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BRIEF REPORT

Improving Antimicrobial Stewardship by Antibiotic Allergy Delabeling: Evaluation of Knowledge, Attitude, and Practices Throughout the Emerging Infections Network

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Antibiotic allergy testing (AAT) practices of Emerging Infections Network infectious disease physicians were surveyed. Although AAT was perceived to be necessary for removal of inappropriate or unnecessary allergy labels, there was limited access to any form of testing. In this study, we discuss current antibiotic allergy knowledge gaps and the development of AAT practices within antimicrobial stewardship programs, which will potentially improve antimicrobial prescribing.

Keywords. adverse drug reaction; antibiotic allergy; hypersensitivity; skin prick testing; stewardship; penicillin allergy.

Antibiotic allergy labels that reflect either immune- and/or nonimmune-mediated adverse drug reactions are prevalent in 10%–30% of hospitalized patients. Whilst often inaccurate, they are also associated with inappropriate antimicrobial prescribing, microbiological resistance, higher antimicrobial costs, and suboptimal patient outcomes [1–4]. Inappropriate labeling of drug side effects, suboptimal allergy history taking, incorrect antibiotic allergy recording in electronic medical records, and poor clinician understanding have previously been identified as contributing factors [5–7].

The Infectious Diseases Society of America (IDSA) antimicrobial stewardship guidelines highlight the burden of antibiotic allergy and propose the incorporation of antibiotic allergy assessment into stewardship progams [8]. Antibiotic allergy delabeling programs have been shown to effectively remove >90% of patient labels, and hence such programs could aid stewardship measures [9–12]. We distributed a survey to members of the Emerging Infections Network (EIN) of IDSA to ascertain current availability of antibiotic allergy services and the receptiveness for incorporating antibiotic allergy testing (AAT) strategies into stewardship programs.

METHODS

The EIN is a provider-based network of practicing adult and pediatric infectious diseases (ID) physicians from all 50 states, the District of Columbia, and Canada [13]. A 10-item survey (Appendix 1) to evaluate current practices and knowledge was developed in consultation with ID physicians, hospital pharmacists, immunologists, and key stakeholders of the EIN. The survey was piloted amongst staff of the EIN. The EIN distributed the survey and study objectives between September 15 and October 13, 2015. An opt-out option and 2 e-mail reminders at 1-week intervals were provided. Demographic information was available for each EIN respondent.

Survey responses were analyzed using Stata, version 13 (StataCorp, College Station, TX) using the χ^2 test for categorical variables and paired *t* test or Wilcoxon signed-rank tests for continuous variables. A *P* value of <.05 was deemed statistically significant.

RESULTS

Characteristics of Participants

In this study, 736 of 1545 (48%) respondents were active EIN members: 75% (558 of 736) were adult physicians, 20% (154 of 736) were pediatricians, and 3.2% (24 of 736) were both. Further baseline characteristics of respondents and nonrespondents are provided (see Supplementary Table 1).

Antibiotic Allergy Prevalence and Availability of Allergy Testing

Most repsondents estimated penicillin allergy prevalence to be between 5% and 20% of the their patients (68%, 500 of 736). Although 43% (317 of 736) of the physicians had a skin prick test (SPT) or intradermal test (IDT) available to them, only 27% (204 of 736) had SPT/IDT combined with oral challenge, which is the gold standard (Table 1). Twenty-three percent (171 of 736) of respondents did not have access to any form of testing, including oral challenge or desensitization (Table 1). Penicillin remained the most commonly used allergy-testing reagent (59%, 271 of 460) (Figure 1). Of those who did have AAT

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Table 1. Antibiotic Allergy Testing: Availability and Potential Benefits

Antibiotic Allergy Testing	Responses, n (%)
Antibiotic allergy services available (n = 736)	
Desensitization to ≥1 antibiotic	417 (57%)
Traditional testing (skin prick, intradermal)	316 (43%)
Oral challenge	297 (40%)
None of the above	171 (23%)
Not sure	55 (7%)
Allergy phenotypes were allergy testing preferred (n = 442)	
Immediate/accelerated reactions	294 (67%)
Mild delayed reactions	182 (41%)
Severe delayed reactions	124 (28%)
Any/all reactions	77 (17%)
None	5 (1%)
Potential benefits of antibiotic allergy "label" removal (n = 446)	
Better antibiotic selection	422 (95%)
Improved antibiotic appropriateness	411 (92%)
Improved antibiotic stewardship services	365 (82%)
Safer administration of antibiotics	332 (74%)
Unclear if any measurable improvement	10 (2%)
None	2 (0.4%)
Other	6 (1%)

Note: Respondents were able to select more than 1 response.

services available, 40% (182 of 460) were unaware of the specific nature of available testing.

AAT was most frequently performed in outpatient facilities (63%, 274 of 432). However, a significant proportion of respondents also offered testing either in inpatient units (47%, 202 of 432) and/or intensive care units (50%, 218 of 432). Only 3% (12 of 460) of respondents performed SPT/IDT themselves, and 8% (39 of 460) performed oral challenge. Although years of experience did not impact upon a respondent's likelihood of self-performing SPT/IDT ($P = .47$), those with >15 years clinical experience were more likely to perform oral challenges (8% [27 of 361] vs 3% [12 of 375]; $P = .01$).

Extended β-lactam testing that involved more than just penicillins was less infrequently used (Figure 1), and it was more likely to be offered by federal institutions (19%, 6 of 31) than private practice (4%, 7 of 183) ($P = .01$). Skin prick test/IDT and oral challenge for non-β-lactams was available to 13% (60 of 460) and 30% (141 of 460) of respondents, respectively.

Perceived Value of Allergy Testing

Most respondents believed that it was worthwhile to refer patients for AAT (93%, 410 of 442), and they believed that testing would serve to remove the antibiotic allergy label (78%, 336 of 432). Respondents with <15 year's experience were more likely than those with ≥15 year's experience to believe in the effectiveness of antibiotic testing to remove the antibiotic allergy label (82% [198 of 241] vs 63% [138 of 219]; $P = .0001$). The presence of an immediate/accelerated antibiotic allergy would prompt antibiotic allergy testing by 67% of respondents (294 of 442) (Table 1), and this was not affected by experience (<15 or ≥15 years; $P = .23$).

Knowledge and Current Practices Regarding Management of Antibiotic Allergies

In patients with a remote history of penicillin allergy and where penicillin is the preferred therapy (scenario 1), respondents indicated that in their practice, the single preferred treatment strategy for acute management would be as follows: (1) point-of-care testing (40%, 177 of 442); (2) use of an alternative non-β-lactam antibiotic, even if inferior (13%, 57 of 442); (3) desensitization with maintenance of penicillin allergy label (8%, 37 of 442); or (4) desensitization then allergy clinic referral for penicillin allergy testing (7%, 30 of 442). For a patient with a history of penicillin anaphylaxis within the last 6 months (scenario 2), respondents

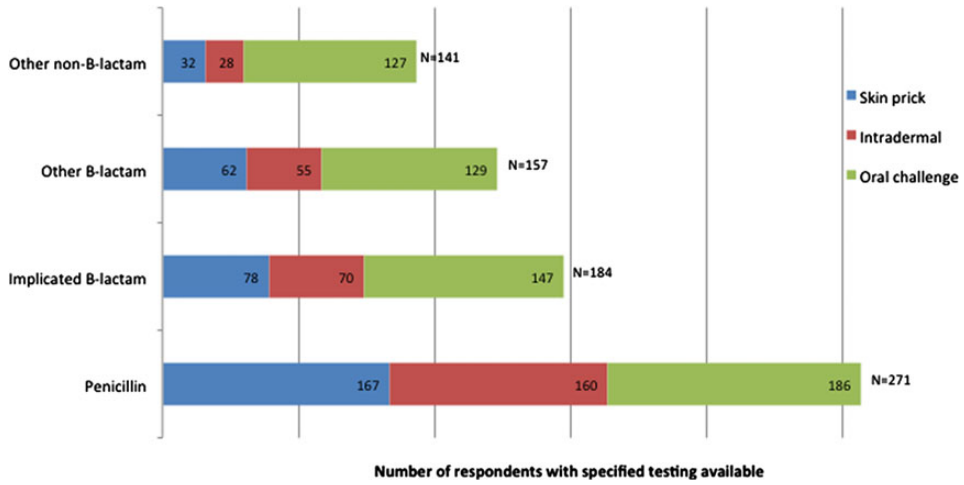

Figure 1. Antibiotic allergy testing procedures available to respondents (n = 460). (Note: 182 of 460 (40%) selected "do not know the specifics of available testing". 278 of 460 (60%) selected at least one of the options available.)

favored using an alternative non-β-lactam antibiotic, even if inferior (51%, 222 of 439), or desensitization with maintenance of penicillin allergy label (28%, 121 of 439). Delabeling approaches such as desensitization then allergy clinic referral for penicillin allergy testing (8%, 36 of 439), point-of-care testing (5%, 22 of 439), and other strategies (6%, 26 of 439) were infrequently used. Experience (<15 or ≥15 years) did not impact upon respondent approaches to scenario 1 ($P = .16$) or scenario 2 ($P = .46$).

Evaluation of Models of Care Including AAT

Most physicians (62%, 277 of 446) thought that antibiotic allergy delabeling would improve clinical practice by enhancing the following: (1) antibiotic appropriateness, (2) safer administration of antimicrobials, and (3) improved antimicrobial stewardship (Table 1). Sixty-eight percent (305 of 449) of respondents agreed that AAT should be incorporated into antimicrobial stewardship programs, and incorporation of AAT into antimicrobial stewardship programs received greater support from those with <15 years' versus those with ≥15 years experience (72% [173 of 241] vs 60% [132 of 219]; $P = .01$). Employment type (federal, military, university, hospital/clinic, or private practice) did not impact upon respondent desire to incorporate AAT into antimicrobial stewardship programs ($P = .3$).

DISCUSSION

Contemporary studies suggest that both outpatient and inpatient AAT programs comprising combinations of SPT/IDT and oral challenge are both cost saving and effective at delabeling patients of antibiotic allergy [1, 14, 15]. Most antibiotic allergy "labels" are inaccurate, because almost 90% of patients with a penicillin allergy history are able tolerate a β-lactam after formal allergy testing [9]. In our survey, antibiotic allergy services were perceived as desirable, particularly in their potential capacity to aid antimicrobial stewardship. However, a minority (43%) of respondents had testing available. The relative inexperience of ID physicians with AAT services and their confidence in these services are juxtaposed against a high perceived burden of antibiotic allergy labels and knowledge gaps centered around antibiotic safety in those with penicillin allergy histories. To our surprise, we found that the overall experience of the ID physician respondents seemed to be negatively correlated with perceived utility and effectiveness of AAT. This finding supports previous studies that illustrated significant inconsistencies in the availability of specialized and standardized AAT services over time. Furthermore, a recent survey of practices amongst Allergy and Immunology specialists in the United States also supports this inconsistency [16].

Although testing may be limited by consistent access to specialty clinics and services [7], simple measures such as direct oral challenge in very low-risk patients and desensitization by published protocols should be available to all ID physicians [17, 18]. Key knowledge gaps were identified via clinicians' responses to common clinical scenarios, irrespective of experience, that could negatively impact on the ability to successfully manage antibiotic allergy. Very few respondents were willing to use, or had access to, point-of-care AAT or follow-up delabeling strategies in patients with a history of recent or remote immediate hypersensitivity, and these respondents also preferred to use inferior antibiotic therapies. Evidence supports <1% cross-reactivity among penicillin, third-generation cephalosporins, and carbapenems [15] and predictable cross-reactivity dependent on β-lactam side chains [15, 19]. Although not addressed in this survey, applying this evidence into clinical practice may help effect change in these common clinicial scenarios [18]. More encouragingly, Blumenthal et al [6] demonstrated that clinician practices could be altered with decision support and a guided education program.

More than 80% of respondents, spanning all areas of clinical practice, believed that AAT would aid antibiotic selection, antibiotic appropriateness, and antimicrobial stewardship. Recent studies have highlighted increased use of restricted antibiotics and inappropriate prescriptions in those with antibiotic allergy labels [2]. The engagement of hospital pharmacists is essential; programs using direct allergy referrals from pharmacy departments have aided delabeling initiatives [12, 20]. A multidisciplinary model involving allergists, immunologists, ID physicians, and pharmacists is most likely to engage clinicians and deliver an effective service [21]. Strategies to manage antibiotic allergy and AAT could be incorporated into existing antimicrobial stewardship programs, even in areas of low antimicrobial resistance [22, 23].

This study does have limitations. Although key stakeholders were surveyed and targeted toward clinicians of teaching hospitals, other members of broader antimicrobial stewardship programs were not. Furthermore, immunologists and allergists were not surveyed, and they form a key role in the provision of antibiotic allergy practices [16]. As with all voluntary surveys, there is a potential for selection bias because those interested in AAT may be more likely to respond. In assessing knowledge gaps, respondents were questioned about their own approaches to clinical antibiotic allergy scenarios, which may in part be impacted by the absence of allergy services. Despite these limitations, the majority of respondents (68%) support the call for AAT to be incorporated into antimicrobial stewardship programs [21, 24].

CONCLUSIONS

These findings demonstrate an urgent need to address both the lack of availability of AAT services and the educational gaps surrounding antibiotic use in labeled patients. Incorporation of allergy teaching into ID training programs and undergraduate medical teaching and the application of clinical guidelines for management of remote allergies are likely to have significant impacts on prescribing in those with antibiotic allergy labels. It

is essential to ensure that allergy labels in the electronic medical record reflect the true nature of the adverse drug reactions, if any attempt at addressing allergy labels is to be successful. To support the feasibility of access to AAT, delabeling services, and incorporation of these into antimicrobial stewardship programs, greater collaboration is needed between allergy service providers and ID physicians as well as between pharmacists who can further contribute to and direct the antibiotic delabeling and stewardship cause. Reorganization of current healthcare services and physician training may be required to foster this collaboration.

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Supplementary Data

Supplementary material is available online at *Open Forum Infectious Diseases online* (http://OpenForumInfectiousDiseases.oxfordjournals.org/).

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