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Diagnostic procedures & practices in drug allergy/hypersensitivity: a survey of 13 Asian countries

Min-Moon Tang [1], Jie Shen Fok [2], Bernard Yu-Hor Thong [3,*], James Yun [4], Philip Hei Li [5], Hye-Ryun Kang [6], Francis Thien [7], Masao Yamaguchi [8], Michaela Lucas [9], Yoon-Seok Chang [10], Byung-Keun Kim [11], Mizuho Nagao [12], Iris Rengganis [13], Yi-Giien Tsai [14], Wen-Hung Chung [15], Ticha Rerkpattanapipat [16], Wasu Kamchaisatian [17], Ting Fan Leung [18], Joo-Yoon Ho [19], Luo Zhang [20], Amir Hamzah Abdul Latiff [21], Takao Fujisawa [22], Mariana C Castells [23], Pascal Demoly [24], Jiu Yao Wang [25], and Ruby Pawankar [26]

[1]Hospital Kuala Lumpur, Kuala Lumpur, Malaysia
[2]Department of Respiratory Medicine, Box Hill Hospital, Eastern Health, Melbourne, Victoria, Australia; Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria, Melbourne, Australia
[3]Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, Singapore
[4]Faculty of Medicine and Health, The University of Sydney, Sydney, Australia; Division of Medicine, Nepean Hospital, Sydney, Australia
[5]Division of Rheumatology and Clinical Immunology, Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong
[6]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, Korea; Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea; Drug Safety Center, Seoul National University Hospital, Seoul, Korea
[7]Eastern Health, Melbourne; Monash University, Melbourne, Australia
[8]Division of Respiratory Medicine and Allergology, Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan
[9]Department of Immunology, Pathwest and Sir Charles Gairdner Hospital, Perth, Australia; Medical School, University of Western Australia, Perth, Australia
[10]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea
[11]Department of Internal Medicine, Korea University Medical Center Anam Hospital, Seoul, Korea
[12]Allergy Center of Mie National Hospital, Tsu, Japan
[13]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[14]School of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
[15]Department of Dermatology, Drug Hypersensitivity Clinical and Research Center, Chang Gung Memorial Hospital, Keelung and Linkou Branches, College of Medicine, Chang Gung University, Taipei, Taiwan
[16]Allergy, Immunology and Rheumatology Division, Department of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
[17]Pediatric Allergy and Immunology Division, Samitivej Children's Hospital, Bangkok, Thailand
[18]Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong
[19]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea
[20]Department of Otolaryngology Head and Neck Surgery, Beijing TongRen Hospital, Capital Medical University, Beijing, China; Beijing Key Laboratory of Nasal Diseases, Beijing Institute of Otolaryngology, Beijing, China
[21]Allergy & Immunology Centre, Pantai Hospital, Kuala Lumpur, Malaysia
[22]Allergy Center of Mie National Hospital, Tsu, Japan
[23]Division of Rheumatology, Immunology, and Allergy, Department of Medicine, Mastocytosis Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[24]Division of Allergy, Department of Pulmonology, Hôpital Arnaud de Villeneuve, University Hospital of Montpellier, Montpellier, France; UPMC Univ Paris 06, UMRS 1136, Equipe - EPAR - IPLESP, Sorbonne Universités, Paris, France
[25]Department of Pediatrics, National Cheng Kung University Hospital, Tainan, Taiwan
[26]Department of Pediatrics, Nippon Medical School, Tokyo, Japan

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***Correspondence to**
Bernard Yu-Hor Thong
Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308344.
Tel: +65-6357-7822
Fax: +65-6357-2686
E-mail: bernard_thong@ttsh.com.sg

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ORCID iDs
Min-Moon Tang
https://orcid.org/0000-0001-7760-3238
Jie Shen Fok
https://orcid.org/0000-0002-3450-0877
Bernard Yu-Hor Thong
https://orcid.org/0000-0002-6338-8482
James Yun
https://orcid.org/0000-0002-3482-5663
Philip Hei Li
https://orcid.org/0000-0002-9155-9162
Hye-Ryun Kang
https://orcid.org/0000-0002-2317-4201
Francis Thien
https://orcid.org/0000-0003-0925-6566
Masao Yamaguchi
https://orcid.org/0000-0001-6167-0591

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Michaela Lucas
https://orcid.org/0000-0001-8881-9990
Yoon-Seok Chang
https://orcid.org/0000-0003-3157-0447
Byung-Keun Kim
https://orcid.org/0000-0001-5147-6306
Mizuho Nagao
https://orcid.org/0000-0003-3557-8761
Iris Rengganis
https://orcid.org/0000-0001-8748-8544
Yi-Giien Tsai
https://orcid.org/0000-0002-6744-1682
Wen-Hung Chung
https://orcid.org/0000-0003-1681-0959
Ticha Rerkpattanapipat
https://orcid.org/0000-0002-6630-2795
Wasu Kamchaisatian
https://orcid.org/0000-0003-0839-7682
Ting Fan Leung
https://orcid.org/0000-0002-6469-1926
Joo-Yoon Ho
https://orcid.org/0000-0002-4645-4863
Luo Zhang
https://orcid.org/0000-0002-0910-9884
Amir Hamzah Abdul Latiff
https://orcid.org/0000-0002-6304-0494
Takao Fujisawa
https://orcid.org/0000-0002-9196-9436
Mariana C Castells
https://orcid.org/0000-0001-6451-0163
Pascal Demoly
https://orcid.org/0000-0001-7827-7964
Jiu Yao Wang
https://orcid.org/0000-0003-4540-9822
Ruby Pawankar
https://orcid.org/0000-0002-3091-7237

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Author Contributions
Conceptualization: Ruby Pawankar, Bernard Y Thong. Data curation: Min Moon Tang, Jie-Shen Fok, Philip Li, James Yun, Bernard Y Thong. Formal analysis: Min Moon Tang, Jie-Shen Fok, Philip Li, James Yun, Bernard Y Thon. Methodology: Ruby Pawankar, Bernard Y Thong. Project administration: Ruby Pawankar, Bernard Y Thong. Writing - original draft: Min Moon Tang, Jie-Shen Fok, Bernard Y Thong. Writing - review & editing: Min Moon Tang, Jie-Shen Fok, Philip Li, James Yun, Hye-Ryun Kang, Francis Thien, Bernard Y Thong.

ABSTRACT

Background: The issues and challenges in the diagnosis of drug allergy/hypersensitivity among children and adults in Asia are likely to be different from non-Asian countries.
Objective: To study the diagnostic modalities used in the evaluation and management of drug allergy/drug hypersensitivity reactions (DHRs) among member societies of the Asia Pacific Association of Allergy, Asthma and Clinical Immunology (APAAACI).
Methods: A questionnaire comprising 41 questions was circulated electronically to member societies and individual members of APAAACI between January 23, 2020 and March 6, 2020.
Results: Twenty-six respondents from 15 member societies and 1 individual member responded. European DHR guidelines were most commonly used. Skin prick and intradermal testing was used by 100%, with only 60% having access to commercial penicillin skin test reagents. *In vitro*-specific IgE tests were used by 75%, and basophil activation test by 56.3% for immediate DHR. Patch tests were used by 75% in contrast to lymphocyte transformation tests by 25% for nonimmediate DHR. Drug provocation tests were used by 68.8%, the most common indication being to exclude hypersensitivity where history/symptoms were not suggestive of drug hypersensitivity/allergy (93.3%). Human leukocyte antigen (HLA) genotype testing was mandatory among 25% respondents before new carbamazepine prescriptions, and 8.3% for allopurinol prescriptions.
Conclusions: There was increased use of skin testing for iodinated contrast media hypersensitivity and patch testing for nonimmediate DHR. HLA genotype testing prior to new carbamazepine, allopurinol and abacavir prescriptions remain variable despite strong associations for severe cutaneous adverse reactions with Asian ethnicity. Results of this survey form a useful framework for developing educational and training needs and for improving access to drug allergy diagnostic and treatment modalities across APAAACI member societies.

Keywords: Anaphylaxis; Contrast media; Penicillins; Pharmacogenetics, Skin tests

INTRODUCTION

Adverse drug reactions account for 1.3% to 6.2% of hospital admissions [1, 2]. The prevalence of physician-reported drug allergies is 7.1% based on population-wide studies in Hong Kong [3]. Up to 14% of hospitalised patients have drug allergy labels [4]. The incidence of drug allergy or drug hypersensitivity reaction (DHR) has been reported to occur in 4.2 per 1,000 hospitalisations, based on a prospective large Asian cohort studies [5]. Drug allergy is an immunologically mediated DHR that should not be confused with intolerance or side effect that is pharmacologically mediated [6]. For example, less than 15% of patients with reported beta-lactam allergies were found to have genuine allergy after evaluation, which is similar to western cohorts [4]. A good understanding of the pathomechanism of an adverse drug reaction is therefore crucial in the correct labelling of a patient's reaction as this has significant implications in clinical management, from choice of appropriate antibiotics to prevention of a catastrophic outcome due to re-exposure [7].

As clarification of history of a drug reaction alone is sometimes insufficient to confirm a diagnosis, additional *in vitro* and *in vivo* testing are often required for further evaluation [8, 9], with the objective of identifying not just the putative active ingredient of the drug, but eventually also define the phenotype and endotype associated with biomarkers of the DHR [10-12]. Comprehensive testing may not be possible in certain locations in the Asia-Pacific

region as specialized immunology/allergy/dermatology centres that provide drug allergy testing services are not always widely available. Furthermore, there is an insufficient critical mass of allergy/immunology specialists or lack of funding in the public health system [13]. Knowledge gaps on drug allergy/hypersensitivity among health care providers [14], infrastructural and access issues in different geographical regions further contribute to heterogeneous practices in drug allergy diagnostics within many geographical regions [15].

In this study, we sought to survey the diagnostic procedures and practices in drug allergy/hypersensitivity among member countries of APAAACI. The specific objectives of this survey were (1) to increase the regional awareness on the requirement of specialized/dedicated allergy clinics/centres for drug allergy testing; (2) to train allergists in performing diagnostic tests; as well as (3) to facilitate exchange of knowledge and research collaborations among society members.

MATERIALS AND METHODS

The questionnaire was initiated and circulated to members of the APAAACI Drug Allergy Special Committee for evaluation in November 2019 through the software SurveyMonkey® (SurveyMonkey, San Mateo, CA, USA). The questions covered both diagnostic and therapeutic practices in drug allergy/hypersensitivity. The final questionnaire comprised a total of 41 questions, which was approved by the entire committee (**Supplementary material 1**). The questionnaire was then converted into a web-based questionnaire by the APAAACI Secretariat and sent electronically to 15 member societies and 3 individual members of APAAACI. All respondents were given 6 weeks (January 23, 2020 to March 6, 2020) to reply with a final reminder at the end of 6 weeks. The responses were then collated by the APAAACI Secretariat, and the numbers and percentages of respondents for each question were collated.

RESULTS

A total of 16 respondents representing 13 Asian countries participated in the survey as shown in **Table 1**. Respondents comprised 13 of 15 member societies and 1 of 3 individual members. Member societies submitted from 1 to 4 responses each as some delegated the respondents to key members from paediatrics or adult allergy, or to other subspecialties primarily involved in the evaluation of drug allergy/hypersensitivity in their country e.g., dermatology. The total of 26 responses were then consolidated. Some respondents left questions which they were unable to answer blank, hence the total number of responses (n) were less than the number of respondents (N) for several questions.

There were dedicated allergy clinics in all countries surveyed to perform drug allergy/DHR tests while 68.8% also performed these tests in dermatology clinics. Among the respondents, there were more of such services in adult (87.4%) than paediatric (75.0%) clinics; with the number of adult clinics ranging from 1 to 37 per country, to 1 to 10 paediatric clinics per country. Various published international or regional guidelines were used by the respondents while performing drug hypersensitivity diagnostic procedures as shown in **Table 2** [16-52]. Among these, the guidelines from The European Academy of Allergy and Clinical Immunology (EAACI) were the most widely used by as shown in **Table 3**, as EAACI's European Network for Drug Allergy (ENDA) had the most number of published drug allergy/hypersensitivity

Table 1. Characteristics of respondents

Characteristic	No. (%)
No. of respondents from the APAAACI Member Society* (n = 26)	
Korean Academy of Asthma Allergy and Clinical Immunology (KAAACI)	4 (15.4)
Allergy and Clinical Immunology Society (Singapore) (ACIS)	3 (11.5)
Hong Kong Institute of Allergy (HKIA)	3 (11.5)
Japanese Society of Allergology (JSA)	3 (11.5)
Australasian Society of Clinical Immunology and Allergy (ASCIA)	2 (7.7)
Malaysian Society of Allergy and Immunology (MSAI)	2 (7.7)
Philippines Society of Allergy, Asthma and Immunology (PSAAI)	2 (7.7)
Allergy, Asthma and Immunology Association of Thailand (AAIAT)	1 (3.8)
Bangladesh Society of Allergy and Immunology (BSAI)	1 (3.8)
Chinese Society of Allergology (CSA)	1 (3.8)
Indian College of Allergy, Asthma and Applied Immunology (ICAAI)	1 (3.8)
Indonesian Society of Allergy and Immunology (ISAI)	1 (3.8)
Mongolian Society of Allergology (MSA)	1 (3.8)
Individual members	1 (3.8)
Composition of APAAACI respondents (n = 26)	
Member society	25 (96.2)
Individual member	1 (3.8)
Types of clinic that perform evaluation of drug hypersensitivity (n = 16)	
Allergy clinic	16 (100)
Dermatology clinic	11 (68.8)
Category of clinics (n = 16)	
Adult	14 (87.5)
Paediatric	12 (75.0)
Tests available (n = 16)	
Skin prick test and intradermal test	16 (100)
Serum tryptase	13 (86.7)
Specific IgE *in vitro* tests	12 (75.0)
Drug patch test	12 (75.0)
Pharmacogenomic tests	12 (75.0)
Drug provocation tests	11 (68.8)
Basophil activation test	9 (56.3)
Lymphocyte transformation test	8 (50.0)

*Nonresponders: Allergy and Immunology Society of Sri Lanka (AISS) and Taiwan Academy of Allergy Asthma and Clinical Immunology (TAAACI).

guidelines pertaining to the evaluation of specific drug classes e.g., beta-lactam antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs).

In the investigation of immediate DHR, measurement of serum tryptase was available among 86.7% of respondents. All clinics performed skin prick and intradermal tests. The drugs most commonly skin-tested were cephalosporins (86.7%), penicillins (80.0%), general anaesthesia (73.3%), and local (66.7%) anaesthetic agents as shown in **Table 4**. Majority obtained penicilloyl polylysine (PPL) (60.0%) and minor determinant mix (66.7%) commercially. In most instances, the clinicians (allergists/dermatologist) prepared the drugs themselves for skin tests. Commercially available specific IgE *in vitro* tests such as ImmunoCAP (Phadia AB, Uppsala, Sweden) (92.9%) and Radioallergosorbent test (25.7%) were available in 10 countries. In-house preparation of specific IgE tests was produced in 5 countries. The drugs commonly tested using these *in vitro* methods included penicilloyl G (61.5%); penicilloyl V, ampicilloyl, amoxicilloyl (55.5% respectively), and cefaclor (46.2% respectively). The basophil activation test was available for 60.0% respondents.

Drug patch testing was available to 75.0% respondents for the investigation of nonimmediate (delayed) DHR. Antibiotics (beta-lactams and non–beta-lactams) (83.3%) and antiepileptics

Table 2. Guidelines used for references (n = 16)

Guideline	No.
Drug allergy	
EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity 2019	13
Drug allergy: an updated practice parameter 2010	7
Drug allergy passport and other documentation for patients with drug hypersensitivity – an ENDA/EAACI Drug Allergy Interest Group Position Paper 2016	3
In vitro tests for drug hypersensitivity reactions: an ENDA/EAACI Drug Allergy Interest Group position paper 2016	2
BSACI guidelines for the management of drug allergy 2009	1
EAACI task force report: recognising the potential of the primary care physician in the diagnosis and management of drug hypersensitivity 2018	1
Antibiotic allergy	
Towards a more precise diagnosis of hypersensitivity to beta-lactams — an EAACI position paper	11
Hypersensitivity reactions to non–beta-lactam antimicrobial agents, a statement of the WAO special committee on drug allergy 2013	4
Update on the evaluation of hypersensitivity reactions to beta-lactams. Allergy 2009	3
Diagnosis of Immediate Allergic Reactions to Beta-Lactam Antibiotics 2003	3
NSAIDs hypersensitivity	
Hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) – classification, diagnosis and management: review of the EAACI/ENDA and GA2LEN/HANNA	9
Statement of the Spanish Society of Allergology and Clinical Immunology on provocation tests with aspirin/nonsteroidal anti-inflammatory drugs 2020	2
Intraoperative anaphylaxis/anaesthetic agents	
EAACI position paper on the investigation of perioperative immediate hypersensitivity reactions 2019	9
BSACI guidelines for the investigation of suspected anaphylaxis during general anaesthesia 2010	2
Radiocontrast media	
Management of hypersensitivity reactions to iodinated contrast media 2005	5
Clinical practice guidelines for diagnosis and management of hypersensitivity reactions to contrast media 2016	3
Vaccine adverse reactions	
Administration of influenza vaccines to egg allergic recipients: a practice parameter update 2017	7
Adverse reactions to vaccines practice parameter 2012 update	3
Skin tests	
In vivo diagnosis of allergic diseases -- allergen provocation tests 2015	7
Skin test concentrations for systemically administered drugs -- an ENDA/EAACI Drug Allergy Interest Group position paper 2013	5
ASCIA skin prick test manual 2016	5
Patch testing in nonimmediate drug eruptions 2008	1
Allergy diagnostic testing: an updated practice parameter 2008	4
In vitro tests	
In vitro tests for drug hypersensitivity reactions: an ENDA/EAACI Drug Allergy Interest Group position paper 2016	4
The clinical utility of basophil activation testing in diagnosis and monitoring of allergic disease 2015	2
Drug provocation test	
Risk and safety requirements for diagnostic and therapeutic procedures in allergology: World Allergy Organization Statement 2016	6
EAACI/GA2LEN guideline: aspirin provocation tests for diagnosis of aspirin hypersensitivity 2007	4
Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations 2003	4
Desensitization	
Desensitization in delayed drug hypersensitivity reactions -- an EAACI position paper of the Drug Allergy Interest Group 2013	8
General considerations on rapid desensitization for drug hypersensitivity - a consensus statement 2010	3
Pharmacogenomic testing	
Clinical pharmacogenetics implementation consortium of the pharmacogenomics	3
Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis	
UK guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults 2016	4
Mastocytosis and mast cell activation syndromes	
Drug hypersensitivity in clonal mast cell disorders: ENDA/EAACI position paper 2015	3
Mastocytosis and allergic diseases 2014	1
Paediatric drug allergy	
Diagnosis and management of drug-induced anaphylaxis in children: an EAACI position paper 2019	7
Drug allergy: diagnosis and management of drug allergy in adults, children and young people 2014	4
EAACI/ENDA position paper: diagnosis and management of hypersensitivity reactions to NSAIDs in children and adolescents 2018	3
The RCPCH care pathway for children with drug allergies: an evidence and consensus based national approach 2011	1

EAACI, European Academy of Allergy and Clinical Immunology; ENDA, European Network for Drug Allergy; BSACI, British Society of Allergy and Clinical Immunology; WAO, World Allergy Organization; ASCIA, Australasian Society of Clinical Immunology and Allergy; GA2LEN, Global Allergy and Asthma European Network; RCPCH, Royal College of Paediatrics and Child Health.

Table 3. Clinical guidelines used by respondents in the assessment of drug hypersensitivity (n = 16)

Guideline	No. (%)
EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity 2019	13 (81.3)
Towards a more precise diagnosis of hypersensitivity to beta-lactams — an EAACI position paper	11 (68.8)
Hypersensitivity to nonsteroidal anti-inflammatory drugs – classification, diagnosis and management: review of the EAACI/ENDA and GA2LEN/HANNA	9 (56.3)
EAACI position paper on the investigation of perioperative immediate hypersensitivity reactions 2019	9 (56.3)
Desensitization in delayed drug hypersensitivity reactions -- an EAACI position paper of the Drug Allergy Interest Group 2013	8 (50.0)
Diagnosis and management of drug-induced anaphylaxis in children: an EAACI position paper 2019	7 (43.8)
In vivo diagnosis of allergic diseases--allergen provocation tests 2015	7 (43.8)
Drug allergy: an updated practice parameter 2010	7 (43.8)
Administration of influenza vaccines to egg allergic recipients: a practice parameter update 2017	7 (43.8)
Risk and safety requirements for diagnostic and therapeutic procedures in allergology: World Allergy Organization Statement 2016	6 (37.5)
Skin test concentrations for systemically administered drugs -- an ENDA/EAACI Drug Allergy Interest Group position paper 2013	5 (31.3)
Management of hypersensitivity reactions to iodinated contrast media 2005	5 (31.3)
ASCIA skin prick test manual 2016	5 (31.3)

EAACI, European Academy of Allergy and Clinical Immunology; ENDA, European Network for Drug Allergy; GA2LEN, Global Allergy and Asthma European Network; HANNA, European Network on Hypersensitivity to Aspirin and Non-Steroidal Anti-Inflammatory Drugs; ASCIA, Australasian Society of Clinical Immunology and Allergy.

(58.3%) were the most frequently patch-tested drugs as shown in **Table 5**. Stevens-Johnson syndrome (SJS) (75.0%), drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms (DRESS) (66.7%), acute generalized exanthematous pustulosis (AGEP), and maculopapular eruptions (58.3% respectively) were the common indications for drug patch testing. Most (75.0%) used the commercialized form of drugs prepared in-house, in both 10% and 30% dilution using petrolatum (or aqueous) to perform the patch test. Less than half of the respondents tested the colouring (41.7%), and preservative (33.0%). All performed the first patch test reading after 48 hours of occlusion. Only 69.2% performed the second reading at 96 hours, and 15.4% performed a day-7 reading.

Lymphocyte transformation test (LTT) was only used in research settings among 75% of respondents, while only 12.5% used LTT for research and clinical care. The drugs tested by LTT were mainly NSAIDs and selective cyclooxygenase (COX)-2 inhibitors (42.9% respectively); beta-lactam antibiotics and antituberculous drugs (28.6% respectively).

Drug provocation test (DPT) was performed by 93.8% respondents mainly to exclude the diagnosis of drug hypersensitivity for nonsuggestive history or nonspecific symptoms (93.3%) as shown in **Table 6**. Preparation of drugs for drug provocation was done mainly by doctors (80.0%). Almost all performed open DPT (93.3%) with only 33.3% doing single-blind placebo control DPT. None routinely performed double blind placebo control drug provocation. The most common route of administration of the challenge drug was oral using tablet, syrup, or capsule. For the diagnosis of aspirin hypersensitivity, aspirin provocation was performed in all countries with oral provocation (100.0%) as the most common route used.

Pharmacogenetics testing for HLA-B*15:02 prior to prescribing carbamazepine, HLA-B*58:01 for allopurinol, and HLA-B*57:01 for abacavir, was not mandatory or recommended by local pharmacoregulatory agencies in the majority of countries in the region as shown in **Table 7**.

Table 4. Investigations for immediate drug hypersensitivity

Characteristic	No. (%)
Skin prick test and intradermal test	
Drugs commonly tested (n = 15)	
Cephalosporins	13 (86.7)
Penicillin	12 (80.0)
General anaesthetic agents	11 (73.3)
Local Anaesthetic agents	10 (66.7)
Radiocontrast media	9 (60.0)
NSAIDs	6 (40.0)
Carbapenems	4 (26.7)
Non–beta-lactam antibiotics	4 (26.7)
Source of penicilloyl polylysine (n = 10)	
Diater®	6 (60.0)
In-house	3 (30.0)
Source of minor determinant mix (n = 9)	
Diater®	6 (66.7)
In-house	3 (33.3)
Persons who prepare the drugs for skin testing (n = 15)	
Allergist	15 (100)
Nurse/clinicians/specialist	4 (26.7)
Pharmacist	3 (20.0)
Dermatologist	1 (6.7)
Specific IgE *in vitro* tests	
Types of available assay (n = 15)	
Commercial	8 (53.3)
In-house preparation	3 (20.0)
Both	2 (13.3)
Neither	2 (13.3)
Types of commercial assay used (n = 14)	
CAP-FEIA (Phadia ImmunoCAP®)	13 (92.9)
RAST (Radioallergosorbent test®)	5 (35.7)
Drugs commonly tested using these *in vitro* methods (n = 13)	
Penicilloyl G	8 (61.5)
Penicilloyl V	7 (53.8)
Ampicilloyl	7 (53.8)
Amoxicilloyl	7 (53.8)
Alfa-gal	6 (46.2)
Cefaclor	6 (46.2)
Chlorhexidine	2 (15.4)
Gelatin	2 (15.4)
General anaesthetic agents	2 (15.4)
NSAIDs	2 (15.4)
Suxamethonium	2 (15.4)
Cephalosporins	1 (7.7)
Morphine	1 (7.7)
Pholcodine	1 (7.7)
No. with serum tryptase available for test (n = 15)	13 (86.7)
No. with basophil activation test available for drug hypersensitivity (n = 15)	9 (60.0)

NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 5. Investigations for nonimmediate (delayed) drug hypersensitivity

Characteristic	No. (%)
Drug patch test	
Drugs commonly tested (n = 12)	
Antibiotics (beta-lactam)	10 (83.3)
Antibiotic (non–beta-lactams)	10 (83.3)
Antiepileptics	7 (58.3)
Antituberculous drugs	5 (41.7)
NSAIDs and Selective COX-2 inhibitor	5 (41.7)
Cotrimoxazole	5 (41.7)

(continued to the next page)

Table 5. (Continued) Investigations for nonimmediate (delayed) drug hypersensitivity

Characteristic	No. (%)
Radiocontrast media	2 (16.7)
Hydroxyzine	1 (8.3)
Corticosteroids	1 (8.3)
Indications (n = 12)	
Stevens-Johnson syndrome	9 (75)
Drug-induced hypersensitivity syndrome	8 (66.7)
Acute generalized exanthematous pustulosis	7 (58.3)
Maculopapular eruption	7 (58.3)
Toxic epidermal necrolysis	6 (50.0)
Fixed drug eruption	6 (50.0)
Drug-induced immune-bullous eruptions	3 (25.0)
Drug-induced lupus erythematosus	3 (25.0)
Symmetrical drug-related intertriginous and flexural exanthema	3 (25.0)
Drug-induced vasculitis	3 (25.0)
Used in clinical or research setting (n = 13)	
Clinical	9 (69.2)
Research	2 (15.4)
Both	2 (15.4)
Formulation of drugs (n = 12)	
Commercialized form of drugs	9 (75.0)
Pure substance	5 (41.7)
Dilution of drugs (n = 13)	
10% and 30%	8 (61.5)
1%	6 (46.2)
5%	3 (23.1)
0.1%	3 (23.1)
Vehicle used (n = 13)	
Petrolatum	11 (84.6)
Water	5 (38.5)
Alcohol	1 (7.7)
Source of drugs for patch test (n = 13)	
In-house	9 (69.2)
Chemotechnique®	3 (23.1)
Commercial	2 (15.4)
Other agent tested (n = 12)	
Photoallergen	7 (58.3)
Colouring	5 (41.7)
Preservative	4 (33.3)
Excipient	3 (25.0)
Reading of patch test (n = 13)	
48 Hours	13 (100)
96 Hours	9 (69.2)
20 Minutes	2 (15.4)
Day 7	2 (15.4)
Lymphocyte transformation test (LTT)	
Type of LTT service (n = 8)	
Research	6 (75.0)
Clinical	1 (12.5)
Clinical and research	1 (12.5)
Facility that provide LTT (n = 8)	
In-house	4 (50.0)
Another facility within the country	4 (50.0)
Drugs tested using LTT (n = 7)	
NSAIDs and Selective COX-2 inhibitor	3 (42.9)
Contact allergens	3 (42.9)
Antibiotics (beta-lactam)	2 (28.6)
Antituberculous drugs	2 (28.6)
Antibiotic (non–beta-lactams)	1 (14.3)
Antiepileptics	1 (14.3)

NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 6. Drug provocation tests

Characteristic	No. (%)
Indications (n = 15)	
To exclude hypersensitivity (for nonsuggestive history/nonspecific symptoms)	14 (93.3)
To exclude cross-reactivity of related drugs in proven hypersensitivity (e.g., cephalosporin in a penicillin allergic)	12 (80.0)
To provide safe pharmacologically/structurally nonrelated drugs in proven hypersensitivity (e.g., beta-lactam)	11 (73.3)
Definitive diagnosis in suggestive history with negative, nonconclusive or nonavailable allergological tests	11 (73.3)
Preparation of drugs (n = 15)	
Doctor	12 (80.0)
Pharmacist	6 (40.0)
Nurse	5 (33.3)
Types of provocation (n = 15)	
Open challenge	14 (93.3)
Single blind placebo control	5 (33.3)
Routes of administration (n = 15)	
Oral	
Tablet	14 (93.3)
Syrup	11 (73.3)
Capsule	8 (53.3)
Intravenous	9 (60.0)
Subcutaneous	6 (40.0)
Intramuscular	1 (6.7)
The common routes of aspirin provocation (n = 15)	
Oral	15 (100)
Bronchial (inhalation) L-lysine-aspirin challenge	1 (6.7)

Table 7. Pharmacogenetics testing

Characteristic	No. (%)
Mandatory testing before prescribing (n = 12)	
None of the drugs below	7 (58.3)
HLA-B*1502 (carbamazepine)	3 (25.0)
HLA-B*5701 (abacavir)	2 (16.7)
HLA-B*5801 (allopurinol)	1 (8.3)
Recommended testing before prescribing (n = 11)	
None of the drugs below	5 (45.5)
HLA-B*5801 (allopurinol)	4 (36.4)
HLA-B*1502 (carbamazepine)	3 (27.3)
HLA-B*5701 (abacavir)	0 (0)

HLA, human leukocyte antigen.

DISCUSSION

Since the World Allergy Organization (WAO) International Survey on Diagnostic Procedures and Therapies in Drug Allergy/Hypersensitivity was carried out and published almost a decade ago [53], there have been several other physician surveys on the diagnosis and management of drug allergy/hypersensitivity to date. By far the area with the highest priority has been on penicillin [54] and beta-lactam allergy [55], with surveys led by EAACI's ENDA group and the British Society of Allergy and Clinical Immunology [56]. There have also been other surveys done specifically by specialists involved in the management of specific DHRs, e.g., aspirin desensitization for coronary artery disease among interventional cardiologists [57], and SJS/toxic epidermal necrolysis among directors managing Burns Units in the United States [58].

In the WAO 2009 survey, APAAACI member countries comprised 26.4% of the 82 responses from the then 77 regional and national member societies of WAO. Since then, there have

been several significant changes in the practice of drug allergy/DHR in our region. Firstly, we have had new member societies join APAAACI since the 2009 survey: Bangladesh Society of Allergy and Immunology, Mongolian Society of Allergology and Allergy and Clinical Immunology Society of Sri Lanka. In addition, we also have 2 individual members from Pakistan and 1 from Myanmar, representing countries with emerging interests in allergy and clinical immunology. As such this is likely to contribute to an increase in the number of new allergy/immunology practices within our region.

Secondly, there are now also many more published international and regional guidelines on important areas in drug allergy/hypersensitivity, including risk and safety requirements for diagnostic and therapeutic procedures [23], desensitization [44,45], pharmacogenetic testing [46], and paediatric drug allergy [50-52]. In contrast to 2009 where the American Academy of Allergy Asthma and Immunology/American College of Allergy Asthma and Immunology Practice Parameters were the most commonly accessed, this has since been overtaken by the EAACI/ENDA guidelines.

In terms of diagnostic tests, the use of skin prick and intradermal tests for immediate DHR appears to be similar to 2009, with similar types of drugs being the most commonly tested (beta-lactam antibiotics, general and local anaesthetic agents). However, in our current survey, there are 2 interesting trends. Firstly, there were marginally more respondents who answered to do skin testing for cephalosporins than penicillins. This may be a reflection of the increasing use of cephalosporins in Asia and hence increase in DHR [59]; intermittent difficulties in accessing commercial PPL and minor determinants, and emerging safety data of direct amoxicillin oral provocation tests in low-risk patients without the need for prior skin testing [60]. Secondly, iodinated contrast media (ICM) has now emerged as one of the "new" drugs for which skin testing has become increasingly used, likely for several reasons. These include the increasing incidence of solid organ cancers in the region, in particular with our ageing population; the increasing need for repeated computed tomography scans/magnetic resonance imaging for follow-up and surveillance increasing the risk of developing DHR, and because of the extensive work done by our colleagues in Korea on ICM hypersensitivity [61].

For nonimmediate DHR, in contrast to 2009, there is now increased use of drug patch tests in particular for beta-lactam and non–beta-lactam antibiotics, antiepileptic drugs and antituberculous drugs; and for selected patients with more severe reactions like SJS, DRESS, and AGEP [62]. These are much easier to carry out and interpret when performed by physicians trained in doing and interpreting these tests e.g., dermatologists, than setting up *in vitro* assays like LTT and enzyme-linked immunosorbent spot (Elispot) assays [63]. Many of the *in vitro* tests for nonimmediate reactions remain limited in their use to academic medical centres with links to research laboratories which carry out these tests. With the recognition of phenotypes and endotypes in various DHR, measurement of different cytokines, such as gamma-interferon, interleukin (IL)-5, IL-6, and IL-10 may in future be increasingly useful for the diagnosis of nonimmediate reactions [9, 11].

In the area of pharmacogenomic testing, even though there has been increasing interest in the risk of severe cutaneous adverse reactions (SCAR) in Asians with the use of carbamazepine and allopurinol, it may appear unusual that to date less than half the countries in the APAACI region mandate HLA genotype testing prior to prescription. This is likely to be due to heterogeneous ethnicities even within the same geographical region limiting the positive predictive value of testing, different health care financing systems,

relatively high costs of HLA testing which may not be government subsidized, and limited availability to alternative lower-cost drugs that make mandatory testing not cost-effective, especially in countries where healthcare financing is based on a copayment system rather than universal health care [64-68]. Nonetheless, nongenetic risk factors (e.g., chronic kidney disease) [69] and other HLA-genetic risk factors [70] need to be considered in the risk stratification for high-risk drugs like allopurinol.

There are several limitations in this survey. Firstly, the difficulties with validation, equity, and interpretation of responses. For instance, one centre in a large country with a large population that performs all the possible investigations available may seem to suggest that all types of tests are widely available. However, this is not the case as a vast majority of the population will not be able to access the service due to limited availability or difficulties accessing specialist centres e.g., rural practices. Likewise, for economies of scale, there may only be 1 or 2 centres in each country that performs ICM skin tests versus multiple centres in one country that performs ICM skin tests but none in others. Thus, the overall results of this survey will need to be geographically contextualized.

Secondly, we did not look at the discrepancies among responses within a member society, nor ask that each society consolidate responses on behalf of the member society. The survey was administered unfortunately when Asia was just at the start of the COVID-19 outbreak, so it was not feasible to coordinate responses. Discrepancies may or may not be present depending on whether the respondents consolidated responses on behalf of his/her geographical region or forwarded to members actively involved in managing drug allergy patients, and if so whether adult or paediatrics or both.

Thirdly, the types and frequency of tests used may be a result of differences in the type of practice of the respondents, and composition of the base-specialties in the allergy/immunology community managing drug allergy/hypersensitivity in the region. Between adult and paediatric allergists, the scope of procedures used (e.g., direct amoxicillin challenges being safe in low-risk children without a need for skin tests [71]); and the scope of drugs tested may differ (e.g., anaphylaxis to general anaesthetic agents being more common among adults than children). Some practices may also manage both children and adults. Likewise, allergists with dermatology as a base-specialty may also perform patch tests more frequently than nondermatologists.

Fourthly, there are other areas in which this survey has merely provided preliminary information for which further details are lacking. Examples include differences between adult and paediatric drug allergy/hypersensitivity clinical practices, the use of intradermal testing with delayed readings for nonimmediate reactions, and variations in DPT protocols e.g., the use a single dose versus multidose DPT, in particular beta-lactam allergy. As this survey was already considerably lengthy, follow-up surveys on these specific areas of interest will be considered.

In conclusion, notable changes in the past decade in drug allergy/hypersensitivity diagnostics within our region include increased use of European guidelines from EAACI/ENDA, use of skin testing for ICM hypersensitivity and drug patch testing for nonimmediate drug hypersensitivity. The use of HLA genotype testing prior to new carbamazepine, allopurinol and abacavir prescriptions remain variable throughout the region despite strong associations of SCAR with Asian ethnicity for a variety of reasons. The results of this survey form a useful

framework for developing educational and training needs and for improving access to drug allergy diagnostic and treatment modalities across APAAACI member societies.

SUPPLEMENTARY MATERIAL

Supplementary material 1 can be found via https://apallergy.org/src/sm/apallergy-10-e36-s001.pdf

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REFERENCES

1. Carroll R, McLean J, Walsh M. Reporting hospital adverse events using the Alfred Hospital's morbidity data. Aust Health Rev 2003;26:100-5.
PUBMED | CROSSREF
2. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998;279:1200-5.
PUBMED | CROSSREF
3. Li PH, Yeung HHF, Lau CS, Au EYL. Prevalence, incidence, and sensitization profile of β-lactam antibiotic allergy in Hong Kong. JAMA Netw Open 2020;3:e204199.
PUBMED | CROSSREF
4. Li PH, Siew LQC, Thomas I, Watts TJ, Ue KL, Rutkowski K, Lau CS. Beta-lactam allergy in Chinese patients and factors predicting genuine allergy. World Allergy Organ J 2019;12:100048.
PUBMED | CROSSREF
5. Thong BY, Leong KP, Tang CY, Chng HH. Drug allergy in a general hospital: results of a novel prospective inpatient reporting system. Ann Allergy Asthma Immunol 2003;90:342-7.
PUBMED | CROSSREF
6. Smith W. Adverse drug reactions - allergy? side-effect? intolerance? Aust Fam Physician 2013;42:12-6.
PUBMED
7. Shakib S, Caughey GE, Fok JS, Smith WB. Adverse drug reaction classification by health professionals: appropriate discrimination between allergy and intolerance? Clin Transl Allergy 2019;9:18.
PUBMED | CROSSREF
8. Romano A, Atanaskovic-Markovic M, Barbaud A, Bircher AJ, Brockow K, Caubet JC, Celik G, Cernadas J, Chiriac AM, Demoly P, Garvey LH, Mayorga C, Nakonechna A, Whitaker P, Torres MJ. Towards a more precise diagnosis of hypersensitivity to beta-lactams - an EAACI position paper. Allergy 2020;75:1300-15.
PUBMED | CROSSREF
9. Broyles AD, Banerji A, Castells M. Practical guidelines for the evaluation and management of drug hypersensitivity: general concepts. J Allergy Clin Immunol Pract 2020;8 (9 Suppl):S3-15.
PUBMED | CROSSREF
10. Castells M, Khan DA, Phillips EJ. Penicillin Allergy. N Engl J Med 2019;381:2338-51.
PUBMED | CROSSREF
11. Castells M. Diagnosis and management of anaphylaxis in precision medicine. J Allergy Clin Immunol 2017;140:321-33.
PUBMED | CROSSREF
12. Jakubovic BD, Vecillas LL, Jimenez-Rodriguez TW, Sanchez-Sanchez S, Castells M. Drug hypersensitivity in the fast lane: what clinicians should know about phenotypes, endotypes, and biomarkers. Ann Allergy Asthma Immunol 2020;124:566-72.
PUBMED | CROSSREF
13. Lee TH, Leung TF, Wong G, Ho M, Duque JR, Li PH, Lau CS, Lam WF, Wu A, Chan E, Lai C, Lau YL. The unmet provision of allergy services in Hong Kong impairs capability for allergy prevention-implications for the Asia Pacific region. Asian Pac J Allergy Immunol 2019;37:1-8.
PUBMED
14. Wang Y, Zhu R, Huang N, Li W, Yang L, Zhang S, Liu G. Knowledge, attitudes, and practices survey of drug allergy among healthcare practitioners in central China: a multicenter study. Asia Pac Allergy 2016;6:105-11.
PUBMED | CROSSREF

15. Thong BY, Lucas M, Kang HR, Chang YS, Li PH, Tang MM, Yun J, Fok JS, Kim BK, Nagao M, Rengganis I, Tsai YG, Chung WH, Yamaguchi M, Rerkpattanapipat T, Kamchaisatian W, Leung TF, Yoon HJ, Zhang L, Latiff AHA, Fujisawa T, Thien F, Castells MC, Demoly P, Wang JY, Pawankar R. Drug hypersensitivity reactions in Asia: regional issues and challenges. Asia Pac Allergy 2020;10:e8.
PUBMED | CROSSREF

16. Brockow K, Ardern-Jones MR, Mockenhaupt M, Aberer W, Barbaud A, Caubet JC, Spiewak R, Torres MJ, Mortz CG. EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity. Allergy 2019;74:14-27.
PUBMED | CROSSREF

17. Kowalski ML, Makowska JS, Blanca M, Bavbek S, Bochenek G, Bousquet J, Bousquet P, Celik G, Demoly P, Gomes ER, Niżankowska-Mogilnicka E, Romano A, Sanchez-Borges M, Sanz M, Torres MJ, De Weck A, Szczeklik A, Brockow K. Hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) - classification, diagnosis and management: review of the EAACI/ENDA(#) and GA2LEN/HANNA*. Allergy 2011;66:818-29.
PUBMED | CROSSREF

18. Garvey LH, Ebo DG, Mertes PM, Dewachter P, Garcez T, Kopac P, Laguna JJ, Chiriac AM, Terreehorst I, Voltolini S, Scherer K. An EAACI position paper on the investigation of perioperative immediate hypersensitivity reactions. Allergy 2019;74:1872-84.
PUBMED | CROSSREF

19. Atanaskovic-Markovic M, Gomes E, Cernadas JR, du Toit G, Kidon M, Kuyucu S, Mori F, Ponvert C, Terreehorst I, Caubet JC. Diagnosis and management of drug-induced anaphylaxis in children: an EAACI position paper. Pediatr Allergy Immunol 2019;30:269-76.
PUBMED | CROSSREF

20. Agache I, Bilò M, Braunstahl GJ, Delgado L, Demoly P, Eigenmann P, Gevaert P, Gomes E, Hellings P, Horak F, Muraro A, Werfel T, Jutel M. In vivo diagnosis of allergic diseases--allergen provocation tests. Allergy 2015;70:355-65.
PUBMED | CROSSREF

21. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology. American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol 2010;105:259-73.

22. Greenhawt M, Turner PJ, Kelso JM. Administration of influenza vaccines to egg allergic recipients: A practice parameter update 2017. Ann Allergy Asthma Immunol 2018;120:49-52.
PUBMED | CROSSREF

23. Kowalski ML, Ansotegui I, Aberer W, Al-Ahmad M, Akdis M, Ballmer-Weber BK, Beyer K, Blanca M, Brown S, Bunnag C, Hulett AC, Castells M, Chng HH, De Blay F, Ebisawa M, Fineman S, Golden DB, Haahtela T, Kaliner M, Katelaris C, Lee BW, Makowska J, Muller U, Mullol J, Oppenheimer J, Park HS, Parkerson J, Passalacqua G, Pawankar R, Renz H, Rueff F, Sanchez-Borges M, Sastre J, Scadding G, Sicherer S, Tantilipikorn P, Tracy J, van Kempen V, Bohle B, Canonica GW, Caraballo L, Gomez M, Ito K, Jensen-Jarolim E, Larche M, Melioli G, Poulsen LK, Valenta R, Zuberbier T. Risk and safety requirements for diagnostic and therapeutic procedures in allergology: World Allergy Organization Statement. World Allergy Organ J 2016;9:33.
PUBMED | CROSSREF

24. Doña I, Caubet JC, Brockow K, Doyle M, Moreno E, Terreehorst I, Torres MJ. An EAACI task force report: recognising the potential of the primary care physician in the diagnosis and management of drug hypersensitivity. Clin Transl Allergy 2018;8:16.
PUBMED | CROSSREF

25. Brockow K, Aberer W, Atanaskovic-Markovic M, Bavbek S, Bircher A, Bilo B, Blanca M, Bonadonna P, Burbach G, Calogiuri G, Caruso C, Celik G, Cernadas J, Chiriac A, Demoly P, Oude Elberink JN, Fernandez J, Gomes E, Garvey LH, Gooi J, Gotua M, Grosber M, Kauppi P, Kvedariene V, Laguna JJ, Makowska JS, Mosbech H, Nakonechna A, Papadopolous NG, Ring J, Romano A, Rockmann H, Sargur R, Sedlackova L, Sigurdardottir S, Schnyder B, Storaas T, Torres M, Zidarn M, Terreehorst I. Drug allergy passport and other documentation for patients with drug hypersensitivity - an ENDA/EAACI Drug Allergy Interest Group Position Paper. Allergy 2016;71:1533-9.
PUBMED | CROSSREF

26. Mayorga C, Celik G, Rouzaire P, Whitaker P, Bonadonna P, Rodrigues-Cernadas J, Vultaggio A, Brockow K, Caubet JC, Makowska J, Nakonechna A, Romano A, Montañez MI, Laguna JJ, Zanoni G, Gueant JL, Oude Elberink H, Fernandez J, Viel S, Demoly P, Torres MJ; In vitro tests for Drug Allergy Task Force of EAACI Drug Interest Group. In vitro tests for drug hypersensitivity reactions: an ENDA/EAACI Drug Allergy Interest Group position paper. Allergy 2016;71:1103-34.
PUBMED | CROSSREF

27. Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, Khan DA, Lang DM, Park HS, Pichler W, Sanchez-Borges M, Shiohara T, Thong BY. International Consensus on drug allergy. Allergy 2014;69:420-37.
PUBMED | CROSSREF

28. Mirakian R, Ewan PW, Durham SR, Youlten LJ, Dugué P, Friedmann PS, English JS, Huber PA, Nasser SM; BSACI. BSACI guidelines for the management of drug allergy. Clin Exp Allergy 2009;39:43-61.
PUBMED | CROSSREF

29. Sánchez-Borges M, Thong B, Blanca M, Ensina LF, González-Díaz S, Greenberger PA, Jares E, Jee YK, Kase-Tanno L, Khan D, Park JW, Pichler W, Romano A, Jaén MJ. Hypersensitivity reactions to non beta-lactam antimicrobial agents, a statement of the WAO special committee on drug allergy. World Allergy Organ J 2013;6:18.
PUBMED | CROSSREF

30. Blanca M, Romano A, Torres MJ, Férnandez J, Mayorga C, Rodriguez J, Demoly P, Bousquet PJ, Merk HF, Sanz ML, Ott H, Atanasković-Marković M. Update on the evaluation of hypersensitivity reactions to betalactams. Allergy 2009;64:183-93.
PUBMED | CROSSREF

31. Torres MJ, Blanca M, Fernandez J, Romano A, Weck A, Aberer W, Brockow K, Pichler WJ, Demoly P; ENDA; EAACI Interest Group on Drug Hypersensitivity. Diagnosis of immediate allergic reactions to beta-lactam antibiotics. Allergy 2003;58:961-72.
PUBMED | CROSSREF

32. Brockow K, Garvey LH, Aberer W, Atanaskovic-Markovic M, Barbaud A, Bilo MB, Bircher A, Blanca M, Bonadonna B, Campi P, Castro E, Cernadas JR, Chiriac AM, Demoly P, Grosber M, Gooi J, Lombardo C, Mertes PM, Mosbech H, Nasser S, Pagani M, Ring J, Romano A, Scherer K, Schnyder B, Testi S, Torres M, Trautmann A, Terreehorst I; ENDA/EAACI Drug Allergy Interest Group. Skin test concentrations for systemically administered drugs -- an ENDA/EAACI Drug Allergy Interest Group position paper. Allergy 2013;68:702-12.
PUBMED | CROSSREF

33. Brockow K, Christiansen C, Kanny G, Clément O, Barbaud A, Bircher A, Dewachter P, Guéant JL, Rodriguez Guéant RM, Mouton-Faivre C, Ring J, Romano A, Sainte-Laudy J, Demoly P, Pichler WJ; ENDA; EAACI interest group on drug hypersensitivity. Management of hypersensitivity reactions to iodinated contrast media. Allergy 2005;60:150-8.
PUBMED | CROSSREF

34. Australasian Society of Clinical Immunology and Allergy (ASCIA). Skin prick testing for the diagnosis of allergic disease: a manual for practitioners. Balgowlah (Australia): ASCIA; 2016

35. Izquierdo-Domínguez A, Bobolea I, Doña I, Campo P, Segura C, Ortega N, González R, Delgado J, Torres MJ, Dordal MT; SEAIC Rhinoconjunctivitis Committee. Statement of the Spanish Society of Allergology and Clinical Immunology on provocation tests with aspirin/nonsteroidal anti-inflammatory drugs. J Investig Allergol Clin Immunol 2020;30:1-13.
PUBMED | CROSSREF

36. Ewan PW, Dugué P, Mirakian R, Dixon TA, Harper JN, Nasser SM; BSACI. BSACI guidelines for the investigation of suspected anaphylaxis during general anaesthesia. Clin Exp Allergy 2010;40:15-31.
PUBMED | CROSSREF

37. Rosado Ingelmo A, Doña Diaz I, Cabañas Moreno R, Moya Quesada MC, García-Avilés C, García Nuñez I, Martínez Tadeo JI, Mielgo Ballesteros R, Ortega-Rodríguez N, Padial Vilchez MA, Sánchez-Morillas L, Vila Albelda C, Moreno Rodilla E, Torres Jaén MJ. Clinical practice guidelines for diagnosis and management of hypersensitivity reactions to contrast media. J Investig Allergol Clin Immunol 2016;26:144-55.
PUBMED | CROSSREF

38. Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J, Cox L, Khan D, Lang DM, Oppenheimer J, Portnoy JM, Randolph CR, Schuller DE, Spector SL, Tilles SA, Wallace D. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol 2012;130:25-43.
PUBMED | CROSSREF

39. Romano A, Viola M, Gaeta F, Rumi G, Maggioletti M. Patch testing in non-immediate drug eruptions. Allergy Asthma Clin Immunol 2008;4:66-74.
PUBMED | CROSSREF

40. Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, Sicherer S, Golden DB, Khan DA, Nicklas RA, Portnoy JM, Blessing-Moore J, Cox L, Lang DM, Oppenheimer J, Randolph CC, Schuller DE, Tilles SA, Wallace DV, Levetin E, Weber R; American Academy of Allergy, Asthma and Immunology. American College of Allergy, Asthma and Immunology. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol 2008;100 (3 Suppl 3):S1-148.

41. Hoffmann HJ, Santos AF, Mayorga C, Nopp A, Eberlein B, Ferrer M, Rouzaire P, Ebo DG, Sabato V, Sanz ML, Pecaric-Petkovic T, Patil SU, Hausmann OV, Shreffler WG, Korosec P, Knol EF. The clinical utility of basophil activation testing in diagnosis and monitoring of allergic disease. Allergy 2015;70:1393-405.
PUBMED | CROSSREF

42. Nizankowska-Mogilnicka E, Bochenek G, Mastalerz L, Swierczyńska M, Picado C, Scadding G, Kowalski ML, Setkowicz M, Ring J, Brockow K, Bachert C, Wöhrl S, Dahlén B, Szczeklik A. EAACI/GA2LEN guideline: aspirin provocation tests for diagnosis of aspirin hypersensitivity. Allergy 2007;62:1111-8.
PUBMED | CROSSREF

43. Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J, Brockow K, Pichler WJ, Demoly P; European Network for Drug Allergy (ENDA); EAACI interest group on drug hypersensitivity. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations. Allergy 2003;58:854-63.
PUBMED | CROSSREF

44. Scherer K, Brockow K, Aberer W, Gooi JH, Demoly P, Romano A, Schnyder B, Whitaker P, Cernadas JS, Bircher AJ; ENDA, the European Network on Drug Allergy and the EAACI Drug Allergy Interest Group. Desensitization in delayed drug hypersensitivity reactions -- an EAACI position paper of the Drug Allergy Interest Group. Allergy 2013;68:844-52.
PUBMED | CROSSREF

45. Cernadas JR, Brockow K, Romano A, Aberer W, Torres MJ, Bircher A, Campi P, Sanz ML, Castells M, Demoly P, Pichler WJ; European Network of Drug Allergy and the EAACI interest group on drug hypersensitivity. General considerations on rapid desensitization for drug hypersensitivity - a consensus statement. Allergy 2010;65:1357-66.
PUBMED | CROSSREF

46. Clinical Pharmacogenetics Implementation Consortium (CPIC) [Internet]. CPIC; 2020 [cited 2020 Sep 28]. Available from: https://cpicpgx.org/

47. Creamer D, Walsh SA, Dziewulski P, Exton LS, Lee HY, Dart JK, Setterfield J, Bunker CB, Ardern-Jones MR, Watson KM, Wong GA, Philippidou M, Vercueil A, Martin RV, Williams G, Shah M, Brown D, Williams P, Mohd Mustapa MF, Smith CH, McHenry PM, Hughes JR, Griffiths M, Gibbon K, McDonagh AJ, Buckley DA, Nasr I, Swale VJ, Duarte Williamson CE, Levell NJ, Leslie T, Mallon E, Wakelin S, Ungureanu S, Hunasehally P, Cork M, Towers K, Donnelly J, Saunders C, Brain AG. U.K. guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults 2016. Br J Dermatol 2016;174:1194-227.
PUBMED | CROSSREF

48. Bonadonna P, Pagani M, Aberer W, Bilò MB, Brockow K, Oude Elberink H, Garvey L, Mosbech H, Romano A, Zanotti R, Torres MJ. Drug hypersensitivity in clonal mast cell disorders: ENDA/EAACI position paper. Allergy 2015;70:755-63.
PUBMED | CROSSREF

49. Bonadonna P, Lombardo C, Zanotti R. Mastocytosis and allergic diseases. J Investig Allergol Clin Immunol 2014;24:288-97.
PUBMED

50. Kidon M, Blanca-Lopez N, Gomes E, Terreehorst I, Tanno L, Ponvert C, Chin CW, Caubet JC, Soyer O, Mori F, Blanca M, Atanaskovic-Markovic M. EAACI/ENDA Position Paper: Diagnosis and management of hypersensitivity reactions to non-steroidal anti-inflammatory drugs (NSAIDs) in children and adolescents. Pediatr Allergy Immunol 2018;29:469-80.
PUBMED | CROSSREF

51. National Clinical Guideline Centre (UK). Drug allergy: diagnosis and management of drug allergy in adults, children and young people. London: National Institute for Health and Care Excellence (UK); 2014.

52. du Toit G, Lloyd K, Sinnott L, Forster D, Austin M, Clark C, Tuthill D, Lucas JS, Brathwaite N, Warner J; Science and Research Department, Royal College of Paediatrics and Child Health. The RCPCH care pathway for children with drug allergies: an evidence and consensus based national approach. Arch Dis Child 2011;96 Suppl 2:i15-8.
PUBMED | CROSSREF

53. Thong BY, Mirakian R, Castells M, Pichler W, Romano A, Bonadonna P, Diana D, Kowalski M, Yanez A, Lleonart R, Sanchez-Borges M, Demoly P. A world allergy organization international survey on diagnostic procedures and therapies in drug allergy/hypersensitivity. World Allergy Organ J 2011;4:257-70.
PUBMED | CROSSREF

54. Sousa-Pinto B, Blumenthal KG, Macy E, Bavbek S, Benić MS, Alves-Correia M, Dursun AB, Jerschow E, Kong-Cardoso B, Kopač P, Lefèvre S, Lombardo C, Marraccini P, Moral L, Norton AE, Petrişor C, Poziomkowska-Gęsicka I, Regateiro FS, Santos N, Saretta F, Turkalj M, Veličković J, Wöhrl S, Yazicioglu M, Zidarn M, Pereira M, Rebelo-Gomes E, Pereira AM, Delgado L, Almeida Fonseca J. Diagnostic testing for penicillin allergy: a survey of practices and cost perceptions. Allergy 2020;75:436-41.
PUBMED | CROSSREF

55. Torres MJ, Celik GE, Whitaker P, Atanaskovic-Markovic M, Barbaud A, Bircher A, Blanca M, Brockow K, Caubet JC, Cernadas JR, Chiriac A, Demoly P, Garvey LH, Merk HF, Mosbech H, Nakonechna A, Romano A. A EAACI drug allergy interest group survey on how European allergy specialists deal with β-lactam allergy. Allergy 2019;74:1052-62.
PUBMED | CROSSREF

56. Richter AG, Nasser SM, Krishna MT. A UK national survey of investigations for beta-lactam hypersensitivity - heterogeneity in practice and a need for national guidelines - on behalf of British Society for Allergy and Clinical Immunology (BSACI). Clin Exp Allergy 2013;43:941-9.
PUBMED | CROSSREF

57. Bianco M, Bernardi A, D'Ascenzo F, Cerrato E, Omedè P, Montefusco A, DiNicolantonio JJ, Zoccai GB, Varbella F, Carini G, Moretti C, Pozzi R, Gaita F. Efficacy and safety of available protocols for aspirin hypersensitivity for patients undergoing percutaneous coronary intervention: a survey and systematic review. Circ Cardiovasc Interv 2016;9:e002896.
PUBMED | CROSSREF

58. Richard EB, Hamer D, Musso MW, Short T, O'Neal HR Jr. Variability in management of patients with SJS/TEN: a survey of burn unit directors. J Burn Care Res 2018;39:585-92.
PUBMED | CROSSREF

59. Versporten A, Zarb P, Caniaux I, Gros MF, Drapier N, Miller M, Jarlier V, Nathwani D, Goossens H, Koraqi A, Hoxha I, Tafaj S, Lacej D, Hojman M, Quiros RE, Ghazaryan L, Cairns KA, Cheng A, Horne KC, Doukas FF, Gottlieb T, Alsalman J, Magerman K, Marielle GY, Ljubovic AD, Coelho AA, Gales AC, Keuleyan E, Sabuda D, Boswell JL, Conly JM, Rojas A, Carvajal C, Labarca J, Solano A, Valverde CR, Villalobos-Vindas JM, Pristas I, Plecko V, Paphitou N, Shaqiri E, Rummukainen ML, Pagava K, Korinteli I, Brandt T, Messler S, Enimil A, Iosifidis E, Roilides E, Sow MS, Sengupta S, George JV, Poojary A, Patil P, Soltani J, Jafarpour Z, Ameen H, Fitzgerald D, Maor Y, Chowers M, Temkin E, Esposito S, Arnoldo L, Brusaferro S, Gu Y, El-Hajji FD, Kim NJ, Kambaralieva B, Pavare J, Zarakauska L, Usonis V, Burokiene S, Ivaskeviciene I, Mijovic G, Duborija-Kovacevic N, Bondesio K, Iregbu K, Oduyebo O, Raka D, Raka L, Rachina S, Enani MA, Al Shehri M, Carevic B, Dragovac G, Obradovic D, Stojadinovic A, Radulovic L, Wu JE, Wei Teng Chung G, Chen HH, Tambyah PA, Lye D, Tan SH, Ng TM, Tay HL, Ling ML, Chlebicki MP, Kwa AL, Lee W, Beović B, Dramowski A, Finlayson H, Taljaard J, Ojeda-Burgos G, Retamar P, Lucas J, Pot W, Verduin C, Kluytmans J, Scott M, Aldeyab MA, McCullagh B, Gormley C, Sharpe D, Gilchrist M, Whitney L, Laundy M, Lockwood D, Drysdale SB, Boudreaux J, Septimus EJ, Greer N, Gawrys G, Rios E, May S; Global-PPS network. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Lancet Glob Health 2018;6:e619-29.
PUBMED | CROSSREF

60. Stone CA Jr, Trubiano J, Coleman DT, Rukasin CR, Phillips EJ. The challenge of de-labeling penicillin allergy. Allergy 2020;75:273-88.
PUBMED | CROSSREF

61. Cha MJ, Kang DY, Lee W, Yoon SH, Choi YH, Byun JS, Lee J, Kim YH, Choo KS, Cho BS, Jeon KN, Jung JW, Kang HR. Hypersensitivity reactions to iodinated contrast media: a multicenter study of 196 081 patients. Radiology 2019;293:117-24.
PUBMED | CROSSREF

62. Bergmann MM, Caubet JC. Role of in vivo and in vitro tests in the diagnosis of severe cutaneous adverse reactions (SCAR) to drug. Curr Pharm Des 2019;25:3872-80.
PUBMED | CROSSREF

63. Doña I, Torres MJ, Montañez MI, Fernández TD. In vitro diagnostic testing for antibiotic allergy. Allergy Asthma Immunol Res 2017;9:288-98.
PUBMED | CROSSREF

64. Zhou Y, Krebs K, Milani L, Lauschke VM. Global frequencies of clinically important HLA alleles and their implications for the cost-effectiveness of preemptive pharmacogenetic testing. Clin Pharmacol Ther 2020 Jun 14 [Epub].
PUBMED | CROSSREF

65. Pruis SL, Jeon YK, Pearce F, Thong BY, Aziz MI. Cost-effectiveness of sequential urate lowering therapies for the management of gout in Singapore. J Med Econ 2020;23:838-47.
PUBMED | CROSSREF

66. Chong HY, Lim YH, Prawjaeng J, Tassaneeyakul W, Mohamed Z, Chaiyakunapruk N. Cost-effectiveness analysis of HLA-B*58: 01 genetic testing before initiation of allopurinol therapy to prevent allopurinol-induced Stevens-Johnson syndrome/toxic epidermal necrolysis in a Malaysian population. Pharmacogenet Genomics 2018;28:56-67.
PUBMED

67. Rattanavipapong W, Koopitakkajorn T, Praditsitthikorn N, Mahasirimongkol S, Teerawattananon Y. Economic evaluation of HLA-B*15:02 screening for carbamazepine-induced severe adverse drug reactions in Thailand. Epilepsia 2013;54:1628-38.
PUBMED | CROSSREF

68. Ke CH, Chung WH, Wen YH, Huang YB, Chuang HY, Tain YL, Wang YL, Wu CC, Hsu CN. Cost-effectiveness analysis for genotyping before allopurinol treatment to prevent severe cutaneous adverse drug reactions. J Rheumatol 2017;44:835-43.
PUBMED | CROSSREF

69. Jung JW, Song WJ, Kim YS, Joo KW, Lee KW, Kim SH, Park HW, Chang YS, Cho SH, Min KU, Kang HR. HLA-B58 can help the clinical decision on starting allopurinol in patients with chronic renal insufficiency. Nephrol Dial Transplant 2011;26:3567-72.
PUBMED | CROSSREF

70. Shim JS, Yun J, Kim MY, Chung SJ, Oh JH, Kang DY, Jung JW, Cho SH, Kang HR. The presence of HLA-B75, DR13 homozygosity, or DR14 additionally increases the risk of allopurinol-induced severe cutaneous adverse reactions in HLA-B*58:01 carriers. J Allergy Clin Immunol Pract 2019;7:1261-70.
PUBMED | CROSSREF

71. Banks TA, Tucker M, Macy E. Evaluating penicillin allergies without skin testing. Curr Allergy Asthma Rep 2019;19:27.
PUBMED | CROSSREF

Supplementary material 1

ASIA PACIFIC ASSOCIATION OF ALLERGY ASTHMA AND CLINICAL IMMUNOLOGY (APAAACI) SURVEY ON DRUG ALLERGY DIAGNOSTIC PROCEDURES & PRACTICES 2020

Thank you for spending some time to fill in this questionnaire. The objective of this is to survey the types of diagnostic procedures and practice parameters being used by APAAACI members for evaluation of drug allergy/hypersensitivity in both adults and children. It is our hope that the results of this survey will facilitate collaboration and education among the different allergy centres, and help develop care guidances that are specific to our region.

Please check all answers that apply.

Name of Society:

1	APAAACI Member Society	Australasian Society of Clinical Immunology and Allergy (ASCIA)	☐
		Asthma Allergy and Clinical Immunology Association of Thailand	☐
		Allergy and Clinical Immunology Society (Singapore) ACIS	☐
		Allergy and Immunology Society of Sri Lanka	☐
		Bangladesh Society of Allergy and Immunology	☐
		Chinese Society of Allergology	☐
		Hong Kong Institute of Allergy	☐
		Indian College of Allergy, Asthma and Applied Immunology	☐
		Indonesian Society of Allergy and Immunology	☐
		Japanese Society of Allergology (JSA)	☐
		Korean Academy of Asthma Allergy and Clinical Immunology (KAACI)	☐
		Malaysian Society of Allergy and Immunology (MSAI)	☐
		Mongolian Society of Allergology	☐
		Philippines Society of Allergy, Asthma and Immunology	☐
		Taiwan Academy of Allergy Asthma and Clinical Immunology	☐
		Individual members	☐
2	Do the Allergy Clinics in your country carry out evaluation for drug hypersensitivity/allergy?	Yes	☐
		No	☐
3	Do the Dermatology Clinics in your country carry out evaluation for drug hypersensitivity/allergy?	Yes	☐
		No	☐
4	If they do, which of the following guidelines are used?		

1. DRUG ALLERGY

1.1 EAACI 2019: EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity

1.2 EAACI 2018: Recognizing the potential of the primary care physician in the diagnosis and management of drug hypersensitivity

1.3 ENDA/EAACI 2016: Drug allergy passport and other documentation for patients with drug hypersensitivity – An ENDA/EAACI Drug Allergy Interest Group Position Paper

1.4 ENDA/EAACI 2016: In vitro tests for Drug Hypersensitivity Reactions. An ENDA/EAACI Drug Allergy Interest Group Position Paper (2016)

1.5 ICON 2014: International Consensus on Drug Allergy

1.6 AAAAI 2010: Drug allergy: an updated practice parameter

1.7 BSACI 2009: BSACI guidelines on the management of drug allergy

2. ANTIBIOTIC ALLERGY

2.1 EAACI 2019: Towards a more precise diagnosis of hypersensitivity to beta-lactams - an EAACI position paper

2.2 WAO 2013: Hypersensitivity reactions to non beta-lactam antimicrobial agents, a statement of the WAO special committee on drug allergy

2.3 EAACI 2009: Update on evaluation of hypersensitivity reactions to betalactams

2.4 EAACI 2003: Diagnosis of immediate allergic reactions to beta-lactam antibiotics

3. NSAID HYPERSENSITIVITY

3.1 SEAIC 2019: Position Statement of the Spanish Society of Allergology and Clinical Immunology on Provocation Tests with Aspirin/Nonsteroidal anti-inflammatory drugs

3.2 EAACI 2013: Hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) – classification, diagnosis and management: review of the EAACI/ENDA(#) and GA2LEN/HANNA*

4. INTRA-OPERATIVE ANAPHYLAXIS/ ANAESTHETIC AGENTS

4.1 EAACI 2019: Position paper on the investigation of perioperative immediate hypersensitivity reactions

4.2 Spanish Society of Allergology and Clinical Immunology (2018): Practical guidelines for perioperative hypersensitivity reactions

4.3 SFAR 2011: Reducing the risk of anaphylaxis during anesthesia: 2011 updated guidelines for clinical practice

4.4 BSACI 2009: BSACI guidelines for the investigation of suspected anaphylaxis during general anaesthesia

5. RADIOCONTRAST MEDIA

5.1 Spanish Society of Allergology and Clinical Immunology 2015: Clinical practice guidelines on the diagnosis and management of hypersensitivity reactions to contrast media

5.2 EAACI 2005: Management of hypersensitivity reactions to iodinated contrast media

6. VACCINE ADVERSE REACTIONS

6.1 Practice parameter 2017: Administration of influenza vaccines to egg allergic recipients

6.2 AAAAI 2012: Adverse reactions to vaccines 2012 parameter update

7. SKIN TESTS

7.1 ASCIA 2016: Skin prick testing for the diagnosis of allergic diseases (practitioner's manual)

7.2 EAACI 2015: In-vivo Diagnosis of Allergic Diseases – Allergen Provocation Tests

7.3 EAACI 2013: Skin test concentrations for systemically administered drugs — an ENDA/EAACI Drug Allergy Interest Group position paper

7.4 Patch testing in non-immediate drug eruptions by Romano A (2008)

7.5 AAAAI 2008: Allergy diagnostic testing: an updated practice parameter

8. IN-VITRO TESTS

8.1 EAACI 2016: In-vitro tests for drug hypersensitivity reactions

8.2 EAACI 2015: The Clinical Utility of Basophil Activation Testing in Diagnosis and Monitoring of Allergic Disease

9. DRUG PROVOCATION TESTS

9.1 WAO 2016: Risk and safety requirements for diagnostic and therapeutic procedures in allergology

9.2 EAACI/GA^{2}LEN guideline 2007: Aspirin provocation tests for diagnosis of aspirin hypersensitivity

9.3 EAACI 2003: Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations

10. DESENSITIZATION

10.1 EAACI 2013: Desensitization in delayed drug hypersensitivity reactions — an EAACI position paper of the Drug Allergy Interest Group

10.2 EAACI 2010: General considerations on rapid desensitization for drug hypersensitivity – a consensus statement

11. PHARMACOGENOMIC TESTING

Clinical Pharmacogenomics Implementation Consortium (CPIC) Guidelines & Publications

12. STEVENS-JOHNSON SYNDROME/TOXIC EPIDERMAL NECROLYSIS

12.1 British Association of Dermatologists Guidelines 2016

13. MASTOCYTOSIS AND MAST CELL ACTIVATION SYNDROMES

13.1 EAACI 2015: Drug hypersensitivity in clonal mast cell disorders

13.2 Mastocytosis and allergic diseases (2015)

14. PAEDIATRIC DRUG ALLERGY

14.1 EAACI 2019: Diagnosis and management of drug induced anaphylaxis in children: an EAACI position paper

14.2 EAACI 2018: Diagnosis and management of hypersensitivity reactions to NSAIDs in children and adolescents

14.3 NICE 2014 : Diagnosis and management of drug allergy in adults, children and young people

14.4 Royal College of Paediatrics and Child Health (RCPCH) 2012: Allergy Care pathway for Children – Drug Allergy

5	Are there adult drug allergy centres/clinics in your country?	Yes: please specify the number: No	☐ ☐
6	Are there paediatric drug allergy centres/clinics in your country?	Yes: please specify the number: No	☐ ☐
7	Which of the following tests for drug allergy/hypersensitivity are available in your country?	Skin prick and intradermal test → go to section (A) Specific IgE in-vitro tests → go to section (B) Other tests for immediate reactions → go to section (C) Lymphocyte transformation test → go to section (D) Patch testing → go to section (E) Pharmacogenomic tests → go to section (F) Drug provocation tests → go to section (G)	☐ ☐ ☐ ☐ ☐ ☐ ☐

(A) SKIN TESTING

8	Do you have access to penicillin skin test reagents?	Yes No	☐ ☐
9	From where do you obtain your skin test reagent for benzylpenicilloyl polylysine (PPL)?	In-house Diater ® Others – specify:	☐ ☐ ☐
10	From where do you obtain your skin test reagent for minor determinant mix (MDM)?	In-house Diater ® Others – specify:	☐ ☐ ☐
11	Which drugs are commonly skin tested in your country?	Penicillins Cephalosporins	☐ ☐

		Carbapenems	☐
		Non-beta lactam antibiotics	☐
		General anaesthetic agents	☐
		Local anaesthetic agents	☐
		Radiocontrast media (RCM)	☐
		NSAIDs	☐
		Others – specify: Corticosteroids, Insulins	☐
12	Who prepares the drugs for skin testing?	Allergist	☐
		Dermatologist	☐
		Pharmacist	☐
		Nurse clinician/specialist	☐
		Others – specify:	☐

(B) SPECIFIC IgE IN-VITRO TESTS

13	Are in-house or commercial assays available for these tests?	Commercial	☐
		In-house	☐
		Both	☐
		Neither	☐
14	Which commercial tests are available in your country?	CAP-FEIA (Phadia ImmunoCAP®)	☐
		RAST (Radioallergosorbent test®)	☐
		Euroimmune Allercoat 6 ELISA	☐
		FLOW-CAST (Buhlmann Labs®)	☐
		FLOW-2-CAST (Buhlmann Labs®)	☐
		CAST-ELISA (Buhlmann Labs®)	☐
		Others – specify:	☐
15	Which drugs are commonly tested using these in-vitro methods?	Alfa-gal	☐
		Ampicilloyl	☐
		Amoxicilloyl	☐
		Cefaclor	☐
		Cephalosporins	☐
		Chlorhexidine	☐
		Chymopapain	☐
		Gelatin	☐
		General anaesthetic agents	☐
		Insulin porcine, human, bovine	☐
		Morphine	☐
		NSAIDs	☐
		Penicilloyl G	☐
		Penicilloyl V	☐
		Pholcodine	☐
		Protamine	☐
		Suxamethonium	☐
		Tetanus toxoid	☐
		Others – specify:	☐

(C) OTHER TESTS FOR IMMEDIATE REACTIONS

16	Is serum total tryptase available in your country?	Yes No	☐ ☐
17	Is the basophil activation test (BAT) available in your country?	Yes No	☐ ☐

(D) LYMPHOCYTE TRANSFORMATION TESTS (LTT)

18	Is LTT used in the clinical or research setting?	Clinical Research Both clinical and research	☐ ☐ ☐
19	Where are these tests done?	In-house Sent to another facility in the same region/country Sent to another facility out of the region/country	☐ ☐ ☐
20	What drugs are commonly tested using LTT in your country?	Antibiotics (beta-lactams) Antibiotics (non-beta lactams) Anti-epileptics ACE inhibitors Anti-tuberculous drugs Diuretics NSAIDs & selective COX-2 inhibitors Pyrazolones Local anaesthetic agents HMG-CoA reductase inhibitors Opioids Neuromuscular blockers Contact allergens Others - specify:	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
21	For what types of delayed reactions are LTT commonly used for diagnosis?	Acute generalized exanthematous pustolosis (AGEP) Blood dyscracias (cytopaenias) Drug induced hypersensitivity syndrome (DiHS) Fixed drug eruption (FDE) Hepatitis Immunobullous eruptions Interstitial nephritis Maculopapular exanthems (MPE) Stevens Johnson syndrome Toxic epidermal necrolysis Vasculitis Others – specify:	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

(E) PATCH TESTS

22	Is this used in the clinical or research setting?	Clinical Research Both clinical and research	☐ ☐ ☐
23	What formulation of the drug is used for testing?	Pure substance Commercialized form of the drug Others – specify:	☐ ☐ ☐

24	What dilutions of the drug are used	0.1%	☐
		1%	☐
		5%	☐
		10% and 30%	☐
25	What vehicle is used?	Petrolatum	☐
		Water	☐
		Alcohol	☐
26	How do you obtain the drugs for patch testing?	In-house	☐
		Chemotechnique®	☐
		Commercial - specify:	☐
		Others - specify:	☐
27	Which of the following are also tested?	Preservative	☐
		Colouring	☐
		Excipient	☐
		None of the above	☐
28	When is the patch test reading done?	20 minutes	☐
		48 h (Day 2)	☐
		96 h (Day 4)	☐
		Day 7 if Day 2,4 negative	☐
29	Is photo patch testing done for photoallergens?	Yes	☐
		No	☐
30	What drugs have you used for patch testing?	Antibiotics (beta-lactams)	☐
		Antibiotics (non-beta lactams)	☐
		Anti-epileptics	☐
		Anti-tuberculous drugs	☐
		Aciclovir, valaciclovir	☐
		Corticosteroids	☐
		NSAIDs & selective COX-2 inhibitors	☐
		Cotrimoxazole	☐
		Diltiazem	☐
		Hydroxyzine	☐
		Heparin derivatives	☐
		Pseudoephedrine	☐
		Radiocontrast media	☐
		Statins	☐
		Tetrazepam	☐
		Others - specify:	☐
31	For what types of delayed reactions have you used patch testing to help in diagnosis?	Acute generalized exanthematous pustolosis (AGEP)	☐
		Drug induced hypersensitivity syndrome (DiHS)	☐
		Drug induced lupus erythematosus (DILS)	☐
		Fixed drug eruption (FDE)	
		Immunobullous eruptions	☐
		Maculopapular exanthems (MPE)	☐
		Stevens Johnson syndrome	☐
		Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE)	☐
		Toxic epidermal necrolysis	☐
		Vasculitis	☐
		Others – specify:	☐

(F) PHARMACOGENOMIC TESTS

32	Which tests are **mandatory** in your country before prescribing?	HLA-B*5701 (Abacavir) HLA-B*5801 (Allopurinol) HLA-B*1502 (Carbamazepine) Others – specify:	☐ ☐ ☐
33	Which tests are **recommended** in your country before prescribing?	HLA-B*5701 (Abacavir) HLA-B*5801 (Allopurinol) HLA-B*1502 (Carbamazepine) Others – specify:	☐ ☐ ☐ ☐

(G) DRUG PROVOCATION TESTS

34 What are the main indications for drug provocation tests in your centre/country?

Exclude hypersensitivity (non-suggestive history/non-specific symptoms)	☐
Provide safe pharmacologically/structurally non-related drugs in proven hypersensitivity (e.g. beta-lactams)	☐
Exclude cross-reactivity of related drugs in proven hypersensitivity (e.g. cephalosporin in a penicillin allergic)	☐
Definitive diagnosis in suggestive history with negative, non-conclusive or non- available allergological tests	☐
Others - specify:	☐

35	Who prepares the drug used for provocation testing?	Pharmacist Nurse clinician Doctor (IV/SC) Others – specify:	☐ ☐ ☐ ☐
36	What are the types of provocation tests used?	Open challenge Single blind placebo control Double blind placebo control Others – specify:	☐ ☐ ☐ ☐
37	What are the common routes of administration used?	Oral (tablet) Oral (capsule) Oral (syrup) Intramuscular Subcutaneous Intravenous Others – specify:	☐ ☐ ☐ ☐ ☐ ☐
38	What are the common routes of administration for aspirin provocation tests ?	Oral aspirin challenge Bronchial (inhalation) l-lysine-aspirin (l-ASA) challenge Nasal l-ASA challenge	☐ ☐ ☐

DESENSITIZATION

39	What are the common drugs for which desensitizations are done ?	Betalactam antibiotics	☐
		Non-betalactam antibiotics –specify:	☐
		Chemotherapeutic agents	☐
		Monoclonal antibodies	☐
		High-dose aspirin (chronic rhinosinusitis+/-nasal polyposis)	☐
		Low-dose aspirin (coronary artery disease)	☐
		Others – specify:	☐
40	Which are the common modes of desensitization ?	Rapid	☐
		Slow	☐
		Both rapid and slow	☐
41	Where are these commonly done ?	Inpatient general wards	☐
		Inpatient high dependency/ intensive care units	☐
		Outpatient day ward	☐
		Outpatient clinic	☐
		Others: specify:	☐

Thank you for completing this survey.

Drug Allergy Committee, APAAACI