

Safety, Efficacy, and Clinical Impact of Penicillin Skin Testing in Immunocompromised Cancer Patients



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What is already known about this topic? The impact of penicillin skin testing (PST) in immunocompetent patients with penicillin allergy is well described. Immunocompromised patients are at increased risk for infections, and documented allergies are associated with worse outcomes including increased mortality.

What does this article add to our knowledge? Inpatient PST is safe and effective in ruling out IgE-mediated penicillin allergy in severely immunocompromised patients with cancer and profound neutropenia and results in the increased use of preferred antimicrobial agents in this population.

How does this study impact current management guideline? Immunocompromised patients with penicillin allergies should undergo PST. Those with negative results should be switched to preferred β -lactam therapies. Implementation of PST at cancer centers is vital to improve clinical management and enhance antimicrobial stewardship.

BACKGROUND: Use of penicillin skin testing (PST) to rule out penicillin (PCN) allergies is safe and effective in immunocompetent patients; however, data on immunocompromised patients are limited.

OBJECTIVE: We aimed to determine safety, efficacy, and clinical impact of PST in immunocompromised patients with cancer.

METHODS: A quality improvement process establishing a PST service was implemented at MD Anderson Cancer Center. Adult patients admitted to leukemia and genitourinary medical oncology (GUMO) services with history of possible type I reactions to PCN were eligible for testing.

RESULTS: Between April and October 2017, 218 patients with reported PCN allergies were screened; 100 met inclusion criteria and underwent PST (67 leukemia, 33 GUMO). The most

common reported allergy was to PCN (64%), with 61% reporting cutaneous reactions and 79% reporting reactions more than 20 years ago. PST with oral challenge results were overwhelmingly negative (95%); only 4% tested positive, and 1 test result was indeterminate (negative histamine control). After negative PST and oral challenge results, 51% patients were transitioned to PCN-based antibiotics during the same hospitalization. During the follow-up period (median 177 days), 65 of 95 patients were readmitted (185 total readmissions), and 51 patients required antibiotic therapy, with 37 receiving a PCN-based antibiotic (accounting for 336 days of therapy). No patient who received PCN-based antibiotics experienced an immediate-type allergic reaction.

CONCLUSIONS: Our findings support PST use in immunocompromised hosts. The widespread use of PST in patients with cancer will allow for optimal use of antimicrobial therapy and stewardship, which are vital in a population at increased risk for infections. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:2185-91)

Key words: Allergy to penicillin; Penicillin skin testing; Immunocompromised patients; β -Lactam allergy; Allergy testing

Penicillin (PCN) allergy is the most commonly reported drug allergy, with up to 10% of outpatients and as many as 20% of inpatients self-reporting allergic reactions.^{1,2} However, after appropriate testing, approximately 10% of those who self-report allergies are found to have a true IgE-mediated reaction. More recent studies suggested even lower rates of true positivity at between 1% and 4%.^{1,3}

When practitioners avoid using β -lactam antibiotics because of self-reported PCN allergies, they must turn to second-line, and

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Abbreviations used

ANC- Absolute neutrophil count
 EMR- Electronic medical record
 GUMO- Genitourinary medical oncology
 ID- Infectious diseases
 PBA- Penicillin-based antibiotics
 PCN- Penicillin
 PPL- Penicilloyl-poly-lysine
 PST- Penicillin skin testing

often broad-spectrum, antimicrobial regimens that are associated with increased risk for *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant enterococcus infections.⁴⁻⁷ Antimicrobial use in patients with PCN allergies is also associated with higher costs and readmission risk and longer hospital stays than use in patients without PCN allergy.^{1,8} A recent study by Huang et al⁹ revealed that hospitalized patients with a hematological malignancy and reported β -lactam allergy versus those without a reported allergy had a longer median length of stay (11.3 days vs 7.6 days), higher mortality rate at 30 days (7.6% vs 5.3%) and 180 days (15.8% vs 12.2%), higher 30-day readmission rate (19.2% vs 15.1%), increased rate of *C. difficile* infection (17.7% vs 11.6%), and a higher median total initial encounter charge (\$223,046 vs \$173,256).

PCN is the only antibiotic for which a standardized skin test is safe and effective to evaluate for IgE-mediated allergy, with a negative predictive value of 97% to 99% in immunocompetent patients.^{2,10,11} IgE-mediated reactions, also known as type I reactions, lead to symptoms such as urticarial rash, cutaneous pruritus, flushing, angioedema, wheezing, gastrointestinal symptoms, altered mental status, and hypotension.¹²

Although penicillin skin testing (PST) has been validated in immunocompetent patients, its safety and feasibility has not been established in immunocompromised patients. In a recent study, Trubiano et al¹³ used PST and included immunocompromised patients; however, these patients represented less than one-half of the cohort, and specific group results were not discussed thoroughly.

The objective of this project was to assess the safety and efficacy of PST in immunocompromised patients with solid tumor and hematologic malignancies and to evaluate the impact of PST on antimicrobial therapy.

METHODS**Study design and setting**

A PST quality improvement initiative was implemented at The University of Texas MD Anderson Cancer Center, a 681-bed comprehensive cancer center in Houston, Texas. A dedicated PST team was established, and PST was used to evaluate for IgE-mediated PCN allergy and to guide antibiotic use between April and October 2017. Before this initiative, there was no use of inpatient PST at our institution. The study was approved by the institutional Quality Improvement Assessment Board, and the PST team was led by an infectious diseases (ID) attending physician and included an ID fellow, ID pharmacist, and 2 ID advanced practice providers. Each day, a report detailing patients admitted to leukemia and genitourinary medical oncology (GUMO) services for whom an active PCN (PCN, ampicillin, dicloxacillin, amoxicillin, amoxicillin/clavulanate,

naftillin, piperacillin/tazobactam) allergy was documented in their electronic medical record (EMR) was generated. Leukemia and GUMO services were selected because they represent the wide spectrum of immunosuppression found in patients with cancer. Patients with leukemia generally are considered severely immunocompromised, whereas those with genitourinary malignancies are regarded as less immunocompromised and often do not experience substantial myelosuppression.

Patients with documented allergies were screened Monday through Friday by the ID pharmacist. If a patient was eligible for testing based on a thorough drug allergy history, verbal consent was obtained before the procedure. Patients were eligible for testing if they were at least 18 years old with a history of possible IgE-mediated type I reactions (such as urticaria, pruritic rashes, angioedema, or anaphylaxis) or an unknown reaction to a PCN. Patients were excluded if they were older than age 85, did not have a history consistent with a possible IgE-mediated allergy, did not have a true allergy (eg, gastrointestinal intolerance), had an anaphylactic reaction to a PCN within the last 5 years, or were taking an antihistamine agent that could not be discontinued. Patients with non-IgE-mediated reactions included but not limited to Steven-Johnson syndrome, vasculitis, interstitial nephritis were excluded. Patients in the intensive care unit or with hemodynamic instability were also excluded. PST was performed by the ID physician, ID fellow, or ID advanced practice providers using standard methodology described elsewhere.¹⁴ PST involved a 2-step process for which the testing team received training. Skin prick and intradermal testing involved the PCN major determinant (penicilloyl-poly-lysine [PPL]; ALK Abello, Round Rock, Tex), the minor determinant PCN G potassium (PenG, 10,000 U/mL), and normal saline (negative control). The skin prick test also used a positive control with histamine (Histatrol; ALK Abello). Skin testing results were considered positive if a wheal was at least 3 mm larger than the negative control at 15 minutes for either the major or minor PCN determinant. If a reaction to a PCN determinant was noted at any time, testing was suspended and the patient's result was considered positive for PCN allergy. If the patient had negative results on skin prick and intradermal tests, 250 mg of amoxicillin was administered as an oral challenge and the patient was observed closely for 1 hour for signs of hypersensitivity reaction. If there was no reaction, PST results were considered negative for allergy, and the PCN allergy was removed from the EMR and the procedure results were documented in the EMR. The primary oncology teams were notified of testing results so that desired antimicrobial changes could be made, although the PST team did not make direct recommendations. Patients were given a pocket card on which test results were documented and could be shared with their health care providers at other institutions.

To assess the long-term impact of PST on antimicrobial management, patients with negative PST results were followed prospectively for subsequent admissions for 11 months.

Data collection

The following data points were collected on PST admission: basic demographic information, allergy description, admission and discharge dates, complete cell count with differential on day of PST, history of colonization with resistant bacteria within 6 months before PST admission, use of steroids, and recent chemotherapy or immunotherapy before PST. During the PST admission and on any subsequent readmission, data were collected on antimicrobial therapy, indication for therapy, and culture results. Prophylactic antibiotic use was not included in the data set.

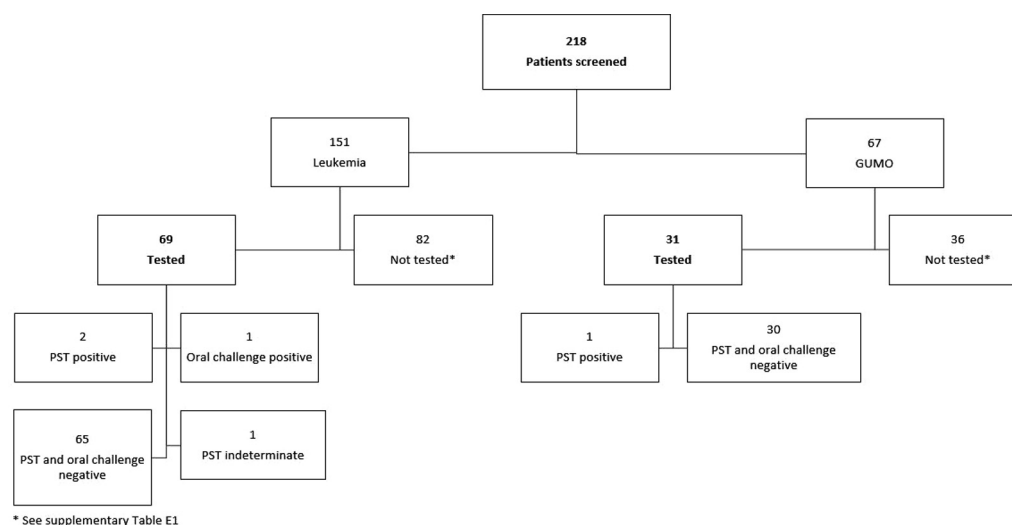


FIGURE 1. Screening and penicillin skin testing and oral amoxicillin challenge results among patients with documented penicillin allergies on leukemia and genitourinary medical oncology services. *GUMO*, Genitourinary medical oncology; *PST*, penicillin skin testing.

Definitions

The term penicillin-based antibiotics (PBA) refers to any antibiotic within the immediate PCN families including amoxicillin, ampicillin, amoxicillin/clavulanate, piperacillin/tazobactam, and nafcillin. Non-PCN β -lactams include antibiotics within the cephalosporin or carbapenem family and aztreonam.

Statistical analysis

Descriptive statistics were used to analyze the data. Continuous numeric variables were presented as median and range. Category data were presented as frequencies and percentages. The statistical analyses were performed with SAS version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS

A total of 218 consecutive patients admitted to leukemia and GUMO services with a documented allergy to 1 or more PCN agents between April 2017 and October 2017 (151 [69%] to leukemia services, and 67 [31%] to GUMO services) were screened (Figure 1). Among these patients, 118 were excluded, with the most common reasons being lack of consent for the procedure mainly due to overwhelming cancer diagnosis and associated treatments (28 [24%]), and discharged before eligibility (15 [13%]) (Table E1, available in this article's Online Repository at www.jaci-inpractice.org). Notably, 4 patients (3%) were excluded for having a history of anaphylactic reaction within the last 5 years, and 6 patients (5%) were excluded after screening revealed that the documented allergy actually was an intolerance. PCN allergy was changed from allergy to intolerance in the EMR for those with intolerance without further testing. The remaining 100 patients met eligibility criteria and underwent PST. Most of those tested were white (85%) with a median age of 65 (range, 21-85) (Table I). Most patients from leukemia services had acute myeloid leukemia (51%) or myelodysplastic syndrome (13%); for patients from GUMO services, the most common cancer types were renal cell carcinoma (32%) and bladder cancer (29%). For patients with leukemia, their median absolute neutrophil count (ANC) was 0.78 (0-64.88 k/ μ L), with

TABLE I. Demographics and clinical characteristics of patients who underwent penicillin skin testing

Patient characteristics	N = 100, No. (%)
Age, median (range)	65 (21-85)
Male	58 (58)
Race	
Caucasian	86 (86)
African American	5 (5)
Hispanic	5 (5)
Other	4 (4)
Leukemia*	69 (69)
AML	35 (51)
CLL	8 (12)
MDS	9 (13)
ALL	7 (10)
Other	10 (6)
History of stem cell transplant	9 (9)
Autologous	1 (11)
Matched related	2 (22)
Matched unrelated	5 (56)
Cord	1 (11)
GUMO	31 (31)
RCC	10 (32)
Bladder cancer	9 (29)
Prostate cancer	8 (26)
Other	4 (13)
Corticosteroid during admission	48 (48)
Other immunosuppressive agents during admission	49 (49)

ALL, Acute lymphoblastic leukemia; *AML*, acute myeloid leukemia; *CLL*, chronic lymphocytic leukemia; *GUMO*, genitourinary medical oncology; *MDS*, myelodysplastic syndrome; *RCC*, renal cell carcinoma.

*Patients may have more than 1 malignancy.

28 (41%) of those patients having an ANC lower than 0.5 k/ μ L; the median platelet count was 27 (4.0-284.0 k/ μ L) (Table II). The most commonly reported antibiotic allergy was to PCN (64%). Although most patients only carried documented PCN

TABLE II. Complete blood count and differential results on day of penicillin skin testing for patients using leukemia and genitourinary medical oncology services

	Leukemia, median (range)	GUMO, median (range)
WBC	2.8 (0.2-132.4)	8.2 (3.7-24.8)
ANC	0.78 (0-64.88)	5.64 (0.46-22.4)
ALC	0.80 (0-116.71)	0.92 (0.05-2.93)
PLT	27.0 (4.0-284.0)	225.0 (18.0-400.0)

ALC, Absolute lymphocyte count; ANC, absolute neutrophil count; GUMO, genitourinary medical oncology; PLT, platelets; WBC, white blood cells.

allergies, 29% listed allergies to other antimicrobial classes including sulfonamides (20%) and cephalosporins (9%) (Table III). Sixty-one percent reported cutaneous reactions, and 79% reported reactions that occurred more than 20 years ago. Almost one-half of all patients were taking steroids (48%) or any kind of immunosuppressive therapy (49%) at the time of PST.

Of the 100 patients eligible for testing, only 1 patient could not complete the test because of a negative histamine control (wheal <5 mm). Of the 99 patients who completed the PST, 95 patients were negative for PCN allergy after PST and oral challenge. Four patients had positive results: 2 were positive on the skin prick (PPL), 1 tested positive on the intradermal test (PCN G), and 1 skin test-negative patient developed a mild non-urticarial skin rash within 6 hours after the oral amoxicillin challenge. No patient experienced severe adverse reactions necessitating intervention (Table IV).

The EMR was updated for all 95 patients with a negative PST and oral challenge result. Of these patients, 67 (71%) had been receiving antibiotics before PST, and 50 of these patients (75%) were receiving non-PCN β -lactam therapy including aztreonam (15 patients), carbapenems (9 patients), and cephalosporins (26 patients). Eleven patients had antibiotics discontinued the day of PST testing. Of the 39 patients who continued antibiotics, 20 (51%) were changed to PBA immediately after negative PST and oral challenge results, with piperacillin/tazobactam being the most commonly prescribed agent (13 patients, 65%) (Figure 2). Sixteen patients continued to receive non- β -lactam agents such as fluoroquinolones and were not switched to a β -lactam therapy after PST primarily because of the need for oral agents with high bioavailability or prescriber preference. One patient who was taking vancomycin was switched to ampicillin to treat enterococcal bacteremia. The most common indications for antibiotic treatment were pneumonia (30%) and bacteremia (22%), followed by neutropenic fever of unknown etiology (19%). There were 266 days of PBA use as a direct result of PST. No patient experienced a type I allergic reaction while receiving PBA therapy.

Among the 95 patients with negative PST results, 65 were readmitted during the 11-month follow-up period, accounting for a total of 185 admissions. Twenty-four patients had 1 admission, and 41 patients had 2 or more admissions (range, 1-9 admissions) after the initial PST encounter. Fifty-one patients (51 of 65) required antibiotic therapy during 119 of those admissions. Cephalosporin therapy was used in 54 of the 119 readmissions (45%), and a PBA agent was used in 40 of readmissions (34%). Carbapenem therapy was prescribed as the antibiotic of choice in 14% of admissions. There were 1220 days of β -lactam use, including 336 days of PBA therapy. No reported

TABLE III. Types of reported penicillin allergies among patients who underwent penicillin skin testing

	N = 100
Antibiotic allergy	
Penicillin	64
Amoxicillin or amoxicillin-clavulanate	8
Ampicillin	2
Piperacillin	1
Unknown	25
Reaction reported in electronic medical record	
Nonurticarial rash	38
Urticarial rash	28
Anaphylaxis	4
Unknown	17
Other	13
Reaction reported at patient interview	
Nonurticarial rash	32
Urticarial rash	29
Angioedema	11
Unknown	19
Other	9
Timing of allergy	
>20 y ago	79
10-20 y ago	6
5-10 y ago	4
Less than 5 y ago	8
Unknown	3
Other concurrent antibiotic allergies	
Cephalosporins	9
Sulfonamides	20
Quinolones	9
Macrolides	1
Other	9

allergic drug reactions were associated with β -lactam during any of the subsequent admissions.

PCN allergy was re-entered into the EMR system during readmission for 2 of the 95 patients who were delabeled after receiving negative PST results, although neither scenario was attributable to the development of a type I allergic reaction to any PCN agent after PST testing. These patients were the only participants to receive aztreonam at any subsequent readmission.

DISCUSSION

To our knowledge, this is the first large study of PCN allergy skin testing in immunocompromised patients with cancer. The results demonstrate that PST is a safe and reliable procedure for severely immunocompromised patients with cancer and profound neutropenia, a group of patients in whom first-line antibiotic therapy is vital. The extended follow-up period helped to evaluate the impact of PST results on clinical management and patient care, as demonstrated by the increased use of optimal antimicrobials.

Only 4% of patients reported having a history of PCN allergy tested positive when PST and oral challenge were used. This rate is comparable with the most recent data in immunocompetent patients that identified a positivity rate of 1% to 4% overall.^{3,15,16}

TABLE IV. Patients with positive penicillin skin testing and/or oral challenge results

Patient	Age	Cancer diagnosis	Time since initial Allergy (y)	Documented allergy in electronic medical record	ANC at testing (k/ μ L)	Skin prick PPL (wheal)	Skin prick PG (wheal)	Skin prick PG	Intradermal PPL	Intradermal PG (wheal)	Oral amoxicillin
1	76	AML	>20	Nonurticarial rash	0.02	Positive (6 $\times$ 6 mm)	Negative	Negative	Not performed	Not performed	Not performed
2	65	Prostate cancer	>20	Urticaria	5.23	Negative	Negative	Negative	Negative	Positive (5 $\times$ 5 mm)	Not performed
3	22	ALL	>20	Urticaria	1.13	Positive (5 $\times$ 5 mm)	Negative	Negative	Not performed	Not performed	Not performed
4	76	AML	5-10	Erythema, swelling	0.10	Negative	Negative	Negative	Negative	Negative	Positive* (facial flushing and skin rash)

ALL, Acute lymphoblastic leukemia; AML, acute myeloid leukemia; ANC, absolute neutrophil count; PG, penicillin G potassium; PPL, penicilloyl-poly-L-lysine.

*Patient responded to one dose of Benadryl.

PST acceptance for immunocompromised patients has been slow because of concerns regarding accuracy, reliability, and safety in the setting of immunosuppression. Although there has been no reported association between neutropenia and skin test results, many studies excluded patients with ANC <500 from skin testing.^{17,18} Of the 100 patients tested in the quality improvement initiative, only 1 patient who did not have neutropenia (ANC of 0.62 k/ μ L) failed to react to the histamine-positive control with no identifiable cause. Of importance, 2 patients with profound neutropenia (ANC <0.1 k/ μ L) had a positive skin testing result, demonstrating that degree of neutropenia does not affect PST validity. There were also no episodes of excess bleeding or ecchymosis in patients who underwent PST, including those with severe thrombocytopenia. This finding helps to alleviate concerns about adverse bleeding events associated with PST in patients with thrombocytopenia. Moreover, approximately one-half of tested patients were actively taking steroids and/or immunosuppressive cancer therapies without experiencing negative interference with skin testing and results, further supporting the safety and efficacy of PST in immunocompromised patients with cancer.

The literature reports that the negative predictive value of PST exceeds 99% with PST and oral challenge.² Of the 96 patients with negative skin-tests results, only 1 developed reaction to oral challenge, resulting in a negative predictive value of 99%. This suggests that the use of PST in immunocompromised patients with cancer is as reliable as PST use reported in immunocompetent counterparts.

β -Lactam agents including PBA are first-line antibiotics for immunocompromised patients with cancer to manage febrile neutropenia. The rate of reported PCN allergies at MD Anderson is approximately 13% (unpublished data, 2016). These reported allergies often influenced empirical and culture-driven antimicrobial selection, leading to the increased use of non-PCN or non- β -lactam-based therapies. Previous studies demonstrated that alternative antibiotics have suboptimal clinical efficacy and are associated with increased mortality.^{19,20} Aztreonam, a monobactam antibiotic, is safe in PCN allergy yet costs 3 times as much as piperacillin-tazobactam and is associated with decreased rates of *in vitro* susceptibility for *Pseudomonas aeruginosa* isolates.^{15,21-23} Before PST testing, 75% (50 of 67) of study patients were receiving non-PCN β -lactam therapy, with 36% taking aztreonam and carbapenems. However, only 3 of these patients had a history of colonization with extended-spectrum β -lactamase, or carbapenem-resistant organisms, which suggests that non-PCN antimicrobial treatment is largely driven by reported allergies rather than microbiological criteria. Of the 95 patients who were negative on PST and oral challenge, 51 (54%) were successfully prescribed PCN-based antimicrobials during initial admission or throughout the follow-up period, which consequently resulted in decreased aztreonam use.

During the 11-month follow-up period, allergies were re-entered into the EMR for only 2 patients with negative PST results. One patient refused to take PCN agents despite having a negative PST result, and he requested redocumentation of his allergy into the EMR. The second patient tolerated a course of amoxicillin to treat *Enterococcus faecalis* cystitis without experiencing an adverse reaction after having an initial negative PST finding. However, this patient subsequently developed a biopsy-proven leukocytoclastic vasculitis secondary to use of nafcillin for methicillin-susceptible *S. aureus* bacteremia, and a new PCN allergy was added to her EMR. This

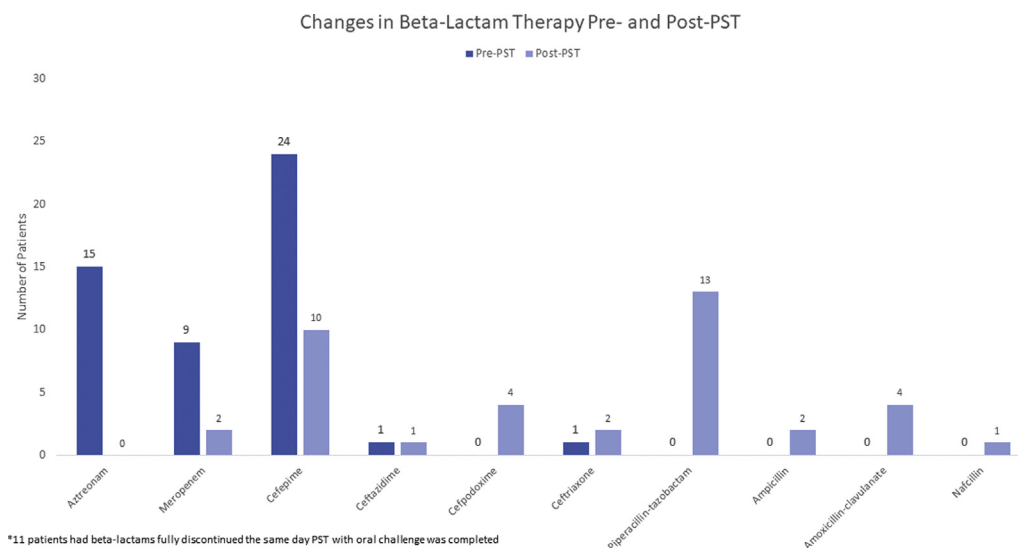


FIGURE 2. Changes in β -lactam therapy before and after a negative penicillin skin testing and oral challenge. *PST*, penicillin skin testing.

scenario emphasizes that a negative PST applies only to IgE-mediated reactions to PCN, and a negative oral challenge result does not preclude the possibility of a delayed-type reaction with a different immunological mechanism.

This single-center study is not without limitations. The study only included patients with leukemia and genitourinary cancers, which limited applicability to other settings and populations. However, selection of these 2 very different cancer populations allowed for testing across a spectrum of immunocompromised states, including severe immunocompromise in patients with leukemia. Although every patient who was admitted to these services Monday through Friday was screened, many patients were discharged before PST. This issue was driven by many factors—primarily delays in eligibility attributable to use of antihistamines, which frequently are used for patients with cancer who receive blood product transfusions or chemotherapy necessitating premedication. Also, investigators could not capture data on antimicrobial use for subsequent admissions or clinic visits outside of MD Anderson, although these numbers are likely low because many patients continue to receive inpatient and outpatient care at MD Anderson for the duration of their cancer care. Although our team was composed of representatives from ID, PST team would also benefit greatly from involvement of allergy and immunology services if such resources are available in the inpatient setting. Moreover, this intervention did not include direct recommendations for antimicrobial change after PST testing results were negative. Changes in antimicrobial therapy were at the discretion of the primary team. If we had made targeted recommendations, we may have seen increased use of PBA and non-PCN β -lactam agents after the procedure. Yet, even without direct intervention, therapy was changed for many patients after PST testing, illustrating the responsiveness of clinicians to allergy reports and this novel, efficient, and safe confirmatory test. Finally, although the safety of direct oral challenges without skin testing in appropriately selected immunocompetent host is reassuring, the safety and efficacy of oral challenge among immunocompromised patients with cancer needs further investigation.

In summary, this study demonstrated that inpatient PCN allergy skin testing is safe and effective in ruling out IgE-mediated PCN allergy in immunocompromised patients with cancer and results in the increased use of optimal and safe antimicrobial therapy. A dedicated, multidisciplinary team is essential to the establishment of a successful PST program in the inpatient setting. Because immunocompromised patients with cancer are at increased risk for infectious complications with frequent readmissions and exposures to prolonged courses of antimicrobials, PST implementation at cancer centers is vital to improve clinical management and should become the standard of care at cancer institutions.

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ONLINE REPOSITORY

TABLE E1. Patients excluded after screening (n = 118)

	Leukemia	GUMO	Total
Recent allergic reaction/positive PST*	4	2	6
Age >85	4	3	7
Allergy updated, erroneous entry	7	0	7
Anaphylaxis to PCN last 5 y	4	0	4
Antihistamine use could not be stopped	4	3	7
β -Blocker therapy	3	3	6
Delayed-type reaction	6	2	8
Discharged before eligibility	9	6	15
GI Intolerance	7	0	7
ICU	2	1	3
Refusal	17	11	28
Other (total)	15	5	20
Deceased	2	0	
Allergy previously deleted	5	2	
Hospice	1	0	
Active rash	4	0	
Skin too fragile	1	0	
Stroke	0	1	
Anaphylaxis (non-PCN last 4 wk)	0	1	
<i>Clostridium difficile</i> diarrhea	1	0	
Questionable rash	1	0	
Hallucinations	0	1	

GI, Gastrointestinal; GUMO, genitourinary medical oncology; ICU, intensive care unit; PCN, penicillin; PST, penicillin skin testing.

*Five patients had inpatient, physician-observed reactions to a penicillin agent at MD Anderson within the last 3 months; 1 patient had a positive PST within the last 6 months at a different institution.

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