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ANAPHYLAXIS AND DRUG ALLERGY (DA KHAN AND M CASTELLS, SECTION EDITORS)

Evaluation of Penicillin Allergy in the Hospitalized Patient: Opportunities for Antimicrobial Stewardship

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Abstract
Purpose of Review Penicillin allergy is often misdiagnosed and is associated with adverse consequences, but testing is infrequently done in the hospital setting. This article reviews historical and contemporary innovations in inpatient penicillin allergy testing and its impact on antimicrobial stewardship.
Recent Findings Adoption of the electronic medical record allows rapid identification of admitted patients carrying a penicillin allergy diagnosis. Collaboration with clinical pharmacists and the development of computerized clinical guidelines facilitates increased testing and appropriate use of penicillin and related β-lactams. Education of patients and their outpatient providers is the key to retaining the benefits of penicillin allergy de-labeling.
Summary Penicillin allergy testing is feasible in the hospital and offers tangible benefits towards antimicrobial stewardship. Allergists should take the lead in this endeavor and work towards overcoming personnel limitations by partnering with other health care providers and incorporating technology that improves the efficiency of allergy evaluation.

Keywords Penicillin allergy · Drug allergy · Penicilloyl-polylysine · Antimicrobial stewardship · Skin test · Electronic medical record

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Introduction

Penicillin (PCN) allergy is a very common diagnosis, reported by approximately 10–20% of the population in the USA [1, 2]. Despite its high prevalence, less than 10% of patients identifying as allergic have positive skin tests to penicillin and accordingly greater than 90% of such patients are in fact able to tolerate the medication without immediate-type hypersensitivity [3, 4, 5•, 6–8, 9••]. There are many reasons for the persistence of PCN allergy in the patient's minds and medical records. The origin of patients' PCN allergy labels is often remote and the circumstances obscure. Although commonly reported reactions include rash, urticaria, angioedema, and anaphylaxis, a sizable portion of patients are unable to recall specific symptoms that led to the diagnosis [10]. In some cases, PCN is mistakenly blamed for viral exanthems or urticaria secondary to concomitant infection [11]. In others, non-immunologic side effects such as nausea, diarrhea, or headaches are recorded as allergies for lack of an alternative means to document these issues. Although PCN allergy does not follow any clear inheritance pattern, patients may avoid this medication on account of a family member's prior experience. True immunoglobulin E (IgE)-mediated hypersensitivity to PCN also decreases with time, with over half of skin test-positive patients losing sensitivity by 5 years and 80% with histories of PCN allergy by 10 years [12•, 13]. Compounding the issue of penicillin allergy is the avoidance of other β-lactam antibiotics such as cephalosporins by some clinicians, even though they can often be safely administered in the presence of IgE-mediated PCN allergy following a test dose [1].

Why Testing Matters

There is mounting evidence that inaccurate PCN allergy diagnosis brings negative repercussions. A policy statement jointly

published by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America, and the Pediatric Infectious Diseases Society in 2012 called for broad adoption of antimicrobial stewardship nationwide [14]. This was followed up by a 2016 recommendation to incorporate PCN allergy testing where possible as a part of stewardship protocols [15]. PCN allergic patients receive higher rates of vancomycin, fluoroquinolones, clindamycin, and aztreonam [16–18]. Multiple previous studies have indicated the superiority of β-lactams over vancomycin for the treatment of susceptible *Staphylococcus aureus* infections [19]. In addition, Jeffres et al. compared clinical outcomes in β-lactam "allergic" patients receiving empiric treatment for gram-negative bacilli bacteremia and found that patients treated with non-β-lactam antibiotics were more likely to experience treatment failure compared with their counterparts receiving β-lactams with no difference in rates of hypersensitivity [20]. A landmark-matched cohort study on over 100,000 patients by Macy and Contreras revealed that simply being labeled PCN allergic was associated with higher incidences of Clostridium difficile, vancomycin-resistant Enterococcus, and methicillin-resistant *S. aureus* infections along with an increased number of hospital days versus nonallergic controls [21••]. These findings raise substantial concern in an era of increasing in drug-resistant organisms and a lack of development of new antimicrobials. In 2014, a Threat Report published by the Centers for Disease Control and Prevention reported that over two million infections and 23,000 deaths occur annually due to antibiotic-resistant organisms [22].

Addressing PCN allergy may offer financial benefits to patients and health care systems as well. A retrospective study conducted by Picard et al. uncovered additional antibiotic costs of over $15,000 in patients receiving non-β-lactam antibiotics over 1 year within a tertiary hospital setting [23]. Another study identified 38% higher costs for the prescribed antimicrobial treatment regimen to be followed upon discharge [24]. A cost analysis of antibiotic prescribing patterns in the UK by Li et al. demonstrated a 1.82 to 2.58-fold greater expense incurred in patients with the diagnostic label of PCN allergy, even though less than half had a history consistent with actual hypersensitivity after discussion with the patients and their primary physician [25]. Elective testing within a large US health care system in advance of antibiotic need reduced antibiotic costs by 32% between the year before and after the test [26].

Penicillin Skin Testing Protocols

Historically, penicillin skin testing (PST) consisted of skin prick and intradermal testing using the major determinant penicilloyl-polylysine (PRE-PEN®) and minor determinants penicillin G, penicilloate, and penilloate long with positive histamine and negative saline controls. In US studies, PST has a negative predictive value of 97–99%. However, penicilloate and penilloate are not commercially available in the USA. In lieu of this approach, a protocol utilizing penicilloyl-polylysine and penicillin G for skin testing followed by oral amoxicillin challenge makes the diagnosis with similar accuracy and is preferred at the authors' institution [5•, 9••] (Fig. 1).

Properly performed PST along with an oral test dose can be completed in under 2 h and the incidence of adverse reactions is extremely low. The frequency of systemic reactions has been reported at 0.1% in response to skin testing and 0.4–0.8% for patients receiving oral doses of amoxicillin after negative skin tests to penicilloyl-polylysine and penicillin G [5•, 9••, 27]. Furthermore, the rate of resensitization in skin test negative individuals following three courses of PCN was found to be negligible by Solensky et al., indicating that patients cleared of this allergy do not carry an increased future risk compared to the general population [28].

Prior Inpatient Penicillin Allergy Testing Initiatives

Hospitalized patients are an intuitive target for PCN allergy testing and existing studies on this topic are summarized in Table 1. The incidence of PCN allergy is higher in the inpatient population (up to 15%), and these individuals tend to be older and sicker with greater need for antibiotics [16, 17, 29]. Clarifying the allergy status could alter antibiotic therapy immediately and alleviate the need for long courses of more expensive, less effective, and sometimes harmful alternatives. Several pilot studies from the late 1990s through early 2000s have demonstrated the impact of testing initiatives in large health care centers. Harris et al. published the findings of 28 inpatients with expected duration of treatment of greater than 24 h and whose antibiotic regimen was expected to change following testing [30]. Eighty-nine percent tested negative and 82% received post-test β-lactam therapy, consequently reducing vancomycin, fluoroquinolone, and clindamycin usage. No immediate adverse reactions were reported. A retrospective review of 101 consultations for penicillin allergy testing over a 6-year interval also yielded a negative testing rate over 90% [31]. Though small, these were promising studies regarding viable skin testing initiatives in the acute care environment.

Prospective studies have also examined the role of PCN allergy testing with the intensive care unit (ICU). Arroliga et al. conducted a 2-month study of 21 medical ICU patients with a documented PCN allergy. Twenty out of twenty-one patients (95%) had negative skin tests and 10 (48%) saw changes in antibiotic therapy during their stay. Patients reporting histories of immediate-type hypersensitivity were excluded in this study [32]. This was followed up by a second trial expanded to include 96 history positive patients in medical, surgical, and cardiac ICUs including those with histories

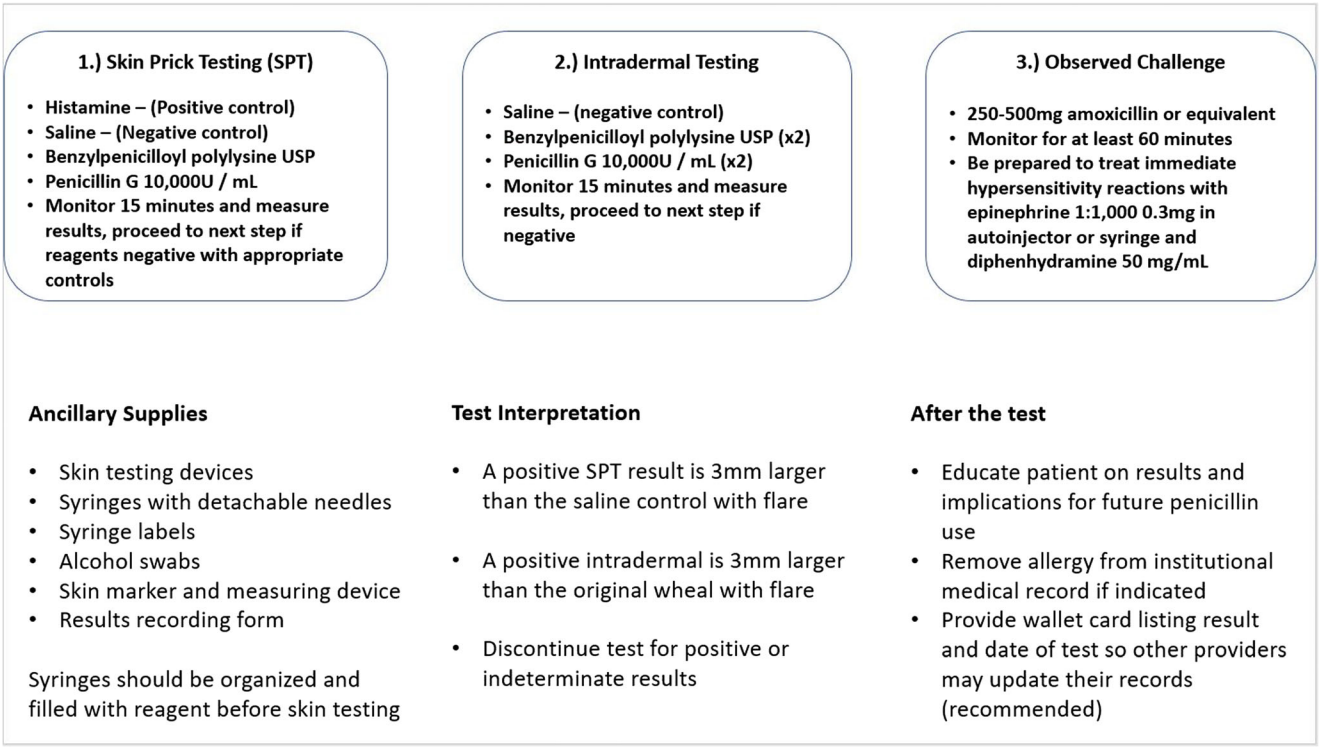

Fig. 1 Penicillin allergy testing protocol outline

of immediate reactions including anaphylaxis. A similar rate of antibiotic modification was seen [33].

These studies provided an encouraging baseline from which to explore the feasibility of more widespread inpatient PCN allergy testing initiatives. However, efforts to this end experienced a significant and unexpected roadblock in 2004 when the sole manufacturer of penicilloyl-polylysine discontinued production, citing costs for maintaining the FDA's strict manufacturing requirements, along with a small market compared to other pharmaceuticals. The world's only other producer based in Europe soon followed suit and that same year, all commercial supplies had been exhausted. From 2004 to 2009, testing was difficult if not impossible outside of select centers with the ability to synthesize their own reagents. However, the substantial efforts of a number of prominent US allergists led to their obtaining the rights to the product and bringing it back to market. The return of penicilloyl-polylysine has opened the door for the current era of PCN allergy testing incorporating other members of the health care team and the electronic medical record.

Recent Approaches to Inpatient Testing

The assessment of PCN allergy, including PST and challenges, has traditionally been under the purview of allergy/immunology consultant services. Hospitals with allergists on staff trained in the performance of PCN allergy can perform tests on request and suggest therapeutic changes on a case-by-case basis. One protocol from an academic institution implements automatic allergy consultations for any patient admitted to the medical wards or ICU with the label of PCN allergy [34]. The consulting allergist would then assess antibiotic needs and other factors including concomitant antihistamine use and comorbid conditions to queue patients for a detailed inpatient or outpatient evaluation. However, the number of patients referred by this system and the results of subsequent inpatient or outpatient testing were not reported. Such an approach is feasible in academic institutions with trainees on call. The obvious problem with reflexing inpatients with PCN allergy for allergist consultation is that not all institutions have an allergist on staff to perform the testing. A survey of the Infectious Disease Society of America Emerging Infections Network found that only 60% of respondents reported having PST available at their institutions [35]. Even in hospitals with allergists on staff, their availability is limited due to outpatient clinical commitments during regular business hours. Although a thorough evaluation including skin testing and challenge can be completed within 2 h, multiple scheduled clinic visits could be accomplished in the same timeframe. Additional opportunity cost is incurred through travel to the hospital from the physician's primary site of practice. In short, stewardship efforts reliant solely on physician allergists for PCN allergy testing may not translate to all practice settings or be cost-effective for the physicians' practice.

Some institutions lacking access to allergy consultants have experimented with inpatient testing by infectious diseases (ID)

Table 1 Summary of inpatient penicillin allergy testing studies

Study	Setting	PCN allergic patients identified	Patients tested	No. (%) positive tests	No. (%) indeterminate or incomplete tests	No. (%) negative tests	Challenged per protocol	Testing performed by	Notes
Harris et al. [30]	Acute care Preoperative	100	44	3 (7)	3 (7)	38 (86)	No	Allergist	Patients without anticipated antibiotic changes from a negative test or expected duration <24 h excluded
Arroliga et al. [32]	ICU	24	21	0 (0)	1 (5)	20 (95)	No	Allergist	Histories of immediate hypersensitivity excluded
Arroliga et al. [33]	ICU	100	96	1 (1)	10 (10)	85 (89)	No	Allergist	
Macy et al. [38]	Acute care	141	141	8 (6)	0 (0)	133 (94)	No	Nurse	1627 PCN allergic patients admitted during study period
Wall et al. [40]	Acute care	26	23	1 (4)	0 (0)	22 (96)	No	Pharmacist	3 patients negative by history
Nadarajah et al. [31]	Acute care	101	101	5 (5)	4 (4)	92 (92)	No	Allergist	Retrospective review of consultation outcomes
Heil et al. [36]	Acute care	90	76	3 (4)	9 (12)	64 (84)	Yes	ID physician	ID fellows ran a penicillin allergy consultation service
Active screening									
Rimawi et al. [8]	Acute care ICU	146	146	1 (1)	0 (0)	145 (99)	No	ID physician	Patients selected from database of 4031 charts reviewed by ID fellows
King et al. [39•]	Acute care	122	50	1 (2)	0 (0)	49 (98)	Yes	Allergist	60% of test subjects on HCBA. Pharmacist assisted with medication review
Chen et al. [9••]	Acute care ICU	1203	247	5 (2)	19 (8)	223 (90)	Yes	Pharmacist	Patients proactively identified and prioritized by EMR algorithm. 5 patients negative by history
Blumenthal et al. [46••]	Acute care ICU	278	43	0 (0)	0 (0)	43 (100)	Yes	Nurses and allergist	Eligibility for skin testing determined by dedicated providers. Many patients unable to be tested

Active screening studies involved testing service-initiated identification of eligible candidates within the inpatient population

EMR electronic medical record, *HBCA* high-cost beta-lactam alternative, *ICU* intensive care unit, *ID* infectious diseases

physicians with a shared interest in antimicrobial stewardship. In a study conducted at a US tertiary care hospital, ID fellows performed skin testing and medication challenges on 146 patients obtained over 4 months from an internal database collecting clinical infection, antibiotic use, microbiology results, and allergy history. There were 145 negative tests and 1 systemic reaction consisting of pruritus, hives, and swelling following intradermal injection of reagents [8]. Another prospective observational study from an academic center utilizing ID fellows with a dedicated PCN allergy pager tested 76 patients of whom 64 had negative tests (84%) and 54 had changes to their antibiotic therapy (64%) [36]. However, personnel limitations still hinder inpatient testing by ID physicians. ID services already carry numerous complex high acuity patients and with decreasing interest by graduates in ID fellowship training (evidenced by 117 of 335 positions going unfilled in the 2015 subspecialties match) many programs may be reluctant to commit additional resources into the training and performance of PCN allergy testing [37]. The authors of the latter study also surveyed ID fellowship program directors regarding the feasibility of PST at their

institution with 92% of respondents reporting a lack of personnel and time as barriers. Another concern is the recognition and treatment of reactions by providers without significant exposure to allergic conditions including anaphylaxis. Although rare, systemic reactions despite negative skin prick and intradermal testing can occur and require prompt examination and treatment that is second nature to allergists but less so to other specialists. Furthermore, deciding for whom testing is not indicated or even contraindicated is best determined by a trained allergist with expertise in nonimmediate hypersensitivity reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP).

Tackling the PCN allergy epidemic warrants cooperation with ancillary health care providers and greater integration of technology within the hospital environment. In a study conducted by Macy et al., an allergy clinic nurse circulated within the hospital and performed skin tests on patients identified by hospital personnel over a 6-month period. One hundred forty-one of 1627 patients were tested (8.7%) and 133 were negative within the tested population (94%). Testing utilized penicilloyl-polylysine, penicillin G, penicilloate, penilloate, and amoxicillin. Comparison of tested patients with 282 age- and sex-matched controls showed significant increases in PCN (17 vs 7%, $p = 0.0016$) and cephalosporin (59 vs 48%, $p = 0.039$) use. Vancomycin use was not significantly changed though this accounted for only 3.5% of antibiotic courses [38]. A barrier to using this method at other institutions is the lack of availability for penicilloate and penilloate minor determinants. As previously mentioned, an amoxicillin challenge may be used in lieu of skin testing with the two unavailable determinants but this adds time to the process and would likely reduce the number of patients that could be tested in a given day. Reliance on other providers to report PCN allergy to the tester may also limit productivity, though this has been alleviated with greater integration of allergy histories into the electronic medical record.

Physician-Pharmacist Collaboration

Collaboration with clinical pharmacists has proven valuable in addressing PCN allergies in the inpatient setting. There are several benefits to employing pharmacists trained by allergy/immunology specialists in the testing process. First, pharmacists make natural partners in antimicrobial stewardship programs, being well versed in adverse antibiotic effects. Second, they are already experienced in acquiring medication and allergy history histories before dispensing physician-ordered drugs. This allows them to identify potential candidates for testing early in their admission as well as concurrent medications that may influence testing outcomes such as antihistamines, certain antipsychotics, or antiemetics with histamine antagonizing properties. In addition, pharmacists are accustomed to educating patients following completion of testing, reconciling the de-labeled allergy in the medical record, and advising primary services on optimal post-test antibiotics. Inpatient pharmacists can also communicate results to their outpatient counterparts, closing the loop with regard to the disproven allergy and thus preventing future PCN avoidance.

The value of pharmacist involvement in patient screening was supported by a study from at a community hospital in which 30 of 50 (60%) of patients were on high-cost β-lactam alternatives, defined as aztreonam, linezolid, daptomycin, or tigecycline. Pharmacists helped screen for PCN allergic patients on these agents and bring them to the attention of the primary and ID physicians, who then consulted allergists to perform PST and challenge. After factoring in the cost of the skin testing reagents antibiotic cost savings was over $11,000, though this did not account for physician charges [39•].

Wall and colleagues described a protocol by which pharmacists conducted skin tests in hospitalized patients with the support of a board-certified allergist who served as the program's medical director. Training included didactic lectures about hypersensitivity reactions and practice guidelines pertaining to drug allergy as well as technical instruction on the administration of skin prick and intradermal tests. This service was offered on a limited basis to 26 patients with three cases ruled out simply by conducting a history and confirming recent use of PCN. In 22 of the 23 remaining cases, the test was negative and the last one indeterminate. All 26 patients received β-lactams afterwards without adverse events. An average of 48 doses of vancomycin per patient was avoided, though the high number was biased by the selection of patients requiring prolonged courses of therapy [40].

A proactive approach to PCN allergy testing combining pharmacist-run testing with EMR-assisted protocols was recently published by the authors of this review [9••]. This study was conducted at an urban 870-bed public hospital serving a large indigent population and was aimed at lowering use of broad-spectrum β-lactam alternatives. The average incidence of PCN allergy among admitted patients was calculated at 8%. A dedicated PCN allergy testing service was managed by a clinical pharmacist following an allergist developed protocol. The pharmacist underwent proficiency training on skin test procedures and attended allergy division meetings for continuing education. The novel advancement was the incorporation of computerized algorithms to select patients who would benefit most from de-labeling of their allergy from a large pool of potential candidates. A daily report of inpatients with PCN allergy diagnoses was filtered automatically for those without active discharge or antihistamine orders. The service pharmacist then checked for patients receiving antibiotics, with priority given to high-value broad-spectrum agents such as carbapenems and aztreonam with additional consideration for immune compromise (defined as diabetes mellitus, human immunodeficiency virus infection, active malignancy, or use of immunosuppressant medications

including chemotherapy). Unlike previous programs, the service pharmacist initiated contact with patients fulfilling the most criteria although providers could request traditional consultations as well. A sample screening methodology is outlined in Fig. 2. The pharmacist would conduct interviews using standardized questions to characterize patients' allergy histories and exclude those with non-IgE-mediated reactions. Skin prick and intradermal tests using penicilloyl-polylysine and penicillin G followed by amoxicillin challenge was performed at bedside. Per protocol, a positive result at any step concluded testing. A medication kit to be used in case of reaction was always carried. The on-call allergist was available by phone for guidance in scenarios not explicitly covered by the protocol. Results of the test were clearly documented in the chart and if negative, the allergy was removed and the primary team notified. The patient then received counseling on the implications for future PCN use.

One thousand two hundred three records were flagged by the system resulting in 252 patient interviews. Nineteen subjects were unable to complete testing, mostly due to indeterminate positive or negative controls. Five patients had their allergies removed after verifying tolerance of PCN during the interview. Of the 228 patients that completed the protocol, 223 (97.8%) were negative and cleared to take PCN with 77 (34%) initiated on a β-lactam in house and 40 (18%) continued as outpatients. An additional eight (3.6%) patients did not initiate β-lactam treatment while admitted but were prescribed one at discharge. Tested individuals saw significant declines in active orders for vancomycin (−33%, $p < 0.001$), clindamycin (−61%, $p < 0.001$), fluoroquinolones (−36%, $p < 0.001$), carbapenems (−50%, $p = 0.049$), and aztreonam (−68%, $p = 0.009$) along with over 20-fold increased PCN use ($p < 0.001$). Patients not previously on a β-lactam accumulated 504 days on PCN or cephalosporins. Outpatient β-lactam prescriptions for the 85 switched patients totaled 648 days. This study demonstrated a framework by which ancillary providers can extend the service of PCN allergy evaluation in the acute care setting without significantly detracting from the physician's other duties.

Although short-term cost savings were not the primary driver of this initiative, the threshold of whom to test can be adapted to the needs of specific institutions. The authors have since refined the published approach by integrating PCN allergy testing with all orders for aztreonam, thus giving recipients higher priority within the testing queue. Preliminary data indicate that this shortens time from admission to testing by two full days with many of these orders placed alongside the initial antibiotic in the emergency department. Projected inpatient medication cost savings are $137.31–$330.67 per patient after switching to a β-lactam [41].

Decision Support for Inpatient Providers

Another avenue to addressing PCN allergy is through clinical decision guidelines that educate existing providers and

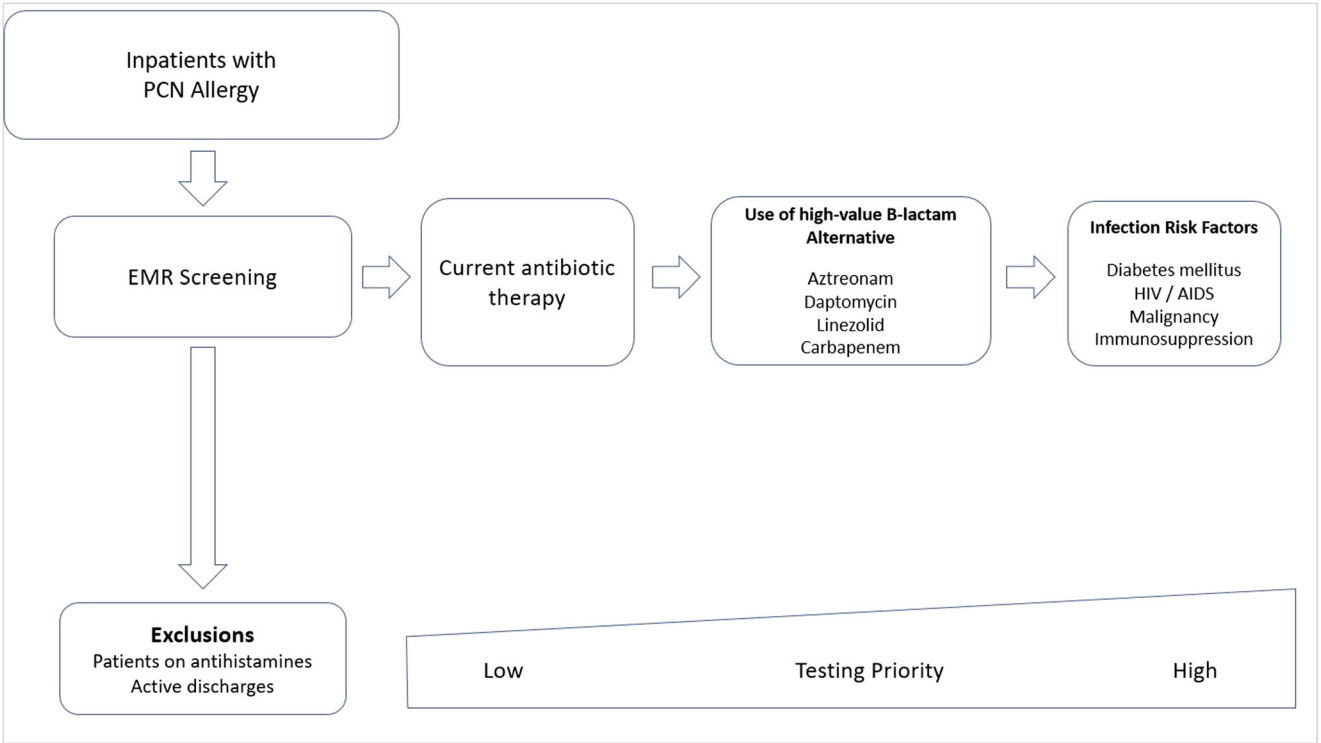

Fig. 2 Sample prioritization algorithm for large-scale inpatient penicillin allergy testing with limited trained personnel

empower them to investigate reported allergies thoroughly before prescribing substitute antibiotics or consulting an allergist. Many inpatient providers lack understanding of the clinical course of PCN allergies and the risk cross-reactivity among β-lactams [42, 43]. A survey conducted at a large academic center found that only 36% of providers knew about skin testing as a valid tool for assessing PCN allergy and 57% mistakenly believed that a PCN allergy was permanent. Encouragingly, many of these providers also expressed a willingness to use tools to better prescribe the appropriate antibiotics for patients reporting such an allergy [44].

Blumenthal and colleagues reported the impact of a hospital-wide guideline to help inpatient clinicians determine which β-lactam antibiotics could be administered to patients with a history of PCN or cephalosporin allergy with a full dose, limited test dose, or only with preceding PST [45•]. This guideline was posted in treatment areas and included a template for obtaining a detailed allergy history that would classify historical reactions as mild reactions of minor clinical significance, immediate-type hypersensitivity, or severe nonimmediate-type hypersensitivity. Cross-reactivity rates among PCN, various cephalosporins, carbapenems, and aztreonam were also provided. Based on the category, the clinician could then avoid PCN or cephalosporins, administer a full or graded test dose to the desired drug, or place an allergy consultation if skin testing was still desired. Previously, an allergy consultation was required for all test doses. Implementation of this guideline was associated with increased test doses and significantly more treatment courses with penicillin (19 vs 2%, $p < 0.001$) and cephalosporins in the first (10 vs 0.6%, $p < 0.001$), third (30 vs 5%, $p < 0.001$), and fourth (32 vs 7%, $p < 0.001$) generations in the following year. Concurrent declines were reported for vancomycin, fluoroquinolones, aminoglycosides, and aztreonam. The total number of allergy consults did not significantly change, though PST was indicated more often in consults received. No difference in adverse events before and after the guideline was reported although the study did not track how often full dose challenges were ordered against guidelines, whether intentionally or not.

This guideline was subsequently adopted at another hospital as an online application easily accessible by mobile electronic devices. Patients treated after its introduction had twofold higher odds of receiving a penicillin or cephalosporin during their inpatient stay versus previous standard of care where allergy evaluations were done only at the request of the primary service. Notably, this intervention did not change the frequency of penicillin or cephalosporin use at discharge, possibly due to some later generation cephalosporins existing only in parenteral formulations. Another cohort proactively assessed by the allergy service for skin testing saw sixfold increased β-lactam use the subset that completed testing per protocol, though rates were not significantly altered in the assessment group as a whole due to inability to coordinate in-house testing for many subjects [46••]. Although shifting penicillin allergic patients to cephalosporins may not yield the long-term benefits that would follow allergy de-labeling, this strategy is still preferable to using non-β-lactams and could be used in institutions without the capacity to perform formal allergy testing.

Maintenance of De-labeling

Patients should receive clear instructions on the implications of a negative penicillin allergy test. Poor communication between health systems or inadequate patient education leads to confusion for the patient and other medical providers and persistence of the allergy label. One retrospective review of hospital-performed PST found passive recommendations in the chart alone to be insufficient, with nearly half of PST negative patients still carrying the label of penicillin allergy at discharge [47]. In an EMR-based environment, active removal of the patient's allergy, clear documentation of test results, and counseling should be the minimum standard of care post-procedure. Rimawi et al. found that 20/55 (36%) patients with negative inpatient testing had their PCN allergy redocumented at a subsequent admission within 1 year without evidence of an interval reaction. Older age, dementia, and long-term care facility residence were associated with redocumentation [48]. A study by Rourke et al. noted only 74/109 (68%) patients with negative testing were reporting their allergy status correctly to their primary care physicians (PCP). Directed counseling after testing and a letter provided to the patient and PCP detailing antibiotics to be used or avoided improved compliance among PST negative patients to 46/54 (85%) [49].

A pilot study at the authors' institution examined several interventions aimed at preventing PCN allergy redocumentation. These included pharmacist counseling at the time of testing (standard of care), post-discharge telephone follow ups to reinforce test results, an electronic alert notifying providers when a penicillin allergy is added back in any patient with documented negative test, and a printed wallet card clearly stating the negative result and date of testing. The standard-of-care group had a 13.8% rate of redocumentation with a mean follow-up time of 280 days while the combination of interventions led to a rate of 6.7%. Statistical significance could not be confirmed given the small sample size and more investigation is needed over a longer follow-up period [50].

Conclusions

Allergists have the most training and experience in handling penicillin allergy and should lead in this endeavor. Although most penicillin allergy testing is performed in the office, the

value of this intervention is perhaps greater in the hospital and should not be overlooked. Generalizable solutions for inpatient testing are inevitably hindered by an inadequate number of capable specialists and the short-term costs in performing the test. The recruitment of supporting health care providers under proper supervision and prudent use of technology will play a significant role in the future of these programs. Pharmacists, midlevel providers, and nurses can serve as onsite testing personnel when appropriately trained and following validated protocols, though it is our recommendation that an allergist serve as a resource for training and acute concerns. Computerized algorithms can optimize allocation of hospital resources needed for testing by identifying high-value testing candidates or enabling front line providers to actively engage the issue. The near-term benefits of inpatient penicillin allergy testing on antibiotic utilization are well established, though studies are needed to quantify long-term outcomes in regard to antibiotic costs, readmission rates, and adverse events. We encourage practicing allergists to adapt the strategies discussed in this review or develop novel initiatives within their own institutions or practices.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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