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ORIGINAL ARTICLE

Penicillin allergy SHACK: Survey of hospital and community knowledge

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Aim: Penicillin allergy accounts for the majority of all reported adverse drug reactions in adults and children. Foregoing first-line antibiotic therapy due to penicillin allergy label is associated with an increased prevalence of infections by resistant organisms and longer hospitalisation. Clinician awareness of allergy assessment, referral indications, management of allergy and anaphylaxis is therefore vital but globally lacking. We aim to assess the knowledge of penicillin allergy, assessment and management in Western Australian health professionals.

Methods: An anonymous survey was distributed to pharmacists, nurses and physicians within Western Australian paediatric and adult Hospitals, Community and General Practice.

Results: In total, 487/611 were completed and included in the statistical analysis. Only 62% (301/487) of respondents routinely assessed for patient medication allergies. Of those who assessed allergy, 9% (28/301) of respondents met the Australian standards for allergy assessment. Only 22% (106/487) of participants correctly cited all indications for management with adrenaline in anaphylaxis to antibiotics and 67% (197/292) of physicians rarely or never referred to an allergy service. Paediatric clinicians had an increased understanding of allergy assessment and anaphylaxis management. Recent penicillin allergy education within a 5-year period led to significant improvements in allergy knowledge.

Conclusion: Overall, knowledge, assessment and management of penicillin allergies among practitioners in Western Australia are currently inadequate in adults and paediatric clinicians to provide safe and effective clinical care. The implementation of a targeted education program for WA health professionals is urgently required and is expected to improve clinician knowledge and aid standardised penicillin assessment (de-labelling) practices.

Key words: allergy; anaphylaxis; antibiotics; education; penicillins.

What is already known on this topic

1 Up to 10% of paediatric and 18% of adult Western Australian inpatients report an antibiotic allergy; however, 90% are not truly allergic.

What this paper adds

1 Knowledge, assessment and management of penicillin allergies among practitioners in Western Australia are currently inadequate in adults and paediatric clinicians to provide safe and effective clinical care.
2 Significantly greater clinical knowledge was demonstrated if targeted education was received within the previous 5 years.

A steady increase of antibiotic prescriptions has been noticed globally and internationally penicillin is used as an effective first-line antibiotic for many adult and paediatric conditions.[1] However, practitioners are frequently and increasingly confronted with patients presenting with a history of a self-reported or parent-reported penicillin allergy. Up to 10% of children and 18% of adult inpatients have an antibiotic allergy label, of which 71% of adults and 79% of children's antibiotic allergies were due to penicillin in Western Australian hospitals.[2–4] This is far in excess of the prevalence of true (confirmed) penicillin allergy. Anaphylaxis is a life-threatening condition requiring immediate resuscitation; fortunately, it is reported in less than 5 per 10 000 cases of penicillin therapy.[5]

Current prescribing practices in response to penicillin allergy drive antimicrobial resistance, leading to significantly higher rates of difficult to treat *Clostridium difficile*, methicillin-resistant

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Staphylococcus aureus and vancomycin-resistant enterococcus infections.[6] Furthermore, second-line antibiotics are often more costly and prove less efficacious, for example, patients' reporting of an allergy to a penicillin is associated with a 50% increase in surgical site infections.[6,7]

In contrast to the high rates of self-reported and parent-reported antibiotic allergy label, following formal assessment and allergy testing, 90% of these patients are found to be not allergic.[8] In penicillin-allergic paediatric populations, true IgE (type 1) hypersensitivity drug allergy was present in just over 1% of children.[9] The adverse outcomes may therefore be avoided with appropriate de-labelling practices. De-labelling penicillin allergies have also demonstrated a significant reduction in length of hospital stay, emergency and outpatient department visits in adults and paediatric care.[6,10,11]

Careful clinical acumen is required to determine the appropriate immunological investigations and antibiotic selection in light of an uncertain/unconfirmed or true/confirmed drug hypersensitivity reactions. A 2016 survey of Australian and New Zealand physicians (predominantly immunologists and infectious disease specialists) and pharmacists demonstrated a lack of awareness of antibiotic allergy testing and penicillin cross reactivity.[12] This research did not specify the inclusion of paediatric health-care professionals. A similar survey of 276 doctors, nurse practitioners and pharmacists conducted in two adult inpatient facilities in North America in 2017 indicated that nearly half of all surveyed health practitioners were unfamiliar with penicillin cross-reactivity, though pharmacists demonstrated superior knowledge. They further highlighted a poor understanding of the indications for penicillin skin-prick testing, desensitisation therapy and immunology consultation.[13]

The reasons sighted for lack of understanding of antibiotic allergies are vastly unexplored in the literature. This study aimed to survey the understanding of penicillin allergies in rural and metropolitan pharmacists, nurses and physicians in all stages of training in community and hospital setting, while also determining if clinician demographics and education factors resulted in superior clinical knowledge. To our understanding, we are the first survey to perform this research in adults and paediatric populations while also assessing the specific impact of rurality and health-care setting on clinician responses.

Materials and Methods

Ethics approval was received by the Child and Adolescent Health Service Ethics Committee (HREC Reference number 2015014EP) and approval to distribute the survey was gained from each health service.

Study design

The research was conducted throughout Western Australia, a state comprising a population of 2.6 million, of which approximately 26% reside in regional/rural areas and 2% in remote communities.[14] Compared to Australian metropolitan areas, rural patients are 2.6 times less likely to have a nearby general practitioner and 5 times less likely to have access to nearby specialty services. Nearby service availability halved again when comparing rural and remote statistics.[15]

Governance approval was received to distribute the anonymous survey by email link to doctors, nurses and pharmacists throughout three metropolitan Western Australian Health Services, the Child and Adolescent Health Service, the Western Australian Country Health Service and their associated community practices. The survey was distributed to service directors and unit managers by global email. It was left to the discretion of service directors and managers to distribute the survey email amongst their staff. As health practitioners are members of multiple emailing groups and not all service directors may have distributed to survey, we were unable to ascertain an overall response rate. All responses were anonymous and did not detail the practitioner's employing institution.

Paediatric and adult care were included. Incomplete surveys were excluded from analysis, no further exclusion criteria were imposed. Responses were collected over a 6-month period from November 2018 to April 2019.

Our survey was based on a North American survey by Staicu *et al.* and adapted for the Australian setting (Appendix S1).[13] It was revised in collaboration between adult and paediatric immunologists, allergists and anaesthetists and refined in discussion with key pharmacists and nursing stakeholders. Gold standard practice was defined by the Australasian Society of Clinical Immunology and Allergy (ASCIA) Guidelines.[16] The survey was developed using SurveyMonkey (Palo Alto, CA) and distributed by email.

The 25 question survey ascertained respondent demographics and critically appraised three key domains; (i) allergy education received, (ii) knowledge of penicillin allergies and (iii) penicillin allergy assessment, referral and management practices.

Statistical analyses

The response variables were binary (yes or no). Consequently, a separate logistic regression model was fitted to each response variable against medical professional characteristics, location and patient characteristics. Statistical significance was taken at 0.05, and odds ratios (ORs) and their 95% confidence intervals (CIs) are reported. All statistical analysis was performed using the R statistical environment.[17]

Results

A total of 487 respondents completed the survey fully, of which 60% were doctors (n = 292/487), 31% were nurses (n = 153/487) and 9% were pharmacists (n = 42/487). For demographics, see Tables 1 and 2.

Education

In total, 79% of participants (n = 386/487) report receiving education on penicillin allergies, of which 68% (n = 261/386) received the education within the past 5 years. Health professionals working within a hospital were 2.9 times more likely to have received education on penicillin allergies compared to health professionals within the community (P = 0.01, CI = (1.39, 6.27)). Workplace penicillin allergy education was reported two times as often in rural compared to metropolitan workplaces (P = 0.04, CI = (1.12, 3.87)) and three times more likely in

Table 1 Demographic data

		Occupation		
		Doctor	Pharmacist	Nurse
Patient population	Adult	105	11	29
	Paediatric	80	15	61
	Adult and paediatric	107	16	63
Rurality	Metropolitan	235	27	71
	Rural	54	13	64
	Remote	3	2	18
Health-care service	Primary	13	3	41
	Secondary	67	12	30
	Tertiary	212	27	82
Speciality	Immunology	4	0	2
	Internal Med	73	2	26
	Peri/surgical	33	0	44
	Critical care	109	0	53
	GP/community	39	2	13
	Other	34	38	15
Years of clinical experience	<1 year	18	1	2
	1–5 years	122	7	29
	5–10 years	58	12	19
	>10 years	94	22	103

Table 2 Demographic data according to the clinicians' patient population

		Patient population		
		Adult and paediatric	Adult	Paediatric
Rurality	Metropolitan	77	103	153
	Rural	90	38	3
	Remote	19	4	0
Health-care service	Primary	30	16	11
	Secondary	71	30	8
	Tertiary	85	99	137
Years of clinical experience	< 1 year	4	16	1
	1–5 years	37	79	41
	5–10 years	29	20	40
	>10 years	115	30	74

paediatric clinicians ($P \leq 0.001$, CI = (1.56–5.56)). Online education was received more often for those in rural (OR = 2.5, CI = (1.23, 5.08)) and remote (OR = 5.7, CI = (1.30, 22.31)) compared with metropolitan environments ($P = 0.01$).

Penicillin allergy knowledge

About 26% ($n = 129/487$) of respondents were aware that overall cross-reactivity between cephalosporin and penicillin is less than 5%, with the majority citing 5–10% cross-reactivity. Clinicians who worked in rural and remote areas were 1.7 times as likely to understand the true penicillin and cephalosporin cross-reactivity ($P = 0.02$, CI = (1.09, 2.78)). Time from penicillin allergy education was negatively correlated with likelihood of knowing the correct cross-reactivity rate of penicillins and cephalosporins. Respondents receiving education within the past year were correct 50% more often than if education was received in the past 5 years ($P = 0.01$, OR = 0.49, CI = (0.28, 0.84)). If education was received more than 5 years ago, the rate of correct answers was further reduced ($P < 0.001$, OR = 0.30, CI = (0.15, 0.57)).

About 36% ($n = 175/487$) of respondents correctly identified that no cross-reactivity exists between macrolides and penicillin. Further, 43% ($n = 210/487$) of health-care professionals understood that care should be taken administering carbapenems to a patient with a true penicillin allergy. The majority of respondents answered the latter two questions with 'I don't know'. Pharmacists' knowledge of antibiotic cross-reactivity far exceeded that of doctors' and nurses' ($P < 0.001$) (Fig. 1).

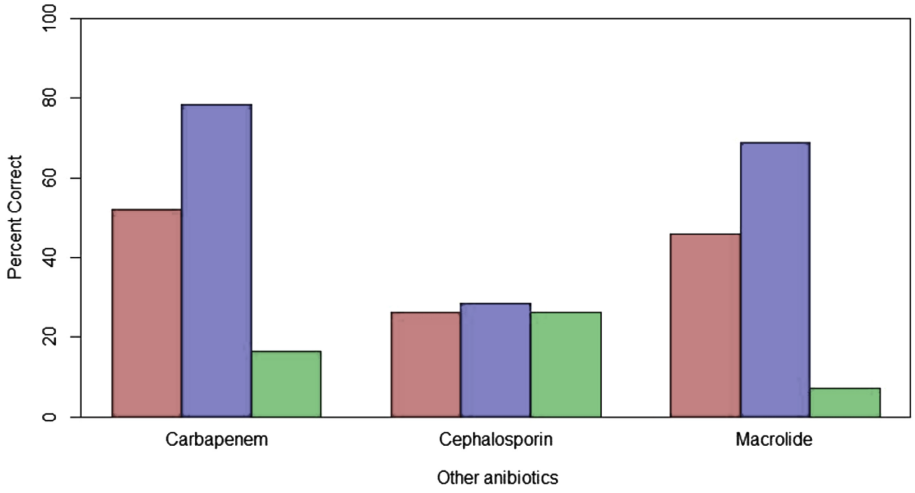

Fig. 1 Percent of clinicians who correctly answered the cross-reactivity between penicillin and alternate antibiotic classes according to profession. (▭), Doctor, (▭), pharmacist and (▭), nurse.

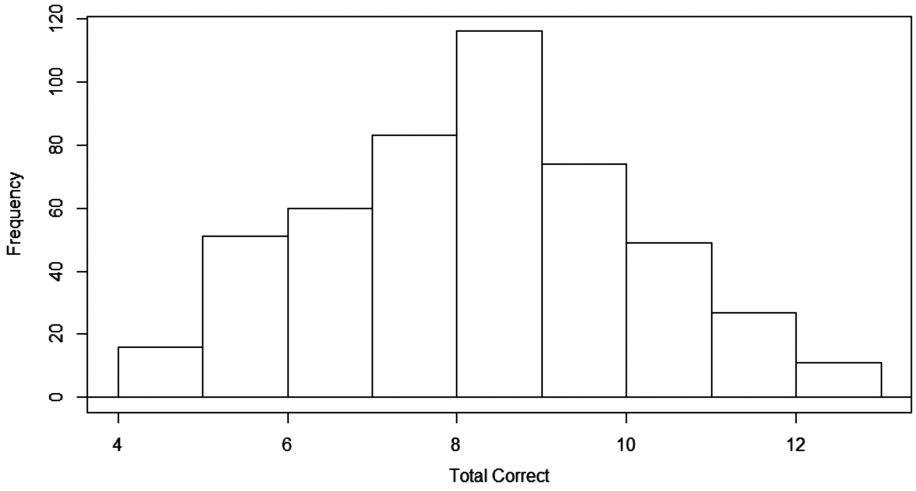

Fig. 2 Frequency of the total correct clinician responses for whether i.m. adrenaline was, or was not indicated for differing clinical signs and symptoms in the setting of penicillin allergy.

Only 23% (112/487) of health-care workers were aware that penicillin allergies can resolve (or wane) over time. Clinicians who had received education within the past 5 years (54%, 261/487) were significantly more likely to recall that 90% of patients with a self-reported penicillin allergy would tolerate penicillin antibiotics ($P = 0.01$). However, in total, only 36% ($n = 173/487$) answered this question correctly.

About 22% ($n = 109/487$) of health-care workers knew that intravenous or oral challenge was considered to be the gold standard for assessing an antibiotic allergy with paediatric clinicians being significantly more likely to give the correct answer than their adult counterparts ($P = 0.008$). Health-care workers who gave the correct answer were four times more likely to have received penicillin allergy education ($P = 0.027$).

Allergy assessment

Of the respondents, 62% (301/487) reported 'always' assessing antibiotic allergy in their patients, while 23% ($n = 116/487$) reported 'rarely' or 'never'. Rural health-care workers were more likely to assess allergy compared to their metropolitan counterparts ($P = 0.04$).

Of those who assessed allergy, only 28 respondents met the Australian gold standards for allergy assessment.[15] Respondents who received penicillin allergy education within the last 5 years were consistently more likely to comply to allergy assessment standards compared to clinicians without allergy education, or where education was received more than 5 years ago ($P = 0.023$).

Allergy management

Clinicians were asked whether the administration of i.m. (intramuscular) adrenaline was indicated for different signs and symptoms in the setting of a presumed penicillin allergy; in six scenarios i.m. adrenaline was indicated, while in seven scenarios, adrenaline was not.[15] On average, 7 of the 13 questions were answered correctly by doctors, nurses and pharmacists (Fig. 2). The analysis of doctors alone revealed an average of nine correct answers. Only 2% ($n = 11/487$) of all respondents answered all 13 questions correctly. Immunologists ($P < 0.001$) and health professionals working with paediatric patients were significantly more likely to answer correctly ($P = 0.001$).

Referral pathway

The likelihood of a clinician referring a patient with a self-reported antibiotic allergy to an allergy service was investigated amongst doctors. About 67% ($n = 197/292$) of doctors rarely or never referred to an allergy service. Doctors with more than 10 years of experience were significantly more likely to 'never' refer to an allergy service ($P = 0.018$). Clinicians working solely with paediatric patients were 11 times more likely to 'always' or 'usually' refer to an allergy service compared to doctors who work solely with adult patients ($P = 0.01$). There was no difference in the likelihood of doctors referring for allergy testing in rural, remote or metropolitan health-care settings and recent allergy education did not influence the result.

Discussion

This research sought to understand the gaps and the factors affecting current knowledge and clinical approaches to self-reported penicillin allergy. Survey results have highlighted the clear deficiencies in understanding of penicillin cross-reactivity, allergy assessment, testing and anaphylaxis management across Western Australia. Understanding the demographic and educational factors that promote optimal care is critical in developing an educational approach.

Our results align with a survey of clinicians in North America, in which more than 50% of clinicians could not accurately recall the cross-reactivity between penicillin with cephalosporins, macrolides and carbapenems.[13] Similar trends were observed in an Australian and New Zealand study.[12] Our survey cohort extended not only to subspecialty physicians and pharmacists, but to all doctors and nurses irrespective of their patient cohort, area of specialty and rurality. The trend of an inadequate understanding of penicillin cross-reactivity in our survey remained true. Improving Australian clinicians' understanding of penicillin cross-reactivity is vital in ensuring safe second-line prescribing in the case of true allergy, reducing morbidity and mortality associated with severe allergy and anaphylaxis, while minimising antimicrobial resistance.

In our study, a clinicians' understanding of antibiotic cross-reactivity was improved if education was received within the past 5 years. This is unsurprising given historic research overestimated the likelihood of antibiotic cross reactivity. It was previously suggested that a 10–25% penicillin cephalosporin cross-reactivity existed, with better pharmaceutical purifications process, it is now estimated to in fact be less than 5%.[18] Recency of education improved all facets of knowledge underpinning penicillin allergy and assessment. This finding is supported by Blumenthal *et al.*, who demonstrated a significant improvement in understanding following an inpatient clinician drug allergy educational initiative.[19]

The odds of the 154 clinicians in rural/remote areas receiving education on penicillin allergy was twice that of metropolitan clinicians, and they were five times more likely to seek online educational resources. Given the correlation shown between education recency and clinical knowledge, this finding may explain why knowledge and allergy assessment are demonstrably superior in rural and remote respondents. Working in a metropolitan area where more specialists and tertiary services are available does not by itself guarantee knowledge is up to date. Hence, this result highlights the urgency to provide, promote and monitor educational resources on penicillin allergies in health practitioners working in the metropolitan area particularly. An emphasis on the development of online resources to ensure ongoing high rates of equitable education access should be considered in the development of penicillin allergy education resources for rural clinicians.

A clinician's years of experience was not associated with greater understanding, assessment or management of penicillin allergies. In fact, physicians with greater than 10 years' experience were less likely to refer to allergy services. This result is echoed by Trubiano *et al.*, who also demonstrated that increasing years of clinical experience did not correlate with superior understanding of penicillin cross-reactivity or allergy testing.[12] Cited reasons for reduced referrals with increasing clinician experience have included an ability to manage more complex clinical cases and a reduced significance placed on a patient's preference for referral.[20] The authors suggest additional factors in our surveyed cohort may include (i) junior clinicians making the referral on behalf of senior clinicians, (ii) a greater utilisation of in-house consultations/s-opinions or clinical guidelines by experienced clinicians, forgoing formal allergy testing. Our research supports the universal argument of continuing professional education. Updated allergy education should be accessible to all clinicians, irrespective of their years of experience.

In our survey, paediatric health-care workers demonstrated statistically significant superior knowledge in the gold standard assessment of allergy and the indications for adrenaline. Furthermore, they were significantly more likely to refer to an allergy service compared to adult clinicians. Paediatric clinicians were three times as likely to have received allergy education in the workplace compared to adult clinicians. As shown in Table 2, 88% (137/156) of paediatric-only clinicians work in a tertiary hospital setting. This finding may reflect the bias of the tertiary paediatric hospital toward allergy education to clinicians given its recent focus on immunology research.

Substantial workplace education and superior clinical knowledge in this paediatric workforce are of particular advantage in driving de-labelling practice. Lucas *et al.* found an oral challenge could safely de-label up to 52% of their Western Australian inpatient paediatric cohort with a self-reported penicillin allergy.[11] Clinicians working with this patient cohort therefore have the capacity to significantly reduce the total allergy-years cumulatively spent in the paediatric and adult health-care system.

The indications for the administration of adrenaline according to the international definition of anaphylaxis were explored.[15] As demonstrated in Figure 2, knowledge was poor, with only 2% of respondents answering all questions correctly. Failure to administer, or inappropriate administration of adrenaline, may be associated with significant morbidity and mortality.[21] Hence, this is a key knowledge gap that urgently requires clinical improvement. Recency of penicillin allergy education did not increase the likelihood of superior management of anaphylaxis. The authors suggest this may be due to the broad nature of the survey question and its interpretation 'have you received education on penicillin allergy within the last five years?'. We did not specifically assess whether education had been received on the management of anaphylaxis. Targeted education on anaphylaxis management may yield promising results. Prompt action should be taken to address this concerning statistic.

Potential limitations of our study include survey fatigue, possibly resulting in substandard answers from respondents. This may have led to an underestimation of clinician knowledge. Additionally, health-care professionals with interest in allergy and antibiotics may have been more likely to respond to the survey creating a selection bias. Therefore, the true rate of knowledge within the wider health-care population might be inferior to that demonstrated by this study, further increasing the significance of our conclusions. And finally, as described in our research methods, we were unable to determine the number of clinicians who received this survey and therefore we cannot determine a response rate to the survey.

The authors acknowledge that a lack of education is only one of many barriers to optimal antibiotic prescribing and de-labelling practices. Currently, in Western Australia, there is an absence of a statewide formal allergy service. Awareness and access to a timely allergy testing service with a formal referral pathway have been shown to remove penicillin allergy labels, increasing the use of first-line narrow-spectrum antibiotics.[10,22–24]

Conclusion

In summary, we have demonstrated the presence of a significant knowledge deficit in the assessment and management of penicillin allergy in adults and for the first time, paediatric clinical care within Australia. A link between recent education and improved clinical understanding has been demonstrated. Greater investment into the implementation of a targeted easily accessible education program for health professionals is expected to aid antibiotic allergy de-labelling practice, thus providing safer care to the individual and encouraging responsible prescribing practices by clinicians. Equity in education accessibility to hospital, community and rural health-care workers irrespective of years of clinical experience is emphasised.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1: Supporting Information.