

# Antibiotic Skin Testing in the Intensive Care Unit: A Systematic Review

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**BACKGROUND** Recent research has shown that a large majority of patients with a history of penicillin allergy are acutely tolerant of penicillins and that there is no clinically significant immunologic cross-reactivity between penicillins and cephalosporins or other  $\beta$ -lactams. The standard test to confirm acute tolerance is challenge with a therapeutic dose. Skin testing is useful only when the culprit antibiotic can haptenate serum proteins and induce an immunoglobulin E–mediated reaction and the clinical history demonstrates such high risk that a direct oral challenge may result in anaphylaxis.

**OBJECTIVE** To review and evaluate the current practice of skin testing for antibiotics (other than penicillin) in critically ill patients by means of a systematic literature review.

**METHODS** This systematic review was performed using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines. Several electronic databases were searched using the following terms: *antibiotics, skin test (tests, testing), intensive care, intensive care unit, ICU, critical care, critical care unit.*

**RESULTS** Twenty-three articles were identified for inclusion in this review. The results indicate a lack of standardized skin testing for all antibiotics in critical care settings. Oral challenge with nonirritating concentrations of antibiotics can be helpful in determining allergy to these drugs.

**CONCLUSIONS** Critical care providers should evaluate antibiotic allergy using nonirritating concentrations before administering antibiotics to patients. Introduction of a standardized skin test for all antibiotics in intensive care unit patients to help select the most appropriate antibiotic treatment regimen might help save lives and reduce costs. (*Critical Care Nurse*. 2019;39[6]:e1-e9)

**A**ntibiotic use is an issue of increasing concern for health care systems in general and intensive care units (ICUs) in particular. Penicillin and other  $\beta$ -lactam antibiotics are the most common cause of medication-induced anaphylaxis.<sup>1</sup> Allergic reactions to penicillin have been reported in up to 10% to 12% of patients.<sup>1</sup> Self-reports of allergic reactions usually arise from historical childhood events or nonallergic adverse events that may be imprecise and unreflective of a true immunoglobulin E (IgE)–mediated allergy.<sup>1,2</sup> Moreover, patients with a well-documented allergy or hypersensitivity may cease to be allergic over time as a result of the loss of antipenicillin IgE antibodies (eg, the allergy may be reduced by about 80% over 10 years).<sup>3</sup> The literature suggests that 10% of documented penicillin allergies are true IgE-mediated reactions, whereas 80% of patients with documented penicillin allergies will have a negative skin test and could subsequently receive penicillin.<sup>3</sup> The standard test to confirm tolerance is an oral amoxicillin challenge and 1 hour of observation to rule out acute hypersensitivity and up to 5 days of observation

to rule out clinically significant T cell–mediated delayed-onset hypersensitivity. Penicillin skin testing (PST) is useful before an oral challenge in individuals with a clinical history that puts them at high risk for anaphylaxis with repeat exposure.<sup>1,4</sup>

Penicillin skin testing has been performed since 1948 and has evolved dramatically over the past 70 years.<sup>3</sup> Following PST, IgE-mediated reactions typically occur within 1 hour of exposure but may occur up to 72 hours afterward; such reactions may include angioedema, urticaria, shortness of breath, rash with pruritus, bronchospasm, and anaphylaxis.<sup>5</sup> Thus, PST must be performed only by a trained health care provider (eg, pharmacist, physician, nurse) and should be completed in a controlled and monitored environment because of possible side effects, such as slightly swollen, red, itchy bumps and, for some, a severe, immediate allergic reaction.<sup>6</sup>

The standard test to confirm current tolerance of an antibiotic to which a patient has been reported to be sensitive or allergic is a drug challenge with a therapeutic dose. Skin testing is useful before drug challenge only in a small subgroup of individuals with a history of an adverse reaction compatible with an IgE-mediated allergy, with the reaction being to an antibiotic that is either a complete antigen or able to haptenate serum proteins and trigger an IgE-mediated reaction. Even under optimal settings,

skin testing can be associated with high rates of both

**A standardized PST procedure is needed to avoid exposing ICU patients to the risk of an allergic reaction.**

false-positive and false-negative results, and the standard test, a challenge (oral when possible), is needed to confirm acute tolerance. Many antibiotics are directly irritating to skin (such as macrolides), directly activate mast cells (such as quinolones), or do not cause IgE-mediated reactions (such as sulfonamides), making skin testing not useful before rechallenge.<sup>7,8</sup> Although PST

has proved to be a reasonable screen, false-negative results may still occur. For instance, 1 study reported a relatively high false-negative rate of skin testing (76%; 13 of 17 who tested negative in PST were positive in a 3-day oral challenge test).<sup>9</sup> Anaphylaxis may occur in patients with false-negative results when oral challenge is not conducted.

Because penicillin allergies have been associated with increased length of ICU stay, antimicrobial resistance, and death,<sup>10,11</sup> it is essential for critical care providers to avoid the use of antibiotics that provoke an allergic response. Unfortunately, patients who require antimicrobial treatment have been reported to have a documented penicillin allergy 15% to 24% of the time.<sup>12</sup> Therefore, a standardized PST procedure is needed to avoid exposing ICU patients to the risk of an allergic reaction, as well as to prevent an unnecessary switch to a non- $\beta$ -lactam antibiotic. The use of PST has been shown to improve patient care and reduce costs in hospitals.<sup>13</sup> A systematic review revealed that the most common clinical outcomes after inpatient PST were a change in antimicrobial therapy, reduced hospital costs, and cost savings for individual patients.<sup>14</sup> The purpose of this project was to examine and evaluate the current practice of antibiotic skin testing in critically ill patients by means of a systematic literature review.

## Methods

This systematic review was performed using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.<sup>15</sup> The following electronic databases were searched: Cumulative Index to Nursing and Allied Health Literature, Health Source: Nursing/Academic Edition, Library Literature & Information Science Full Text (H.W. Wilson), MEDLINE, Shock & Vibration Digest, Academic Search Complete, Food Science Source, SocINDEX with Full Text, PubMed, and Google Scholar. The following search terms were used, in all possible combinations: *antibiotics, skin test (tests, testing), intensive care, intensive care unit, ICU, critical care, critical care unit*.

The focus of this review was antibiotic skin testing in critically ill patients. Articles relevant to the topic of interest were examined to ensure that they met the following inclusion criteria: (1) academic article published in a peer-reviewed scholarly journal, (2) available in the English language, and (3) published between 2003 and

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2018. The purpose of selecting articles published between 2003 and 2018 was to examine only the most recent research conducted on the topic. After articles were identified for inclusion, data pertinent to antibiotic skin testing were extracted. The articles were then analyzed to identify the current practice of antibiotic skin testing in critical care units.

## Results

### Article Selection and Characteristics

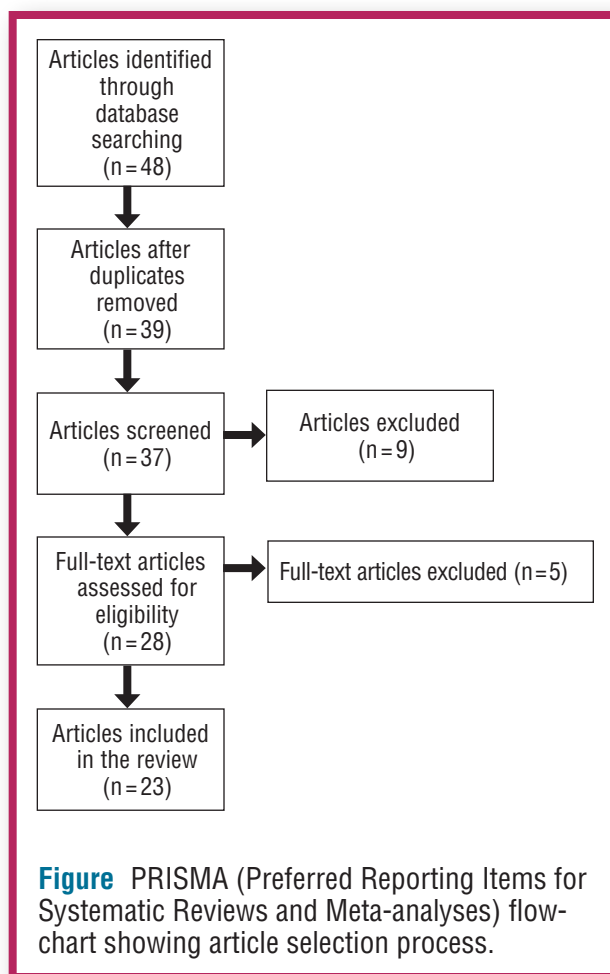
After duplicates were removed, a total of 39 articles were found through the database search. The articles were screened for relevance, and only 2 were excluded after a review of the title and abstract revealed that the article did not address antibiotic skin testing in critical care units. Of the remaining 37 articles, 9 were excluded after full-text review showed that data relevant to the topic were not included. The remaining 28 articles were assessed for study eligibility, of which 5 were excluded for the following reasons: (1) the article did not strictly focus on antibiotic testing but also discussed the long-term use of antibiotics; (2) the article discussed skin tests for neuromuscular blocking agents; (3) the article discussed anaphylaxis reported in infancy; (4) the article described an adverse drug reaction to antibiotics in patients with cystic fibrosis; and (5) the article focused on skin testing for perioperative anaphylaxis. A PRISMA flowchart showing the article selection process appears in the Figure.

Of the 23 included articles, 5 were review articles that provided information about the literature on antibiotic skin testing. Eight articles were interventional studies that examined the effectiveness of antibiotic skin testing. Ten articles outlined the current practice of antibiotic skin testing and the prevalence of drug-induced allergy.

### Summary of Evidence

The Table shows the articles included in this systematic review, with summaries of their results. The articles are discussed here according to the following topics: drug-induced allergy, structured allergy history, antibiotic skin testing, and nonirritating concentration (NIC).

**Drug-Induced Allergy.** The presence of a drug-induced allergy has been associated with increased morbidity, including a higher incidence of multidrug-resistant infections and longer hospital stay. For instance, in a prospective exploratory study that documented cases



**Figure** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flow-chart showing article selection process.

of drug-induced anaphylaxis recorded by the Allergy Vigilance Network from 2002 to 2010, Renaudin et al<sup>16</sup> reported the following allergy incidences: anaphylactic shock (76.6%), severe systemic reactions (10.5%), acute laryngeal edema (9%), severe bronchospasm (2.1%), and death (1.8%). Among drug-induced anaphylaxis cases, antibiotics were responsible for almost 50%.<sup>16</sup> Most of the cases were caused by amoxicillin. Another study indicated that cefazolin was the most frequently reported (6 of 9 cases) cause of hypersensitivity reactions in perioperative patients.<sup>17</sup>

**Structured Allergy History.** The literature contains inconsistent findings on the validity of patient-reported penicillin allergies. For instance, in an interventional study involving perioperative patients, the researchers did not perform antibiotic skin testing or diagnostic challenges but relied solely on the patients' self-reported history of allergy. If no history of allergy was reported, prophylactic cefazolin was used without any serious

**Table** Articles included in the systematic review

Source	Type	Purpose	Participants	Results	Economic savings
Renaudin et al, <sup>16</sup> 2013	Prospective exploratory study	To document cases of drug-induced anaphylaxis	All patients who had drug-induced anaphylaxis	Anaphylactic shock (76.6%), severe systemic reactions (10.5%), acute laryngeal edema (9%), severe bronchospasm (2.1%), and death (1.8%) were recorded. Among drug-induced anaphylaxis cases, antibiotics caused 50%. Most of the cases were caused by amoxicillin.	Not reported
Kuhlen et al, <sup>17</sup> 2016	Prospective study	To determine the success of a comprehensive allergy evaluation plan for patients with hypersensitivity reactions during anesthesia	Perioperative patients	Cefazolin was the most commonly identified (6 of 9 cases) cause of hypersensitivity reactions.	Not reported
Vaisman et al, <sup>18</sup> 2017	Interventional study	To assess the impact of structured allergy histories on patients with self-reported $\beta$ -lactam allergy	Perioperative patients	The authors did not perform antibiotic skin testing or diagnostic challenges. They relied on patients' self-reported history of allergy and used prophylactic cefazolin if patients did not describe a history of type I-mediated or severe reaction without any serious adverse events.	Not reported
Moreno et al, <sup>19</sup> 2017	Review article	To discuss the diagnosis and management of patients with self-reported penicillin allergy		The diagnosis of $\beta$ -lactam allergy relies on a comprehensive medical history, skin tests, and in vitro tests.	Not reported
Raja et al, <sup>12</sup> 2009	Interventional study	To evaluate penicillin allergy skin testing in EDs to verify self-reported allergies	ED patients	The false-positive rate for self-reported penicillin allergy was 91.3%. False-positive self-reports were confirmed by negative PST result. There were no adverse reactions associated with PST.	The median cost of the first-choice and prescribed antibiotics increased from \$30.36 to \$104.16 and from \$30.36 to \$109.76 in patients with a false-positive penicillin allergy according to PST and in patients with a true-positive penicillin allergy history, respectively.
Rimawi and Mazer, <sup>20</sup> 2014	Descriptive study	To determine the prevalence of penicillin allergy	ICU patients	12% of ICU patients had a penicillin allergy history; 17% of them had a negative reaction to the PST. PST is helpful in the ICU setting and may decrease the medical costs.	Not reported
Fox and Park, <sup>5</sup> 2011	Review article	To review the role of PST in the evaluation and management of penicillin allergy		A detailed history of the previous reaction to penicillin is an integral part of the evaluation, but it is not accurate in predicting a positive PST result.	Not reported

*Continued*

**Table** *Continued*

Source	Type	Purpose	Participants	Results	Economic savings
Ramsey and Staicu, <sup>21</sup> 2017	Interventional study	To determine the effectiveness of PAHA and subsequent PST in determining allergy to penicillin	Adult inpatients with penicillin allergy history	If skin test was negative, patients were treated with the first-line $\beta$ -lactam antibiotic therapy without an adverse reaction. If skin test was positive, patients were treated with second-line therapies.	At least 23 hospital days were avoided, with cost savings of \$50 000.
Seitz et al, <sup>22</sup> 2009	Interventional study	To assess whether history alone can determine fluoroquinolone hypersensitivity	Patients with a history of fluoroquinolone hypersensitivity	History alone and/or skin tests lead to a considerable overestimation of fluoroquinolone hypersensitivity. Challenge tests appear to be necessary to definitively confirm or rule out fluoroquinolone hypersensitivity.	Not reported
Unger et al, <sup>3</sup> 2013	Review article	To discuss currently available literature on PST		Up to 10% of patients have a reported penicillin allergy.	Cost savings with PST and a higher economic burden with penicillin allergies, including longer duration of treatment and antibiotic costs up to 63% higher
Schafer et al, <sup>23</sup> 2007	Review article			Penicillin and associated $\beta$ -lactam antibiotics remain a primary cause of anaphylaxis. Patients with suspected penicillin allergy can be treated with antibiotic alternatives. Penicillin allergy skin testing is a simple and effective way to identify true penicillin allergy.	Not reported
Arroliga et al, <sup>24</sup> 2003	Descriptive study	To determine the incidence of true penicillin allergy and the percentage of patients given a $\beta$ -lactam antimicrobial when PST was negative	Patients with penicillin allergy in the ICU	Almost 89% of patients had a negative PST. About 82% received a $\beta$ -lactam antimicrobial after a negative reading. PST is a safe, reliable, and effective strategy to reduce the use of non- $\beta$ -lactam antimicrobials in patients who are labeled as penicillin allergic and admitted to the ICU.	Not reported
Sacco et al, <sup>14</sup> 2017	Systematic review and meta-analysis	To ascertain the validity of PST in the ICU	ICU patients	Penicillin allergy testing is safe and effective in ruling out penicillin allergy in the ICU.	Inpatient penicillin allergy testing was associated with decreased health care cost.
Kavadas et al, <sup>25</sup> 2008	Interventional study	To determine the safety of antibiotic skin testing of children and to describe its potential clinical impact	Pediatric patients	Skin-prick testing is a novel tool in pediatric care that may have an important clinical impact on the accurate diagnosis of antibiotic allergies by guiding provocative challenges.	Not reported
Macy, <sup>26</sup> 2006	Interventional study	To document the safety and utility of PST in pregnant women	Pregnant women with a history of penicillin allergy and group B streptococcus colonization	PST can be performed safely in pregnant women and, if the results are negative, allows penicillin to be used safely at delivery for group B streptococcus prophylaxis.	Not reported

*Continued*

**Table** *Continued*

Source	Type	Purpose	Participants	Results	Economic savings
Lee et al, <sup>27</sup> 2010	Survey	To examine the current practice of antibiotic skin testing in Korea	12 allergists working at hospitals in Korea	The antibiotic skin testing protocols were variable and inconsistent and differed with regard to the type and concentrations of antibiotics, the volume injected, and the interpretation of the results. The protocols also differed from the commonly recommended procedures in the literature.	Not reported
Abdulazeez et al, <sup>28</sup> 2011	Prospective cross-sectional study	To examine the current practice of antibiotic skin testing in the United Arab Emirates	All patients who were prescribed antibiotics	Of 357 patients who received parenteral antibiotics, 238 had a skin test. No standard technique for skin testing existed in the institution, and significant variations were noted between wards.	Not reported
Kavadas et al, <sup>29</sup> 2013	Retrospective chart review	To study the skin reaction at a NIC	Pediatric patients	Through testing with NICs of various antibiotics in children and providing provocative challenges on the basis of negative skin test results, health care providers can select appropriate antibiotic options.	Not reported
Rimawi et al, <sup>30</sup> 2013	Interventional study	To determine the cost-effectiveness of performing PST	Hospitalized patients	146 patients with a history of penicillin allergy and negative PST were treated with $\beta$ -lactam antibiotics. Of these, only 1 patient experienced an allergic reaction.	PST-guided antibiotic modification for these patients resulted in an estimated annual savings of \$82 000.
King et al, <sup>31</sup> 2016	Retrospective analysis study	To determine the cost-effectiveness of performing PST	Adult inpatients with a $\beta$ -lactam allergy who underwent PST and oral challenge performed by an allergist	31 subsequent admissions required antibiotics for patients who tested negative on skin test and oral challenge. A $\beta$ -lactam antibiotic was prescribed in 22 of 31 readmissions.	Overall cost savings were \$11 005 (\$297 per patient switched to a $\beta$ -lactam antibiotic).
Macy and Ho, <sup>32</sup> 2011	Retrospective study	To provide data on antibiotic use and new antibiotic "allergy" incidence after PST	All patients	The highest new antibiotic "allergy" incidence rates in skin test-negative patients were noted for penicillins, 2.9%, and sulfonamides, 2.7%.	Not reported
Brož et al, <sup>33</sup> 2012	Interventional study	To examine whether NICs are helpful to determine allergy to antibiotics	15 healthy volunteers	NICs of the 3 antibiotics (ciprofloxacin, clarithromycin, rifampicin) are helpful in determining allergy to these drugs.	Not reported
Goldberg and Confino-Cohen, <sup>34</sup> 2008	Prospective study	To examine whether penicillin oral challenge for patients with a history of non-life-threatening allergic reaction to penicillin can be well tolerated irrespective of skin test results	All patients	Among 137 patients with a positive skin test result and 135 patients with a negative skin test result, 9 (6.6%) and 5 (3.7%) ( $P = .29$ ), respectively, developed a mild rash in response to oral challenge. At follow-up, 2 to 6 years later, 3 of 55 patients (5.5%) who were given a full treatment course of penicillin developed a mild skin eruption.	Not reported

Abbreviations: ED, emergency department; ICU, intensive care unit; NIC, nonirritating concentration; PAHA, penicillin allergy history algorithm; PST, penicillin skin testing.



adverse events.<sup>18</sup> Similarly, Moreno et al<sup>19</sup> emphasized the importance of allergy history in the diagnosis of  $\beta$ -lactam allergy.

In contrast, other interventional studies indicated that patient-reported penicillin allergies can be unreliable and may result in needless changes in antibiotic therapy. For instance, Raja et al<sup>12</sup> reported that the false-positive rate for self-reported penicillin allergy was 91.3% (137 of 150 patients) in emergency department settings. Similarly, Rimawi and Mazer<sup>20</sup> reported that whereas 12% of ICU patients had a penicillin allergy history, 17% of them had a negative reaction to PST. These findings suggest that allergy history is not a reliable diagnostic approach to rule out penicillin allergies. Thus, some authors recommended combining penicillin allergy history and subsequent PST to confirm or rule out allergy to penicillin.<sup>5,21</sup> However, another study indicated that medical history alone and/or skin tests can lead to an inappropriate diagnosis of fluoroquinolone hypersensitivity.<sup>22</sup> The authors concluded that challenge tests are necessary to definitively confirm or rule out fluoroquinolone hypersensitivity.

**Antibiotic Skin Testing.** Study findings suggested that 10% to 12% of patients have a reported penicillin allergy.<sup>3,20</sup> As discussed earlier, drug-induced allergy is a serious condition that must be prevented among critical care patients to save lives and reduce costs. Thus, some researchers concluded that PST to confirm or rule out penicillin allergy should be a routine procedure.<sup>19,23</sup> If the allergy to penicillin is ruled out, patients can receive  $\beta$ -lactam antibiotics.<sup>19,23,24</sup> However, if the allergy to penicillin is confirmed, patients will be given non- $\beta$ -lactam antimicrobials.<sup>19,23</sup>

Many studies suggest that PST is a safe, reliable, and effective strategy to rule out penicillin allergy and reduce the use of non- $\beta$ -lactam antibiotics in patients who are labeled as penicillin allergic.<sup>14,19,23,24</sup> Furthermore, antibiotic skin testing has been found to be safe for use in the pediatric population to rule out or confirm antibiotic allergy.<sup>25</sup> In addition, PST can be performed safely in pregnant women.<sup>26</sup> However, studies indicated a lack of a standardized skin testing protocol for use in clinical practice. For instance, Lee et al<sup>27</sup> found that antibiotic skin testing protocols in Korea were variable and inconsistent and differed with regard to the type and concentrations of antibiotics, the volume injected, and the

interpretation of the results. Moreover, the protocols differed from the commonly recommended procedures in the literature.<sup>27</sup> Similarly, Abdulazeez et al<sup>28</sup> reported a lack of a standard technique for PST in the United Arab Emirates within their institution, with significant variations noted between wards. Similar findings were reported by Kavadas et al.<sup>29</sup>

In spite of the absence of standardized skin testing before treatment of patients with a fluoroquinolone antibiotic, Seitz et al<sup>22</sup> developed a protocol to treat these patients. As stated previously, the authors reported that history alone and/or skin or in vitro tests are not appropriate approaches for treating patients with fluoroquinolone hypersensitivity and that challenge tests are needed to definitively confirm or rule out fluoroquinolone hypersensitivity. This is the only study found that suggests a standardized skin testing protocol in the treatment of

patients with antibiotic allergies. **Drug-induced allergy is a serious condition and must be prevented in the ICU setting through the performance of skin tests and subsequent challenge tests.**

Some articles highlighted the cost-effectiveness of performing PST in clinical practice. For instance, Rimawi et al<sup>30</sup> reported that PST-guided antibiotic modification resulted in an estimated annual savings of \$82 000. In addition, in a retrospective study of the cost-effectiveness of conducting PST in patients with a  $\beta$ -lactam allergy who underwent PST and oral challenge,<sup>31</sup> 31 admissions required antibiotics for patients who had negative skin test and oral challenge. A  $\beta$ -lactam antibiotic was prescribed in 22 of 31 readmissions. The overall cost savings were estimated to be \$11 005 (\$297 per patient switched to a  $\beta$ -lactam antibiotic).

**Nonirritating Concentration.** In a retrospective study, 2.9% of patients who had negative results on a skin test were reported to develop a penicillin allergy.<sup>32</sup> Similarly, 2.7% of those who had a negative skin test result developed an allergy to sulfonamides. Thus, some researchers recommended orally challenging the patient with an NIC of the required antibiotic to rule out or confirm an allergy to that antibiotic. For instance, in one study, investigators tested NICs of 3 antibiotics (ciprofloxacin ~0.0067 mg/mL, clarithromycin ~0.05 mg/mL, rifampicin ~0.002 mg/mL) in 15 healthy volunteers and

indicated that these concentrations are helpful in determining allergy to these drugs.<sup>33</sup> Results from another study indicated that testing NICs of various antibiotics and providing provocative challenges on the basis of negative skin test results are beneficial in selecting appropriate antibiotic options in children.<sup>29</sup>

In a prospective study by Goldberg and Confino-Cohen,<sup>34</sup> among 137 patients who had a positive skin test result and 135 patients who had a negative skin test result, 9 (6.6%) and 5 (3.7%), respectively, developed a mild rash in response to oral challenge ( $P = .29$ ). At follow-up 2 to 6 years later, only 3 of 55 patients (5.5%) who received a full treatment course of penicillin were noted to develop a mild skin eruption. Thus, provocative challenges based on negative or positive skin testing are relatively safe and can help health care providers select an appropriate

antibiotic treatment regimen. The “gold standard” for challenge

is an oral penicillin or amoxicillin dose of up to 500 mg, to be administered if PST is negative and an immediate hypersensitivity reaction must be ruled out.<sup>6,26,34</sup>

**Challenges based on negative or positive skin testing are relatively safe and can help health care providers select an appropriate antibiotic treatment regimen.**

## Discussion

Drug-induced allergy is associated with increased morbidity, including a higher incidence of multidrug-resistant infections and a longer hospital stay. Allergic reactions include a wide variety of symptoms including acute laryngeal edema, severe bronchospasm, severe systemic reactions, and anaphylactic shock and may result in death. Findings on the validity of patient-reported penicillin allergies are inconsistent: although some authors relied on patients' self-reported history of allergy, others suggested that such self-reports of allergies are unreliable and may lead to unnecessary modification in antibiotic therapy. Those authors recommended skin testing and challenge tests to definitively confirm or rule out allergy to an antibiotic. These recommendations are supported by the finding that 80% of patients with a history of penicillin allergy subsequently receive penicillin treatment without experiencing any adverse events.

Penicillin skin testing has been found to be a safe, reliable, and effective strategy to rule out penicillin

allergy and minimize the use of non- $\beta$ -lactam antibiotics in patients who are labeled as penicillin allergic. In addition, performing PST in clinical practice has been shown to be cost-effective. Furthermore, PST has been found to be safe for children and pregnant women. However, evidence for the safety of skin testing for non- $\beta$ -lactam antibiotics in the ICU setting is limited, despite ICU patients being more prone to antibiotic use than other hospital patients.<sup>35,36</sup> Moreover, conducting skin tests in ICU patients is associated with several difficulties, such as the complexity of organ dysfunction or insufficiency experienced by these patients and the multitude of drugs that are simultaneously administered (eg, antihistamines,  $\beta$ -blockers, and epinephrine infusions).<sup>37</sup> In addition, ICU patients have several risk factors for infection with multidrug-resistant organisms, including prolonged hospital stay, mechanical ventilation, and the use of invasive devices.<sup>38,39</sup> Finally, critically ill patients may experience pharmacokinetic-pharmacodynamic challenges due to the alteration of metabolism and clearance and drug interactions.<sup>38-40</sup> All of these considerations point to the need for standardized skin testing for all antibiotics in ICU patients to help health care providers select the most appropriate antibiotics for treatment.

Oral challenges at an NIC can rule out or confirm allergy to a particular antibiotic. Conducting testing with NICs of various antibiotics and providing provocative challenges on the basis of negative skin test results are beneficial in selecting appropriate antibiotic options in children. Provocative challenges based on negative or positive skin testing are relatively safe and can help health care providers design the most appropriate antibiotic treatment regimen.

## Conclusion

Drug-induced allergy is a serious condition and must be prevented in the ICU setting through the performance of skin tests and subsequent challenge tests. Penicillin skin testing is a safe and effective strategy to rule out or confirm penicillin allergy in adults, children, pregnant women, and ICU patients. Although PST is a cost-effective and safe approach, it must be carried out by trained professionals to minimize risks to patients.

Evidence for the safety of skin testing for non- $\beta$ -lactam antibiotics in ICU settings is limited, despite the fact that ICU patients are more prone to antibiotic



use than are other hospital patients. Patients in ICUs have several risk factors for serious infection and are usually hemodynamically unstable. Use of a standardized skin testing protocol to guide selection of antibiotics for treatment of these patients has the potential to save lives as well as decrease costs. **CCN**

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