

Clinical approach to penicillin-allergic patients: a survey

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Background: Approximately 10% of individuals report a history of penicillin allergy.

Objective: We chose to survey various physician groups to determine how they would manage penicillin-allergic patients who present with an infectious process for which penicillin is the drug of choice.

Methods: In situations where penicillin was the drug of choice, physicians were asked to choose the type of antibiotic treatment for patients who presented with diseases of varying severity and who had either vague or convincing penicillin-allergic histories.

Results: A total of 601 surveys were mailed and 93 (16%) were returned. For those patients who present with a vague history of penicillin allergy, 58% and 59% of the physicians surveyed stated that they would choose cephalosporins for individuals with mild and moderate diseases, respectively. In contrast, in the vague penicillin history/severe disease scenario, physicians were split between choosing cephalosporins (42% of responders) and vancomycin (40% of responders). For those patients who present with a convincing history of penicillin allergy, 55% of the physicians chose erythromycin for individuals with mild disease; 44% chose quinolones for individuals with moderate disease, and 63% chose vancomycin for individuals with severe disease. In each of the three disease severities, physicians were significantly more likely to choose cephalosporins for patients with a vague history of penicillin allergy than for patients with a convincing history (each $P < 10^{-5}$).

Conclusion: The choice of antibiotics is influenced both by the type of penicillin allergic history and by the severity of the disease process to be treated. To decrease the use of broad-spectrum antibiotics in patients labeled "penicillin-allergic", an effort should be made to identify, by skin testing, those patients who lack penicillin-specific IgE antibodies.

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INTRODUCTION

The clinician today has several therapeutic options when managing the adult patient who has a history of penicillin (PCN) allergy and who requires

beta-lactam therapy. These options include (1) skin testing to determine if PCN-specific IgE antibodies exist, (2) desensitization if PCN is the drug of choice and the skin test is positive or not available, and (3) choosing an alternative non beta-lactam antibiotic.

Among the questions that a clinician must answer in deciding the appropriate treatment of the PCN-allergic patient is the accuracy of the historical information. Because many times the reaction occurred in the distant past, the history is frequently vague or unknown. For this reason, it is often difficult to determine if the previous reaction was IgE-mediated, mediated by another immunologic mechanism, or

simply a non-immunologic adverse event. In the current study, several physician groups, none of them allergists, were surveyed regarding their approach to PCN-allergic patients. Our purpose was to determine how a history of PCN allergy would influence clinicians' choices of antibiotic treatment when they are confronted with PCN-allergic patients who have disease processes for which PCN is the drug of choice.

METHODS

Four hundred surveys were mailed to the Internal Medicine, General Surgery, Orthopedic Surgery, and OB-GYN hospital-based physicians (faculty and housestaff) at Parkland Memorial Hospital, a large teaching tertiary care hospital, in Dallas, Texas. In addition, 201 surveys were mailed to private practice physicians (in the same four specialties) who had admitting privileges at two community hospitals in a nearby city (Arlington, Texas). Because our initial goal was to evaluate the treatment of adults only, Family Practice and Pediatric physicians were not included in the survey. In clinical situations where PCN was the drug of choice, the physicians were asked to choose an antibiotic for patients who had either vague or convincing histories of PCN allergy, in each of three clinical situations: (1) mild disease or prophylactic use, (2) moderate disease, and (3) severe or life threatening disease. For each clinical scenario, the physicians were asked to choose from the following antibiotic categories: penicillin, semisynthetic penicillins, cephalosporins, erythromycin, sulfonamides, quinolones, vancomycin, and other. The responders also were asked to list their specialty and the percent of patients they see monthly who report an allergy to PCN. In Table 1 a list of the questions in the survey is presented. Since we had paired data, the McNemar chi-squared

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test was used to determine statistical comparisons between the proportions.

RESULTS

A total of 601 surveys were mailed and 93 (16%) were returned. Of the 93 completed surveys, Parkland Hospital physicians completed 53, and community physicians completed 40. The breakdown of the 93 responders by specialty was as follows: 41 Internal Medicine, 10 Surgery, 13 OB-GYN, 9 Orthopedics, and 20 not listed. Overall, the physicians reported that between 0.5% and 40% (mean 10%, with a standard deviation of 8.8) of the patients they see monthly report an allergy to PCN.

Nearly all of the responders provided answers to each of the six questions pertaining to antibiotic choices in the six different clinical scenarios. In instances where responders chose more than one antibiotic for a given clinical scenario, each answer was counted in the analysis. Physicians' responses are summarized in Figures 1 and 2. As shown, the type of history of the previous PCN reaction as well as the severity of the disease process to be treated affected the choice of antibiotics. In patients with a vague history of PCN allergy (Fig 1), physicians were most likely to choose cephalosporins for those who present with mild (58%) or moderate (59%) disease processes and were split between choosing cephalosporins (42%) and vancomycin (40%) for those patients who present with a severe disease process. In patients with a convincing history of PCN allergy (Fig 2), responders were

most likely to choose erythromycin for patients who present with mild disease (55%), quinolones (44%) and erythromycin (29%) for patients who present with moderate disease, and vancomycin for patients who present with severe disease (63%).

In a number of instances, for a given disease severity, the type of PCN-allergy history (vague or convincing) influenced the choice of antibiotics. The most striking example of this influence was in the choice of cephalosporins (Fig 3). For each disease severity, physicians were more likely to choose cephalosporins for those patients who had a vague history of PCN allergy compared with those patients who had a convincing history. These differences were significant for each disease severity: 58% versus 11% in mild disease ($P<10^{-9}$), 59% versus 14% in moderate disease ($P<10^{-10}$), and 42% versus 16% in severe disease ($P<10^{-5}$). Instead of choosing cephalosporins for patients who had convincing histories of PCN allergy, physicians chose to use antibiotics of alternate classes, especially vancomycin, erythromycin, and the quinolones.

When we compared the responses of Parkland Hospital physicians to those of community physicians, a notable difference was observed. In a number of clinical scenarios, community physicians were more likely to choose cephalosporins for PCN-allergic patients than were Parkland Hospital physicians (Fig 4). Although all the differences did not reach statistical significance, they were observed in the situations of vague history/mild dis-

ease, vague history/moderate disease, convincing history/moderate disease, and convincing history/severe disease. In contrast, in these four clinical situations, the Parkland Hospital physicians more frequently chose to use an alternate class of antibiotics, especially erythromycin, quinolones, and vancomycin (data not shown).

DISCUSSION

This survey is the first to evaluate how non-allergy clinicians approach antibiotic treatment in their adult patients who have a history of PCN allergy. We found that physicians in our survey were more likely to choose cephalosporins for patients who had a vague history of PCN allergy, and that they were less likely to choose cephalosporins for those patients who had a convincing history of PCN allergy. This finding was true across all disease severity categories. In addition, we found that physicians frequently choose to treat patients who have a history of PCN allergy with broad-spectrum antibiotics, such as quinolones and vancomycin.

From these data, it is reasonable to conclude that most of the responders are concerned about potential cross-reactivity between PCN and cephalosporins, and that they rely on the type of reaction history to guide them in their decision-making process. Furthermore, while the numbers are small, in a number of clinical scenarios, community physicians were more likely to choose cephalosporins than were Parkland Hospital physicians. Based on these results, it appears that community physicians are less concerned

Table 1. Clinical Scenario Questions in the Survey

Questions 1–3: The patient gives a vague or questionable history of penicillin allergy.			
1. In an outpatient setting, the patient has a mild disease or requires prophylaxis before or after surgery. Which antibiotic class would you choose?			
2. In an outpatient or inpatient setting, the patient has a moderately severe infection. Which antibiotic class would you use?			
3. In an inpatient setting, the patient has a life-threatening condition or illness. Which antibiotic class would you use?			
Questions 4–6: The patient gives a strong history of anaphylaxis or recent (within the last 2 years) allergic reaction to penicillin.			
4. In an outpatient setting, the patient has a mild disease or requires prophylaxis before or after surgery. Which antibiotic class would you choose?			
5. In an outpatient or inpatient setting, the patient has a moderately severe infection. Which antibiotic class would you use?			
6. In an inpatient setting, the patient has a life-threatening condition or illness. Which antibiotic class would you use?			
Each of the six questions was followed by the following choices:			
a. penicillin	b. semisynthetic penicillin	c. cephalosporin	d. erythromycin
e. sulfa	f. quinolone	g. vancomycin	h. other

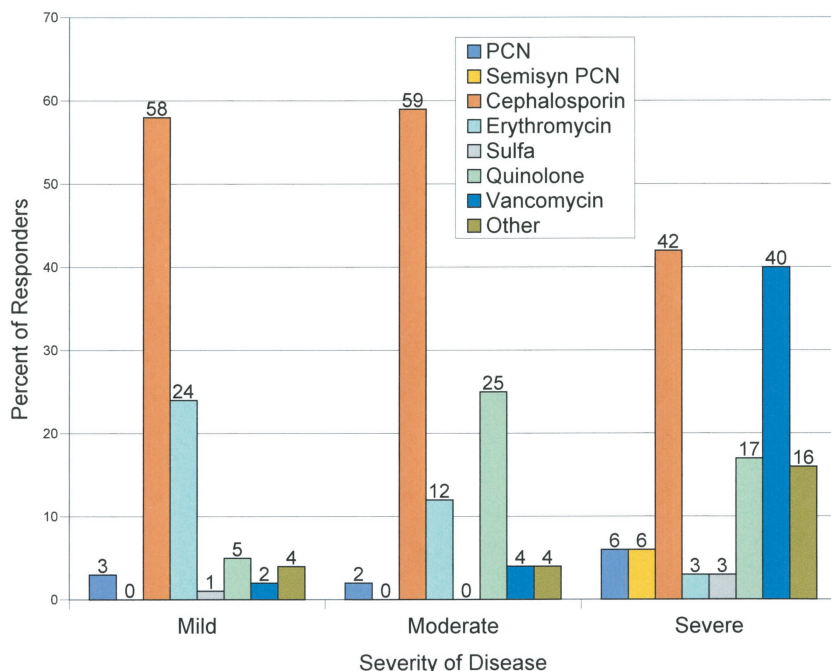


Figure 1. Antibiotic choices in patients with a vague history of penicillin allergy; n = 93.

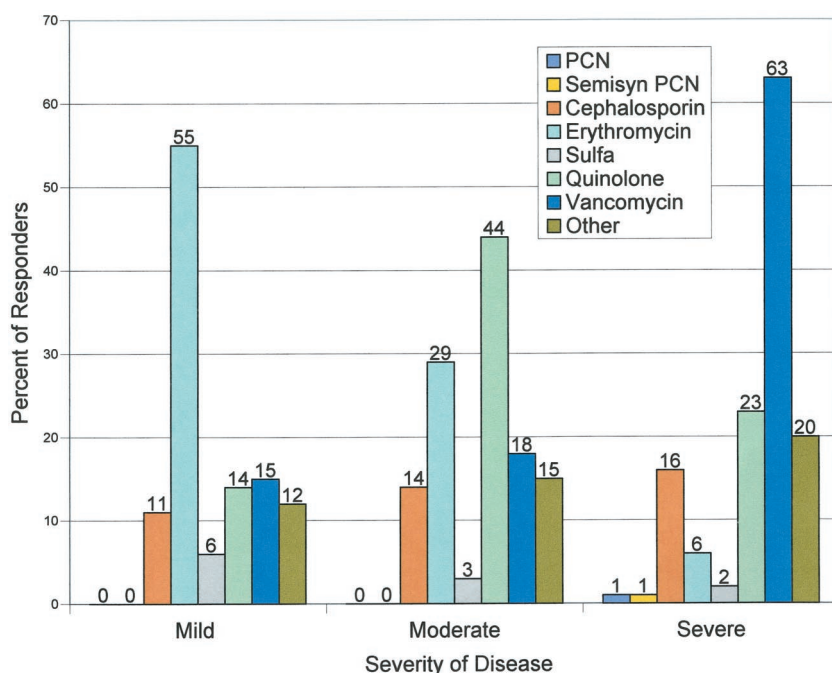


Figure 2. Antibiotic choices in patients with a convincing history of penicillin allergy; n = 93.

about the potential cross-reactivity between PCN and cephalosporins.

The extent of immunologic cross-reactivity between cephalosporins and PCN that may lead to immediate aller-

gic reactions is still not known. Some authors have reported the incidence of allergic reactions in PCN-allergic patients who receive cephalosporins to be no higher than the incidence in the

general population,¹⁻³ whereas in-vitro data suggests that PCN-allergic patients may have a 4 to 8-fold increased risk of an immediate reaction to cephalosporins.⁴⁻⁶ The common use of cephalosporins in PCN-allergic patients is not limited to non-allergists, as was shown in a recent survey of allergists by Wickern et al.⁷ When asked whether they would use cephalosporins in patients with a history of hives to PCN (without first performing a PCN skin test), 26% of allergists stated they would use a first generation cephalosporin; 36%, a second generation cephalosporin; and 48%, a third generation cephalosporin. It has been shown that patients who have a convincing history of PCN allergy are more likely to have a positive PCN skin test than those who have a vague history.⁸⁻¹¹ In a recent review of the literature, however, it also was found that, in history positive patients who have positive PCN skin tests, one-third of these individuals had vague histories of PCN allergy.¹² These findings indicate that one cannot rely on history alone to confirm the presence or absence of PCN-specific IgE antibodies since a significant number of skin test positive patients report a vague drug allergy history. If indeed there is cross-reactivity between PCN and cephalosporins due to the common beta-lactam structure, it would not be prudent to base a decision of whether or not to give cephalosporins to patients with a history of PCN allergy solely on the "strength" of the history.

An interesting and surprising finding of the survey was that some responders chose to use PCN in patients with a history of PCN allergy. Namely, in patients with a vague history of allergy, 3%, 2%, and 6% of responders chose PCN in the scenarios of mild, moderate, and severe disease, respectively. In contrast, only one responder chose PCN in patients with a convincing history of PCN allergy (in the scenario of severe disease). As discussed above, a sizeable proportion of patients who have positive PCN skin tests also have a vague history of PCN allergy. It is therefore, reasonable to conclude

that the practice of giving PCN to patients who have a vague history of PCN allergy, is, despite their history, a potentially dangerous one.

There is a multitude of problems associated with the unnecessary use of broad-spectrum antibiotics in clinical medicine today. Many of these antibiotics are expensive and may have a toxic side-effect profile, such as vancomycin. Another significant problem that has emerged in recent years is the increasing prevalence of multiple-drug resistant bacteria. The emergence of these organisms is largely due to the unnecessary use of broad-spectrum antibiotics.^{13,14} The overall added cost to health care resulting from multiply drug-resistant organisms has been estimated to be over \$4 billion annually.¹⁵ Two notable examples of antibiotic resistance are vancomycin-resistant *Enterococci* (VRE) and vancomycin-resistant *Staphylococcus aureus* (VRSA). These strains represent a major public threat because they are resistant to all clinically available antibiotics, and, in addition, VRE can potentially transmit their antibiotic resistance to other bacteria.¹⁶

It is likely that a considerable proportion of patients who receive broad-spectrum antibiotics are those patients who are labeled "PCN-allergic." At Parkland Memorial Hospital, a recent review of vancomycin order forms, on which a reason for choice of the medication must be submitted, showed that 22% of them were ordered because the patient was labeled "PCN-allergic" (Parkland pharmacy antibiotic subcommittee data). Similarly, in patients receiving vancomycin for prophylaxis, 31% of these individuals were given the antibiotic because they were labeled "PCN-allergic" (Parkland pharmacy antibiotic subcommittee data). In our survey, physicians frequently chose to use vancomycin, especially in the setting of severe disease; 40% and 63% of responders stated they would use it in patients with a vague and convincing history of PCN allergy, respectively.

A control measure that has been recommended by the CDC and others to decrease the spread of vancomycin resistance is more judicious use of van-

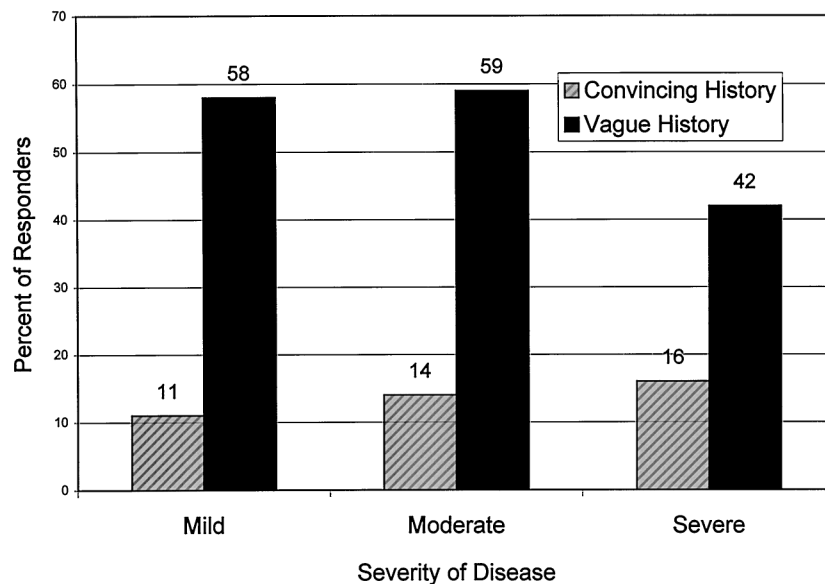


Figure 3. Choice of cephalosporins in patients with vague and convincing histories of penicillin allergy; n = 93.

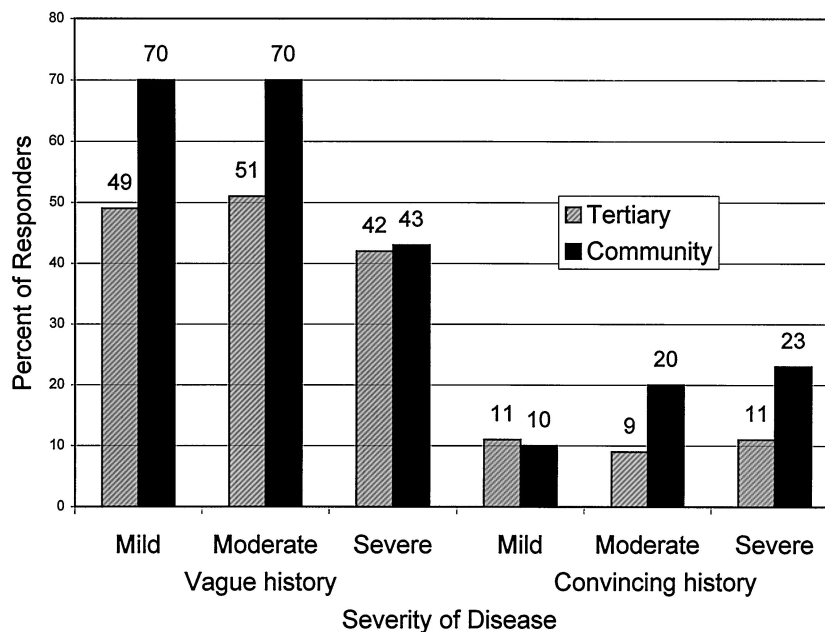


Figure 4. Choice of cephalosporins by tertiary and community physicians; n = 53 (tertiary), n = 40 (community).

comycin and other broad-spectrum antibiotics.^{14,17,18} Numerous studies have shown that the vast majority of patients who have a history of PCN allergy are PCN skin test negative, and that they can safely receive the antibiotic.^{3,9,10,19-23} One method to help achieve the goal of decreasing the spread of antibiotic resis-

tance would be to identify, by skin testing, the many patients labeled "PCN-allergic" who lack PCN-specific IgE antibodies, and who are therefore exposed needlessly to broad-spectrum antibiotics. Nonetheless, recommendations published by the CDC considered the use of vancomycin in patients with "se-

rious allergy to beta-lactam antimicrobials" appropriate, and there was no mention of alternative therapeutic interventions such as PCN skin testing.¹⁸

We realize that both the low response rate and the fact that only physicians in the Dallas metropolitan area were surveyed limit the extent to which our findings can be generalized. Despite these small numbers, the results clearly suggest that both the history of the type of PCN reaction and the severity of the disease process to be treated may influence clinicians' antibiotic choices. Furthermore, although no differences were observed among the physicians' responses in the four specialties, it is possible that a larger sample size may yield differences among these groups.

Penicillin skin testing can play an important and valuable role in decreasing the unnecessary use of broad-spectrum antibiotics in those patients labeled "PCN-allergic," and in turn, helping contain the spread of drug-resistant bacteria. As allergists, we need to continue to make our colleagues aware of the option of PCN skin testing, as well as the fact that most patients with a history of PCN allergy lack PCN-specific IgE antibodies, can safely receive the medication, and therefore are denied access to these antibiotics needlessly.

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