillin allergy diagnostic testing

Testing for penicillin allergy was performed by the service pharmacist at the patient's bedside as follows. All patients had skin testing to the major determinant PRE-PEN (ALK, Round Rock, Tex) used as per package insert, minor determinant penicillin G potassium at a concentration of 10,000 units/mL diluted in normal saline, histamine 6 mg/mL positive control, and 50% glycerin negative control (Hollister-Stier, Spokane, Wash). Prick-puncture testing was performed using a bifurcated needle and drops of each reagent on the volar aspect of the patient's arm with reactions recorded after 15 minutes. A positive response to skin prick was classified as induration of the antigen site $\geq$ 3 mm in diameter in the presence of a positive control site $\geq$ 5 mm and negative control $\leq$ 3 mm. Saline wheals $>$ 3 mm were repeated, and if similar or greater induration was seen on the second attempt, this was classified as dermatographism. A positive control wheal $<$ 5 mm was classified as a negative histamine response. Each of these results terminated the protocol. If the diameter of the antigen wheal was $<$ 3 mm with appropriately sized controls, the prick puncture was recorded as negative and intradermal tests were administered.

Intradermal testing was performed using PRE-PEN, penicillin G, and normal saline reagents. Antigens (0.02-0.03 mL) were drawn in separate tuberculin syringes and injected in duplicate at least 2 cm apart. A single intradermal test to the negative control was placed at least 5 cm away from the antigen sites. The initial wheal diameter was recorded in 2 directions and measured again after 15 minutes. A negative intradermal test was defined as a $<$3-mm increase in the size of the bleb. A positive intradermal test was defined as an increase in size from the original wheal by $\geq$3 mm. An equivocal test was defined as an increase in wheal size by $<$3 mm with a reaction greater than control site or discordant duplicates.

Patients with negative prick-puncture and intradermal tests were openly challenged to amoxicillin 500 mg orally. A 500 mg dose was chosen to allay concerns from the consulting physician for reactions at higher doses. Intramuscular epinephrine 0.3 mg and diphenhydramine were available in case of reaction. Patients on beta-blockers were discussed with the on-call allergist before challenge. All patients were monitored after challenge for 60 minutes. If no reaction had occurred by that point, the penicillin allergy label was removed from the EMR and a clear result note left in the chart. To reinforce these findings, patients and physicians were individually informed of the result and counseled on its implications for future penicillin use.

For each case, in addition to the information collected via the EMR screening and the reaction history, demographic data including age at admission, sex, race, concurrent medication allergies, primary discharge diagnosis, and consulting service were recorded. Primary outcomes were the quantity of patients screened and formally tested, percentage of allergies removed, and inpatient antibiotic usage before and after testing and at discharge. When

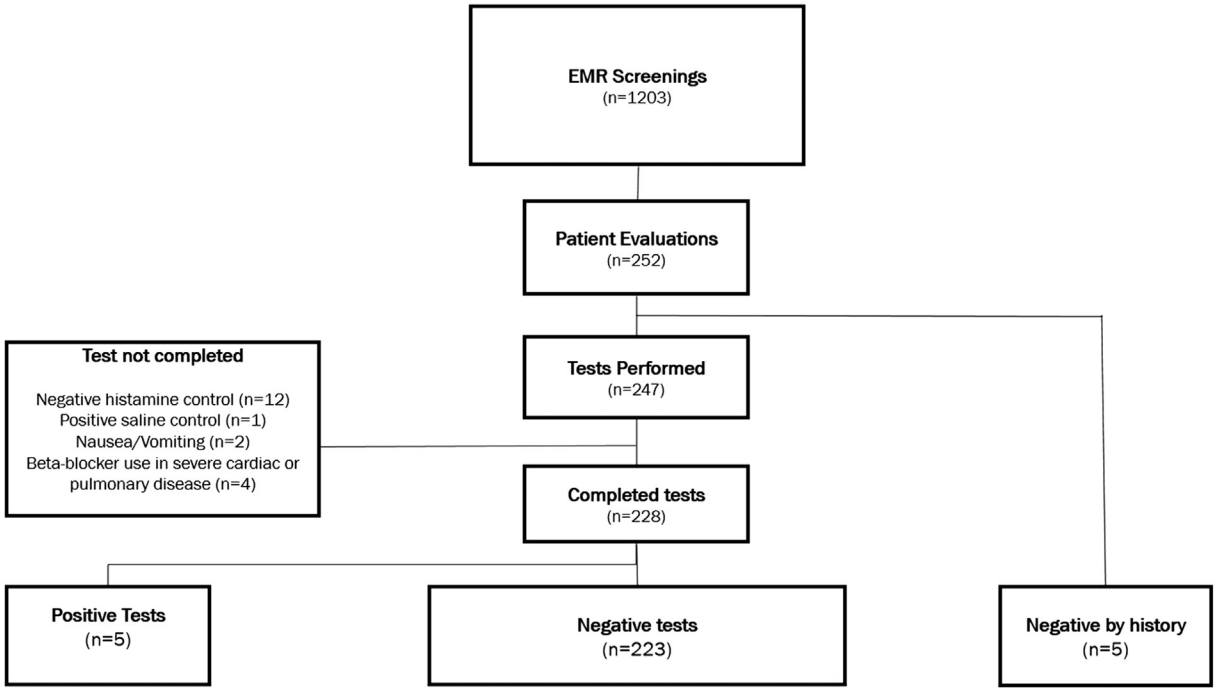


**FIGURE 2.** Numbers of subjects initially screened by EMR, interviewed by the allergy pharmacist, and undergoing the testing protocol. Subjects beginning but not completing the protocol are listed along with the reason for not finishing. *EMR*, Electronic medical record.

applicable, reasons for not completing the protocol were tracked. Subjects were retrospectively assigned to 1 of 10 diagnosis systems groups based on the primary reason for receiving antibiotics as per the discharge summary. Determination of inpatient days on antibiotics was made based on the length of time orders that were active in the EMR, with the exception of long-acting benzathine penicillin G, in which a single dose accounted for 7 days of antibiotic coverage. Descriptive statistics were used to analyze patient demographics. For statistical analysis STATA 14.1 was used to determine statistical differences between the percentage of patients receiving different classes of antibiotics before and after penicillin allergy testing. A McNemar's test was used for paired nominal data.

## RESULTS

Over the study period, 1203 patient records with listed penicillin allergy at admission were flagged by our system. Under our prioritization process, 252 patients were evaluated personally by the service pharmacist. Five patients had allergies removed after verifying prior penicillin tolerance during the interview without need for further testing. A total of 228 patients completed the testing protocol with 223 cleared after negative skin testing and challenge. Only 5 of the 228 patients tested positive, 4 on prick-puncture and 1 developed urticaria within an hour of taking amoxicillin. There were no positive intradermal tests in our cohort. Nineteen patients were not able to complete the protocol for several reasons: negative histamine controls, positive saline control, concurrent beta-blocker use in the setting of severe cardiopulmonary impairment, and nonspecific nausea or vomiting during the challenge. Overall, 228 of the 252 (90.5%) interviewed patients had their allergy removed, for several of these patients this was accomplished simply by taking a detailed history (Figure 2).

The service saw a diverse set of patients, with an average age of 49.3 years ranging from 16 to 87. Our study group had a substantial proportion of African American and Hispanic patients. The majority of patients were hospitalized on primary medical services with sizable portions cared for by surgical and obstetrics/gynecology teams. All but 9 patients received at least one antibiotic while hospitalized. The most common indication for antibiotic use was musculoskeletal-skin/soft tissue infection (28.2%), followed by urinary tract (20.6%) and pulmonary (18.3%) infections. Because of our prioritization process, 150 (60%) of patients evaluated were immunocompromised as defined in the methods section (Table I).

The most common historical reactions to penicillins were urticaria and/or angioedema. Many patients had remote histories, with more than three-fourths describing at least 10 and two-thirds at least 20 years since their last reaction. Three patients denied ever having sensitivity to penicillin despite the chart diagnosis, and 2 had distant histories but had since tolerated use. Most patients had an allergy history to penicillin only, but 37% listed allergies to other medication classes. However, among patients claiming 3 or more drug allergies, all tolerated penicillin. All of those reporting a concomitant cephalosporin allergy had negative skin testing and challenge to penicillin (Table II).

Most patients received non—beta-lactam antibiotics before testing, although 46 were already on a cephalosporin and 3 actually received a penicillin despite their purported allergy. The median time from admission to testing was 2.4 days (interquartile range, 1.23-4.92). Medication administration records after negative testing showed significant declines in active orders for vancomycin (−33%, $P < .001$), clindamycin (−61%, $P < .001$), fluoroquinolones (−36%, $P < .001$), carbapenems (−50%, $P = .049$), and aztreonam (−68%,

**TABLE I.** Demographics of interviewed patients

| | All n = 252 |
|---|---|
| Female, n (%) | 137 (54.4) |
| Age, y | |
| Mean ± SD | 49.3 ± 16.1 |
| Range | 16-87 |
| Ethnicity, n (%) | |
| White | 77 (30.6) |
| Black | 85 (33.7) |
| Hispanic | 88 (34.9) |
| Asian | 2 (0.8) |
| Admitting service, n (%) | |
| Medical | 200 (79.4) |
| Surgical | 33 (13.1) |
| OB-GYN | 16 (6.3) |
| Other | 3 (1.2) |
| Infection risk factors | |
| Diabetes mellitus | 90 (35.7) |
| HIV | 36 (14.3) |
| Malignancy | 24 (9.5) |
| Immunosuppressant | 13 (5.2) |
| Primary diagnosis | |
| Neurology | 6 (2.4) |
| Pulmonary | 46 (18.3) |
| Cardiovascular | 8 (3.2) |
| Abdominal organ | 28 (11.1) |
| Urinary | 52 (20.6) |
| Musculoskeletal/skin | 71 (28.2) |
| Reproductive | 18 (7.2) |
| Hematology/oncology | 10 (4.0) |
| Bloodstream | 4 (1.6) |
| Other | 9 (3.6) |

*HIV*, Human immunodeficiency virus; *OB-GYN*, obstetrics and gynecology; *SD*, standard deviation.
Medical services include general internal medicine, family medicine, cardiology, pulmonary/ICU, oncology, or emergency services observation. Surgical services include trauma, general surgery, colorectal, burn, orthopedics, otolaryngology, and urology. Obstetrics/gynecology includes labor and delivery, gynecology oncology, urogynecology, and maternal-fetal medicine. Other services include inpatient rehabilitation and psychiatry.

**TABLE II.** Allergy histories reported by patients

| | All (n = 252) | Negative test (n = 223) | Positive test (n = 5) | Relabeled (n = 16) |
|---|---|---|---|---|
| Reaction type, n (%) | | | | |
| Nonurticarial rash | 54 (21.4) | 48 (21.5) | 0 (0) | 5 (31.5) |
| Urticaria/ angioedema | 117 (46.4) | 102 (45.7) | 5 (100) | 9 (56.3) |
| Respiratory | 47 (18.6) | 47 (21.1) | 0 (0) | 4 (25) |
| Gastrointestinal | 16 (6.3) | 14 (6.3) | 0 (0) | 2 (12.5) |
| Cardiovascular | 9 (3.6) | 8 (3.6) | 0 (0) | 1 (6.3) |
| Other | 15 (6.0) | 15 (6.7) | 0 (0) | 0 (0) |
| Unknown | 40 (15.9) | 40 (17.9) | 0 (0) | 0 (0) |
| Time since reaction, y | | | | |
| <1 | 9 (3.6) | 8 (3.6) | 1 (20) | 1 (6.3) |
| 1-4 | 19 (7.5) | 19 (8.5) | 0 (0) | 3 (18.8) |
| 5-9 | 25 (9.9) | 19 (8.5) | 2 (40) | 2 (12.5) |
| 10-19 | 32 (12.7) | 25 (11.2) | 1 (20) | 1 (6.3) |
| >20 | 160 (63.5) | 148 (66.3) | 1 (20) | 9 (56.2) |
| Unknown | 4 (1.6) | 4 (1.8) | 0 (0) | – |
| No reaction | 3 (1.2) | – | – | – |
| Drug class allergy, no | | | | |
| 1 | 142 (56.3) | 129 (57.8) | 4 (80) | 7 (43.8) |
| 2 | 57 (22.6) | 47 (21.1) | 1 (20) | 2 (12.5) |
| 3-4 | 39 (15.5) | 34 (15.2) | 0 (0) | 5 (31.3) |
| >5 | 16 (6.3) | 13 (5.8) | 0 (0) | 1 (6.3) |
| Concurrent cephalosporin allergy | 8 (3.2) | 8 (3.6) | 0 (0) | 0 (0) |

Class definitions:
All: Patients evaluated directly by the service pharmacist.
Negative test: Patients with allergy removed after negative skin testing and oral amoxicillin challenge.
Positive test: Patients with allergy not removed after either a positive skin test or amoxicillin challenge.
Relabeled: patients with allergy removed and subsequently added back to the record.

$P = .009$) along with more than 20-fold increased penicillin use ($P < .001$) (Figure 3, *A*). Of the 223 patients with negative tests, 77 (34%) initiated therapy after testing with a penicillin or cephalosporin while admitted, and 40 of these patients were also prescribed a penicillin or cephalosporin at discharge. An additional 8 (3.6%) patients did not initiate beta-lactam treatment while admitted but were prescribed one at discharge. Patients not previously on a beta-lactam totaled 504 inpatient days (377 on penicillins and 127 on cephalosporins). Thirteen patients on cephalosporins before testing were switched to a penicillin for the remainder of their inpatient antibiotic course. Outpatient beta-lactam prescriptions for the 85 switched patients totaled 648 days, with 438 on penicillins and 210 on cephalosporins (Figure 3, *B*).

One notable finding was that 16 of the 223 patients cleared by the protocol (7.2%) had their allergy label added back at a subsequent health care encounter within the study timeframe. However, in most cases, the allergy pharmacist was able to intervene by verifying that no delayed reaction occurred, reeducating the patient, and removing the allergy again from the record.

## DISCUSSION

To our knowledge, this is the largest study of inpatient penicillin testing and the only one in an indigent care setting with high potential for readmission. Traditionally, allergic diseases have rarely been managed in the hospital. Not surprisingly, inpatient providers are deficient in knowledge of penicillin allergy and its evaluation. A study of providers at a tertiary care center found widespread unawareness of skin testing as an assessment tool and the natural history of hypersensitivity.[27] Amongst informed physicians, the clinical need is evident—in a recent survey of infectious diseases specialists, the overwhelming majority indicated a willingness to refer patients for antibiotic allergy testing if it were readily available, with more than two-thirds stating that testing should be incorporated into antimicrobial stewardship efforts.[28] Guidelines published by the Infectious Disease Society of America echo these sentiments.[29] We demonstrate a model for teamwork between allergists and other health care providers for addressing the epidemic of

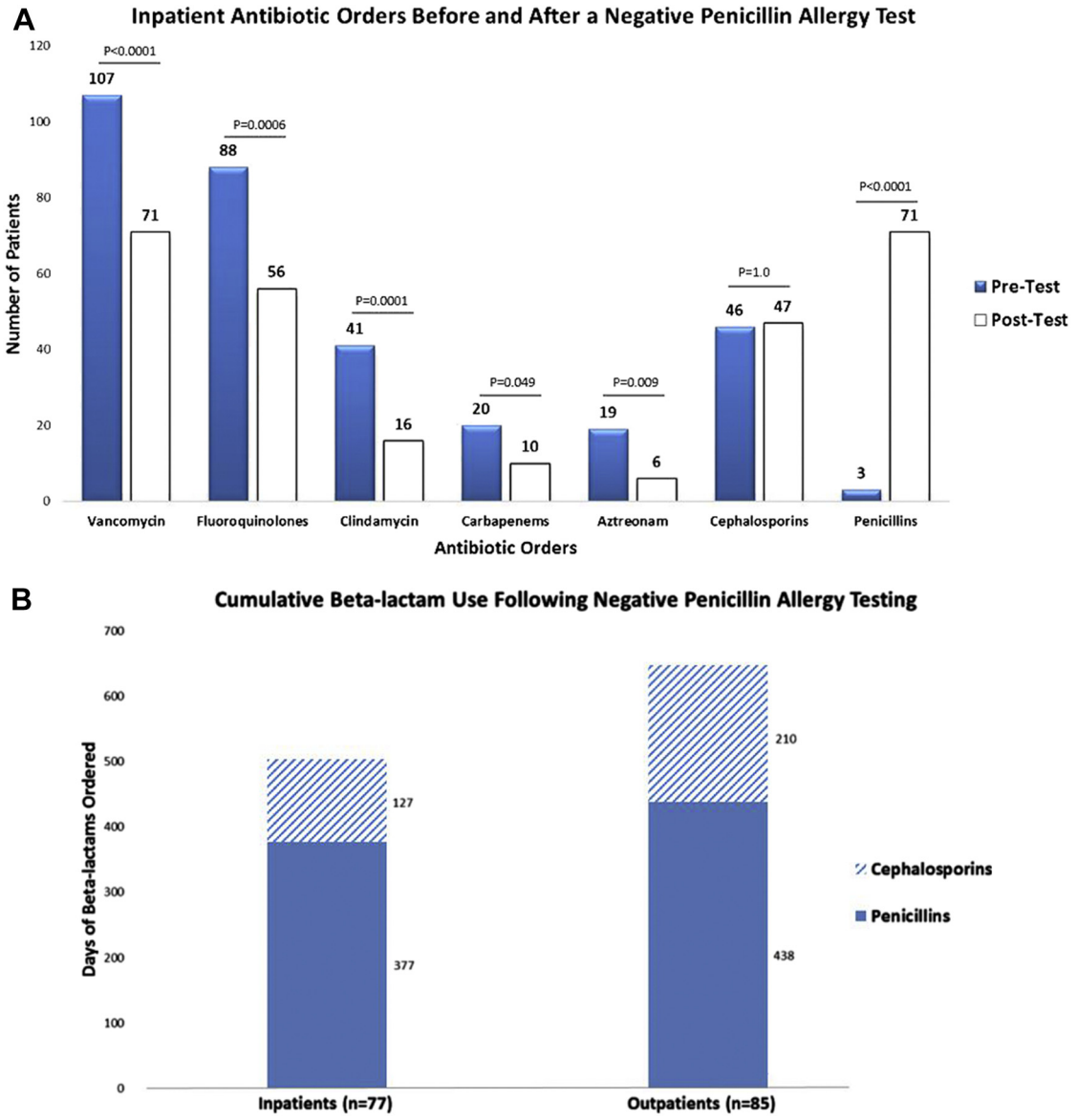


**FIGURE 3.** **A**, Inpatient antibiotic orders for patients before and after negative penicillin allergy testing. **B**, Cumulative patient days on penicillins and cephalosporins during admission and at discharge after negative penicillin allergy testing.

hospitalized patients with penicillin "allergy." Also, we show that the EMR is invaluable in enabling a proactive approach toward identifying testable individuals and directing utilization of testing resources. Finally, our interventions led to meaningful changes in antibiotic prescriptions both inpatient and at discharge.

Previous studies of inpatient penicillin testing have mostly utilized physician allergists with hospital privileges.[20-25] Other institutions may not have an allergist or staff available for testing at all times. This makes the incorporation of other trained professionals paramount, especially in settings with resource limitations. There are a number of advantages to employing pharmacists trained by allergy and/or immunology specialists in the testing process. Although initial screening is largely automated, the final decision on whom to test requires knowledge of a patient's concomitant medications. For instance, many antiemetics or antipsychotics antagonize histamine and beta-blockers could influence the risk associated with a drug challenge. Pharmacists are accustomed to reviewing medications in detail and identifying factors favoring an informative test. Furthermore, pharmacists are well equipped to educate patients after completion of testing, which is an equally important intervention. They may also advise physicians on optimal posttest antibiotics. If future demand is sufficient, throughput could expand by having trained nurses or technicians perform skin tests in a single location within the hospital with the pharmacist coordinating the process.

The penicillin allergy testing service at our institution effectively removed most penicillin allergy labels in our tested population, consistent with many of the smaller studies in the literature. In some instances, gathering a detailed allergy history may confirm tolerance of penicillin and abrogate the need for lengthy testing. Our observations substantiate the continued

relevance of observed challenges, given that one patient reacted on ingestion despite negative prick-puncture and intradermal tests. Although current skin testing reagents are very reliable, the current literature indicates a 0.8% to 2.5% rate of positive challenge in patients with negative skin testing to PRE-PEN and penicillin G.[4,19] Potentially the most valuable action of this service is removing the disproven allergy from the medical record, as previous analyses of hospital-based testing have shown passive recommendation alone to be insufficient to eliminate the allergy label at discharge.[21]

Implementation of an allergy testing service at a large hospital system has uncovered limitations of our approach and also opportunities for process improvement. First, it was not possible to verify patient compliance with outpatient antibiotic therapy, and it is possible that not all expected postdischarge treatment days were achieved. However, the intervention still reduced exposure to agents including clindamycin or fluoroquinolones and their potential adverse effects. Second, the study did not assess whether removal of the allergy directly reduced the length of said hospitalization relative to untested "allergic" patients, but as patients are at times admitted because of a lack of suitable oral treatments, the availability of another medication class with oral options should facilitate faster discharges. Furthermore, given the association between active penicillin allergy and increased hospitalization, the ultimate value of this intervention should arise with subsequent admissions and associated changes in morbidity. One advantage gained from active EMR screening is the attainment of a large comparator pool of patients with penicillin allergies who did not undergo the testing protocol. This may provide the basis for prospective controlled studies assessing the long-term effect of this program on length of stay and complications.

Prior studies have not always demonstrated cost savings associated with penicillin allergy testing of hospitalized patients, and this was a limitation of our study, as testing patients broadly and transitioning from agents such as vancomycin, fluoroquinolones, and clindamycin to beta-lactams may not immediately reduce expenditures. However, this does not adequately capture the costs incurred with increased hospital days, antibiotic resistance, and readmissions seen with suboptimal antibiotic therapy.[30] Our initiative was not driven primarily by drug cost savings, but financially it is sensible to preferentially test patients receiving more expensive beta-lactam alternatives, as we have done in our protocol. A recent study by King et al[31] where most subjects were receiving high-cost broad-spectrum agents found a difference in mean daily antibiotic cost of $297 per patient after testing. With this in mind, we are studying the effect of automatically bundling allergy testing with selected antibiotic orders in penicillin allergic patients.

The issue of previously removed allergies returning to the EMR was observed soon after starting. Although an effort was made to educate each patient about their results, a small percentage continued to report a penicillin allergy at subsequent encounters. Around 1 year into the program, an automated alert was added notifying providers when a penicillin allergy is added back in any patient with a documented negative test. This alert informs providers of the prior result and advises them to investigate why it was added back and to remove the allergy again if appropriate. Secondly, our institution has begun follow-up telephone calls to all patients with negative tests 2-4 weeks after discharge. This effort not only reinforces the education provided before discharge, but also provides an opportunity to assess for any delayed reactions that may have arisen while taking beta-lactam antibiotics. The long-term outcomes of these interventions are currently under active investigation.

Overall, we conclude that a dedicated inpatient penicillin allergy testing program is feasible in the inpatient setting and substantially modifies antibiotic utilization. A proactive approach expands the scope of allergy as a specialty and provides a valuable educational opportunity for physicians and patients alike. Although our framework was developed for use in a large tertiary health system, individual aspects of the protocol may be modified for use in virtually any environment with an EMR. Resource-limited facilities may choose to target patients on only high-cost antibiotics, those with explicit comorbidities, or develop protocols based on local antimicrobial resistances. We encourage the use of this protocol in partnership with local allergy/immunology specialists as a practical resource for any clinician seeking to improve antibiotic stewardship within his or her hospital practice.

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