

Pricking away at penicillin allergy with a dedicated outpatient clinic

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Clinical Implications

- Penicillin skin testing has revolutionized how the question of penicillin drug allergy is evaluated. We created a dedicated penicillin skin testing clinic to improve access to this procedure. Dedicated clinics are efficient, safe, and beneficial to evaluate patients for penicillin allergy.

TO THE EDITOR:

Penicillin (PCN) drug allergy is the most common antibiotic allergy reported by 7% to 10% of the adult US population and 15% to 20% of inpatients.^{1,2} Despite PCN allergy being commonly reported, many patients and clinicians are unaware that most individuals with a history of PCN allergy are not allergic and are able to tolerate PCN.^{3,4} Multiple studies have shown that penicillin skin testing (PST) is not only effective and safe but also reduces health care costs and improves outcomes.⁵⁻⁷ After implementing an inpatient PST program, demand for outpatient evaluation rose. We designed a dedicated outpatient PCN clinic structured so that multiple PCN allergy evaluations could be performed simultaneously. Here, we report our experience to provide allergists with a clinic model that improves access and addresses challenges encountered in clinical practice related to time, provider availability, and space.

We instituted a pilot clinic in May of 2017 to trial feasibility of this model and by August 2017 to July 2018, we incorporated dedicated PST clinics every other week. The clinic was set up to see a maximum of 6 patients scheduled for a 9 AM appointment time slot, with most visits completed by noon. The clinic was staffed by an allergy registered nurse (RN) trained in PST technique and an allergist. One allergy/immunology fellow additionally was available for the start of the first year of the clinic.

Once patients were checked in, the physician performed a focused history and physical reviewing the details of the drug reaction and gave a “green light” for the allergy RN to start PST. Our PCN protocol consisted of skin prick tests to Pre-Pen and PCN G with saline and histamine controls. Skin test results are read after 15 minutes and positive skin prick or intradermal testing result was defined as an increase in wheal size of 3 mm or more in diameter associated with a flare. If the initial skin prick test results were negative with appropriate controls, this was followed by intradermal testing with Pre-Pen, PCN G, and saline control. If intradermal test results were negative with appropriate control, the patient lastly completed a 2-step graded challenge with amoxicillin (400 mg). The patient received 10% (40 mg) of the total dose followed by the remaining 90% (360 mg) of the full dose. The patient was observed for 30 minutes after each step

of the graded challenge. A tolerated and completed oral challenge allowed for the patient to be cleared of their previous allergy. After evaluation, the patient was provided with education including which antibiotics they are able to take. If the patient was cleared of their PCN allergy, the allergy was removed from their medical record. Patients additionally received a wallet card with their allergy designation and test results so that their medical record outside of our system could be updated easily.

During the first year (August 2017-July 2018), we evaluated a total of 104 patients. Patients were referred from transplant, perioperative anesthesia clinic, primary care, and allergy/immunology (Table I). The median referral time was 25 days (interquartile range, 11-44 days). A retrospective chart review at our institution from January 2010 to February 2017 found that we performed PST in 150 outpatients (for an average of 21 evaluations per year) with a median referral time of 56 days (interquartile range, 31-108 days). A number of patients in the dedicated clinic had significant comorbidity including chronic cardiac, pulmonary, and oncologic conditions (Table I). The most commonly reported allergic history was hives or rash followed by an unknown reaction type (Table I). Most patients (n = 87 [84.5%]) reported reactions that occurred 10 or more years before testing.

A total of 95 patients (91.3%) had negative skin testing (Table II) results. Four patients had positive intradermal skin testing results to PCN G and were not challenged. None of the patients with a positive skin test result reported anaphylaxis (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). We had 5 patients (4.9%) who did not mount an appropriate histamine response despite appropriate antihistamine avoidance. One patient opted to perform serum specific IgE testing to penicillin V, penicillin G, and amoxicillin, results for which were negative, but has not returned for oral challenge (Table E1). The other 4 patients were determined to have low pretest probability of IgE-mediated drug allergy, passed a graded oral challenge, and were cleared of their allergy. Therefore, a total of 99 patients (95.2%) passed an oral challenge and cleared their PCN allergy. Two patients reported symptoms such as subjective itching during their challenge; however, they did not show objective findings consistent with an allergic reaction and were cleared of their PCN allergy.

PST is a safe and reliable diagnostic test to use in the outpatient evaluation of penicillin drug allergy. We chose to wait 30 minutes after each dose of the graded challenge, which shortened the appointment time given the low risk of reaction while still allowing for an observed wait time to keep patients safe. We did not have all minor determinants available to test; however, we did not experience allergic reactions during the testing or the challenge as previously shown.^{8,9} It is important to highlight that allergic reactions remain possible; thus, testing should be performed only in a physician's office capable of managing allergic reactions and under physician direct supervision.

This report highlights that a dedicated PST clinic increased referrals from specialty clinics and engages patients to seek education on their drug allergy. We were able to quickly and safely evaluate complex patients with significant comorbidity

TABLE I. Patients' characteristics

Characteristic	Patients (n = 104), n (%)
Age (y), mean $\pm$ SD	54.4 $\pm$ 16.7
Male	35 (33.7)
Female	69 (66.3)
Race	
White	78 (75.7)
Black	23 (22.3)
Hispanic	1 (1.0)
Other	1 (1.0)
Referred by	
Transplant	27 (26.0)
Preoperative	19 (18.3)
Primary care	12 (11.5)
Allergy/Immunology	33 (31.7)
Comorbidities	
Cardiac disease	44 (42.3)
Pulmonary disease	43 (41.3)
Oncologic disease	20 (19.2)
Medication allergy	
PCN	45 (43.3)
Amoxicillin/Augmentin	19 (18.3)
Unknown PCN	34 (32.7)
Cephalosporin	5 (4.8)
Reaction type	
Cutaneous (hives, rash)	83 (79.8)
Respiratory	7 (6.7)
Gastrointestinal	2 (1.9)
Anaphylaxis	3 (2.9)
Unknown	11 (10.6)
Time since reaction (y)	
<1	6 (5.8)
1-4	4 (3.9)
5-9	6 (5.8)
10-19	17 (19.5)
20-29	19 (21.8)
30-39	20 (23.0)
40-49	12 (13.8)
50-59	11 (12.6)
≤ 60	8 (9.2)

outside of the hospital where their care was not complicated by an acute condition or interfering medications. We have partnerships with transplant, infectious disease, and anesthesia and created a streamlined referral process for any provider to request consult to this clinic. We have not observed or recorded any differences in cost associated with the clinic as clinic space and staff costs are shared. Previous time-driven activity-based costing estimated the cost of a 2-step oral challenge after skin testing as \$227.⁶ Moreover, dedicated staff and access have increased the service provided.

It has been rewarding to work with patients whose care is improved by having access to PCN. Even for patients who are

TABLE II. Results

Test result	Patients (n = 104), n (%)
Performed PST	104 (100)
Skin testing negative	95 (91.3)
Histamine nonreactive	5 (4.9)
Intradermal positive	4 (4)
Passed oral challenge*	99 (95.2)
Reported symptoms	2 (1.9)

*Patients were offered an oral challenge if (1) skin testing result was negative or (2) histamine nonreactive but patient with distant history and amenable to oral challenge without skin testing.

not able to be cleared of their PCN allergy, we discussed the role of desensitization should they require a PCN or PCN derivative. This model may be adapted for implementation into any allergy practice. A dedicated clinic provides safe and efficient access for patients and providers seeking to address PCN allergy.

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TABLE E1. Characteristics of subjects with positive or indeterminate PST result

Results and History Details	PosID 1	PosID 2	PosID 3	PosID 4	NegH 1
Evaluation	Positive ID to Pen-G, No oral challenge	Positive ID to Pen-G, No oral challenge	Positive ID to Pen-G, No oral challenge	Positive ID to Pen-G, No oral challenge	Negative histamine, No oral challenge
Medication allergy	Penicillin	“Unknown penicillin”	Amoxicillin	“Unknown penicillin”	Amoxicillin
Reaction type	Cutaneous rash	Cutaneous hives	Cutaneous rash	Cutaneous rash	Cutaneous angioedema
Time since reaction (y)	50	40	5	24	12

ID, Intradermal; Pen-G, penicillin G.

“Unknown penicillin” was noted when subjects could not recall the specific drug to which they reacted.