

Original Article



Piperacillin-Tazobactam Allergies: An Exception to Usual Penicillin Allergy

Jane CY Wong ,¹ Elaine YL Au ,² Heather HF Yeung ,² Chak-Sing Lau ,¹ Philip Hei Li ^{1*}

¹Division of Rheumatology and Clinical Immunology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

²Division of Clinical Immunology, Department of Pathology, The University of Hong Kong, Queen Mary Hospital, Hong Kong



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Correspondence to

Philip Hei Li, MBBS, FHKCP

Division of Rheumatology & Clinical Immunology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong.

Tel: +852-2255-3348

Fax: +852-2816-2863

E-mail: liphilip@hku.hk

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ORCID iDs

Jane CY Wong

<https://orcid.org/0000-0002-6719-6787>

Elaine YL Au

<https://orcid.org/0000-0003-2724-6425>

Heather HF Yeung

<https://orcid.org/0000-0002-5577-5474>

Chak-Sing Lau

<https://orcid.org/0000-0001-6698-8355>

Philip Hei Li

<https://orcid.org/0000-0002-9155-9162>

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ABSTRACT

Purpose: The majority of penicillin allergy labels are false, and skin tests (ST) have high negative predictive value (NPV) of up to 90%. Piperacillin-tazobactam (PT) allergy has been suspected to be an exception to this, but existing literature is scarce. We investigate the epidemiology, clinical characteristics, testing outcomes and predictive value of ST in patients referred for suspected PT allergies.

Methods: The records of all patients referred for suspected PT allergy testing and prescription rates of PT in all Hong Kong public hospitals (2015–2019) were analyzed.

Results: There was an increase in both PT prescriptions and number of newly reported PT allergies between 2015 and 2019. The majority (91.1%) of patients with suspected PT allergy had at least 1 underlying medical co-morbidity or immunosuppressant use leading to increased risk of infections. Thirty-six patients with suspected PT allergy completed ST. Two patients had positive ST, and 32/34 patients with negative ST underwent drug provocation testing (DPT). Nine of these patients were diagnosed with PT allergy based on positive DPT. Overall, 11/34 (32.4%) were diagnosed with PT allergy and the NPV of ST was 71.9%.

Conclusions: There is growing utilization of PT and corresponding cases of suspected allergies. The majority of suspected PT allergies had increased risk for recurrent infections. Unlike other penicillin allergy, there is a high rate of genuine PT allergy (up to 30%) and a poor NPV of ST (up to 70%). DPT remains the gold standard for accurate diagnosis, and all patients with a suspected allergy should undergo thorough allergy workup.

Keywords: Hypersensitivity; drug; anti-bacterial agents; epidemiology; penicillins; skin tests; diagnosis

INTRODUCTION

Penicillins are the most frequently reported cause of drug allergy, with a prevalence of 2.0% and the cumulative incidence of 107 per 100,000 population in Hong Kong.¹ Drug allergy is a type of adverse drug reaction (ADR) which encompasses a spectrum of hypersensitivity reactions. Clinically, drug allergies are categorized into immediate- or delayed-type hypersensitivity reactions. However, most patients labelled with penicillin allergies are found not to be genuinely allergic after evaluation.^{2,7} Inaccurate penicillin allergy labels lead

to obligatory use of less effective antibiotics and are associated with a multitude of adverse consequences.^{8,11} Timely and accurate confirmation of suspected penicillin allergies are therefore imperative. Evaluation for penicillin allergies includes taking a comprehensive history, skin tests (ST) (including skin prick [SPT] and immediate/delayed intradermal tests [IDT]), and if indicated, drug provocation tests (DPT). Overall, ST for penicillin allergy have a high negative predictive value (NPV) (up to 90%) and are useful for predicting the absence of genuine allergy.^{2,3} However, a particular penicillin allergy with piperacillin-tazobactam (PT) has been suspected to be an exception to this—with high rates of genuine allergy and a poor NPV of ST.^{2,12}

Piperacillin is an extended-spectrum, semi-synthetic ureidopenicillin commonly found in combination with the β -lactamase inhibitor tazobactam.¹³ Tazobactam itself is a penicillinate sulfone which shares structural similarity with penicillin.¹⁴ When combined, PT offers excellent coverage against gram-positive and gram-negative bacteria (notably, *Pseudomonas aeruginosa*) compared to first-line aminopenicillins.¹³ PT is therefore the drug of choice for *P. aeruginosa* infections. It is the third most dispensed antimicrobial in Hong Kong and only second to amoxicillin-clavulanate and levofloxacin.^{15,16} We postulate that the increasing use of PT would inadvertently lead to increased sensitization and subsequent allergy.

A pilot study in Hong Kong noted alarmingly high rates of confirmed PT allergy.² Interestingly, all cases of confirmed PT allergy produced a negative ST and required DPT for confirmation. A previous case report also identified a similar phenomenon.¹² However, there have been few dedicated studies on PT allergy and literature remains scarce. To address these areas of uncertainty, we performed this pragmatic retrospective study to investigate the epidemiology, clinical characteristics and allergy testing outcomes of all patients referred for suspected PT allergies in Hong Kong. We also analyzed the performance of ST for PT allergy and reviewed the existing available literature on PT allergy.

MATERIALS AND METHODS

Prescription rates of PT in Hong Kong

The prescription rates of PT were extracted from the electronic records system of the Hong Kong Hospital Authority (HA). Data including the number of unique patients prescribed with PT and sorted by cluster, between January 1, 2015 and December 31, 2019 were analyzed anonymously. HA is the sole public-funded healthcare provider in Hong Kong, serving a population of more than 7 million patients. It is organized into 7 clusters (namely Hong Kong East, Hong Kong West, Kowloon Central, Kowloon East, Kowloon West, New Territories East and New Territories West) based on geographical locations and provide around 90% of inpatient care in Hong Kong.^{17,18} Our data likely capture the vast majority of patients receiving PT in Hong Kong during the study period given that PT can only be administered parentally and likely used in an inpatient setting.

Referrals for suspected PT allergies and data extraction

We reviewed the medical records of all adult patients referred to Queen Mary Hospital (QMH), Hong Kong between January 1, 2015 and March 31, 2020 with suspected PT allergies anonymously. All suspected PT allergies were clarified and reported by the patients' attending physicians into the HA's electronic Clinical Management System. Patients with non-allergic ADR were excluded. Extracted data included: age, sex, allergy history (details of

index reaction: indications for PT; presenting manifestations [rash/urticaria, angioedema, anaphylaxis, gastrointestinal involvement, unknown/others]; suspected type of reaction by attending allergist [immediate/delayed/unknown]; duration since index reaction), presence of concomitant drug allergy labels, medical co-morbidities (including history of asthma or chronic obstructive pulmonary disease [COPD]), bronchiectasis, chronic kidney disease (defined by estimated glomerular filtration rate of < 60 mL/min, cirrhosis, diabetes mellitus, haematological disease, malignancy, rheumatological disease and concurrent use of immunosuppressants) and outcome of allergy testing. “Unknown” manifestation or type of reaction was defined by a confirmed PT allergy label in the patient's medical record, but the index reaction or manifestation could not be retrieved or recalled by the patient. Only patients who consented and completed ST were included.

ST (SPT, immediate/delayed IDT) and DPT were performed in accordance to the British Society for Allergy and Clinical Immunology and Hong Kong Institute of Allergy guidelines^{19,20}: SPT and IDT were performed using a commercially available kit with benzylpenicilloyl-poly-L-lysine (PPL) and the “minor determinant” (MD)—benzylpenicilloate (DAP; Diater, Madrid, Spain), in addition to benzylpenicillin, amoxicillin and PT (piperacillin:tazobactam, 4 g:0.5 g; Aurobindo Pharma Ltd., Hyderabad, India). For PT, SPT was performed with neat concentration (piperacillin:tazobactam, 200 mg:25 mg [*i.e.* 225 mg/mL]) and IDT diluted to piperacillin:tazobactam, 20 mg:2.5 mg (*i.e.* 22.5 mg/mL).

SPT and immediate IDT were performed for immediate-type reactions, and delayed IDT (also known as “late skin test reading”) were performed for delayed-type reactions; as per the European Academy of Allergy and Clinical Immunology recommendations.²¹ For immediate-type reactions, SPT and IDT reactions were read at 20 minutes and results were considered positive if the wheal size expansion was > 3 mm diameter in any direction from the original prick or bleb. For delayed-type reactions, delayed IDT results were read at 48 hours and considered positive if there was any infiltrated erythema with a diameter > 5 mm. Delayed IDT, rather than patch testing, was performed due to its greater sensitivity and ability to diagnose more patients with non-immediate reactions to penicillins.²² If the timing of the index allergy reaction was unclear, SPT as well as both immediate and delayed readings of IDT were performed. Patients with positive SPT or immediate/delayed IDT were diagnosed to be allergic to PT. Those with negative ST proceeded with a graded DPT to confidently exclude allergy.

All DPTs were performed during hospital admissions with close monitoring. DPT protocols were individualized according to the attending allergist's assessment of the patient's risk. In general, PT was administered intravenously in a graded approach (usually at least 3-steps, with 30-minute intervals) until the maximum single unit dose was reached. Patients were observed for at least 2 hours after the final DPT step to observe any immediate reactions. Patients were asked to contact our specialist nurse hotline if there were any delayed reactions and return for the allergist's review. All patients were contacted after DPT by our specialist nurse, after a time interval greater to that of the index reaction, to confirm no reaction (*i.e.* negative DPT). Any immediate and delayed reactions were assessed by the attending allergist and diagnosed accordingly. Patients were diagnosed as non-allergies if they had a negative DPT.

Patients who had a negative ST but did not undergo confirmatory DPT were excluded from analysis. QMH is the only referral center with a formal immunology/allergy service under the HA to provide drug allergy testing services. QMH therefore receives referrals from across the entire territory and this cohort represents almost all referrals for PT allergies in Hong Kong

during the study period. Data extraction was approved by the Institutional Review Board of the University of Hong Kong/HA Hong Kong West Cluster.

Statistical analysis

Categorical variables are expressed as number (percentage), and continuous variables are expressed as either mean (standard deviation) or median (range) when appropriate. The χ^2 statistic and independent *t*-test were used to compare categorical and continuous variables between groups in association analysis, respectively. A *P* value of less than 0.05 was considered statistically significant for the multivariate analysis. SPSS Statistics version 20 (IBM Corp., Armonk, NY, USA) was used for all analyses.

Literature review of existing publications

A comprehensive literature search of relevant literature was conducted using PubMed. The search included articles published between 2000 and 2019. Key search terms included “piperacillin-tazobactam,” “allergy,” “anaphylaxis,” and “hypersensitivity.” Data including manifestations and allergy workup were recorded. All available patient data from publications were reviewed. Only reports published in English and those providing convincing evidence of PT allergy, *e.g.* positive allergy test results (ST, DPT or relevant *in vitro* tests) were included.

RESULTS

A large number of PT prescription with a corresponding increase in newly reported PT allergies between 2015 and 2019

Fig. 1 shows the number of patients prescribed PT and the number of newly reported PT allergies among referrals between 2015 and 2019. There was a steady increase in the number of patients prescribed PT throughout the study period from 39,044 in 2015, with a > 150% increase, to 59,807 in 2019. This growing utilization of PT was consistent longitudinally during the study period as well as geographically across different clusters. Furthermore,

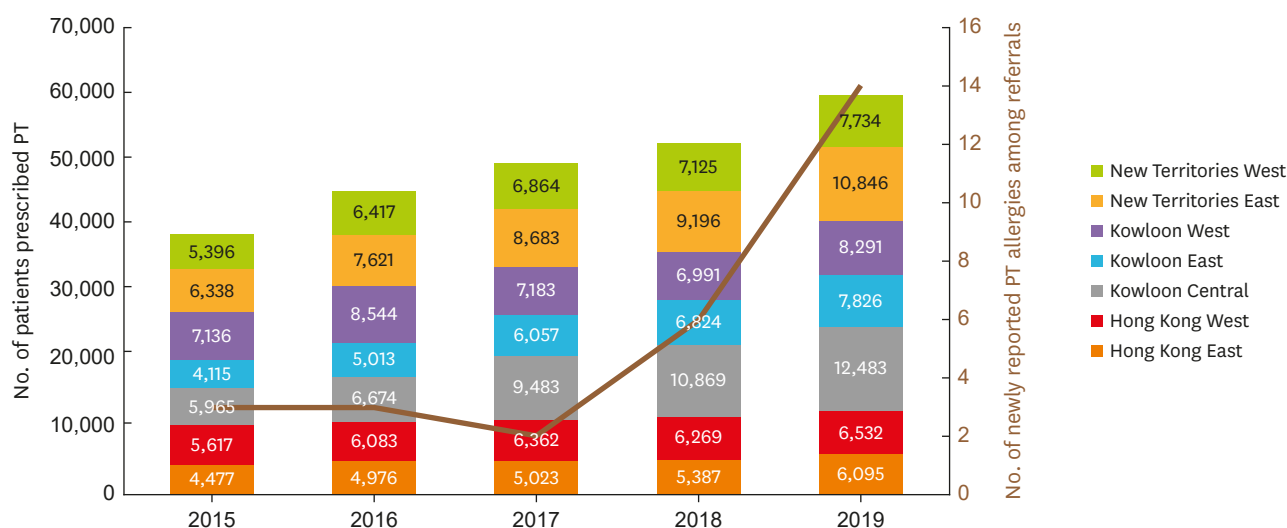


Fig. 1. Number of patients prescribed PT and the corresponding number of newly reported PT allergies among referrals between 2015 and 2019. PT, piperacillin-tazobactam.

Table 1. Demographic and clinical characteristics of 34 patients who completed evaluation for suspected PT allergy

Characteristics	Total (n = 34)	Allergic (n = 11)	Non-allergic (n = 23)	P value
Male sex	14 (41.2)	5 (45.5)	9 (39.1)	0.726
Age (yr)	52 (21–85)	57 (29–78)	44 (21–85)	0.411
Duration since index reaction in years (yr)	1.5 (0–21)	1 (0–15)	2 (0–21)	0.278
Concomitant drug allergy labels	26 (76.5)	7 (63.6)	19 (82.6)	0.222
Medical comorbidities				
Asthma or COPD	2 (5.9)	1 (9.1)	1 (4.3)	0.582
Bronchiectasis	8 (23.5)	2 (18.2)	6 (26.1)	0.611
Chronic kidney disease	7 (20.6)	3 (27.3)	4 (17.4)	0.505
Cirrhosis	2 (5.9)	0	2 (8.7)	0.313
Diabetes mellitus	4 (11.8)	3 (27.3)	1 (4.3)	0.052
Haematological disease	5 (14.7)	3 (27.3)	2 (8.7)	0.152
Malignancy	4 (11.8)	1 (9.1)	3 (13.0)	0.738
Rheumatological disease	5 (14.7)	2 (18.2)	3 (13.0)	0.692
Concurrent use of immunosuppressants	15 (44.1)	7 (63.6)	8 (34.8)	0.113
History of index reaction				
Immediate-type reactions	16 (47.1)	5 (45.4)	11 (47.8)	0.897
Cutaneous	9/14 (64.3)	4/5 (80.0)	7/11 (63.6)	0.889
Respiratory	6/14 (42.9)	3/5 (60.0)	3/11 (24.0)	0.21
Cardiovascular	5/14 (35.7)	4/5 (80.0)	3/11 (27.3)	0.611
Gastrointestinal	0	0	0	-
Delayed-type reactions	10 (29.4)	6 (54.5)	4 (17.4)	0.026
Unknown or forgotten history	8 (23.5)	0	8 (34.8)	0.025

Values are presented as number (%) or median (range).

PT, piperacillin-tazobactam; COPD, chronic obstructive pulmonary disease.

this growth corresponded with an increasing number of newly reported PT allergies among patients referred for allergy workup.

Over 90% of referred patients had underlying medical co-morbidities or concurrent use of immunosuppressants leading to increased risk of infections

Overall, the male-to-female ratio was 0.7, median age was 52 years and median duration from the index reaction to their first allergy workup was 1.5 years. Thirty out of 34 (91.1%) patients with suspected PT allergy had at least 1 underlying medical co-morbidity or concurrent use of immunosuppressants leading to increased risk of infections. Their demographic and clinical characteristics are shown in **Table 1**.

High rate of confirmed PT allergies and a low negative predictive value of ST

A total of 36 patients with PT allergy labels were referred to us and completed ST for suspected PT allergy. **Fig. 2** shows the investigations and outcomes of all 36 referred patients. Notably, 2 patients with negative ST died prior to the completion of allergy workup from pneumonia caused by *Acinetobacter baumannii* and *Enterobacter spp.*

The remaining 34 patients completed full workup for suspected PT allergy, with 11 (32.4%) diagnosed with PT allergy by either positive ST or DPT. Details of the allergy investigation results of 11 patients with positive ST or DPT are shown in **Table 2**. Only 2 patients (18.2%) were diagnosed by positive ST, of which one had selective sensitization to PT, while the other had sensitization to MD, BP and PT (*i.e.* non-selective reactor). The remaining 9 patients were diagnosed with PT allergy based on positive DPTs following negative ST results (*i.e.* false-negative ST). Therefore, the NPV was 71.9%. With our individualized and graded approach, all DPT reactions were mild and only 1 patient required a short course of systemic steroids for the treatment of a delayed morbilliform eruption. There were no cases with severe cutaneous adverse reactions (SCARs). Administration of adrenaline was never required.

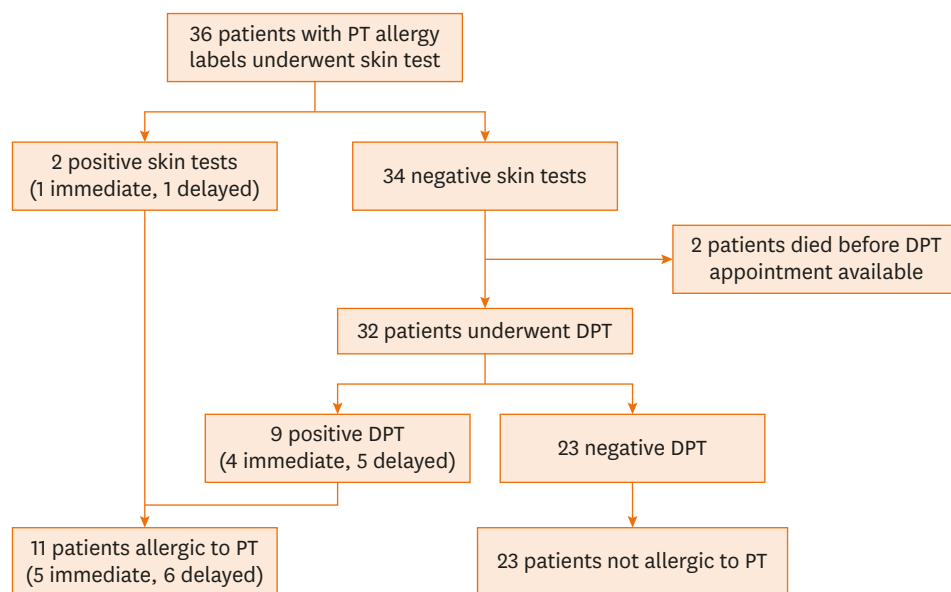


Fig. 2. Investigations and outcomes of 36 patients who were referred for suspected PT allergy testing. PT, piperacillin-tazobactam; DPT, drug provocation tests.

PT-allergic patients more likely have histories of delayed-type reactions and less likely to have unknown/forgotten histories

As shown in **Table 1**, there were no differences in age, sex, duration since the index reaction, presence of concomitant drug allergy labels or medical comorbidities between PT allergic and non-allergic patients. However, PT allergic patients were significantly more likely to have index reactions consistent with delayed-type reactions (54.4% vs. 17.4%, $P = 0.026$) and less likely to have an unknown or forgotten history (0% vs. 34.8%, $P = 0.025$).

Review of the previous literature regarding PT allergy

A total of 12 publications which included allergy testing for PT allergy were found between 2000 and 2019 and are shown in **Table 3**.^{2,12,23-32} There were a total of 29 patients consisting of 7 immediate-type and 22 delayed-type reactions. Eighteen patients had reported ST results: 10/18 (55.6%) patients had positive skin tests (2 immediate-type and 8 delayed-type), the remaining 8 ST negative patients (4 immediate-type and 4 delayed-type) were diagnosed by

Table 2. Allergy investigation results of 11 patients with positive ST or DPT

Patient	Age	Sex	Type of reaction	ST results					DPT result	DPT manifestations
				PPL	MD	Benzylpenicillin	Amoxicillin	PT		
1	29	F	Delayed	-	-	-	-	+ (delayed)	Not done	-
2	35	F	Delayed	-	-	-	-	-	+ (delayed)	Maculopapular rash
3	72	M	Immediate	-	-	-	-	-	+ (immediate)	Urticaria
4	57	F	Delayed	-	-	-	-	-	+ (delayed)	Maculopapular rash
5	60	F	Immediate	-	-	-	-	-	+ (immediate)	Urticaria
6	78	F	Immediate	-	+ (immediate)	+ (immediate)	-	+ (immediate)	Not done	-
7	42	F	Delayed	-	-	-	-	-	+ (delayed)	Maculopapular rash
8	52	M	Delayed	-	-	-	-	-	+ (delayed)	Fixed drug eruption
9	68	M	Immediate	-	-	-	-	-	+ (immediate)	Urticaria
10	65	M	Delayed	-	-	-	-	-	+ (delayed)	Macular rash
11	51	M	Immediate	-	-	-	-	-	+ (immediate)	Urticaria

ST, skin tests; DPT, drug provocation tests; PPL, benzylpenicilloyl-poly-L-lysine; MD, minor determinant; PT, piperacillin-tazobactam.

Table 3. Existing literature on PT allergy during the period 2000–2019

Reference	Year	Type of reaction	No. of patients	SPT or IDT result	Was DPT performed	Other allergy tests	
Romano <i>et al.</i> ²³	2000	Immediate	Anaphylaxis	1	1 positive IDT to PT	No	slgE (penicillin G/V, ampicillin, amoxicillin, piperacillin) negative
Rank and Park ¹²	2007	Immediate	Anaphylaxis	1	1 negative	Yes	
Jurado-Palomo <i>et al.</i> ²⁴	2010	Delayed	DRESS	1	Not done	No	Positive LTT to PT
Song <i>et al.</i> ²⁵	2010	Delayed	MP Rash	1	Not done	Yes	
Kim <i>et al.</i> ²⁶	2011	Immediate	Anaphylaxis	1	Not done	No	Positive piperacillin-human serum albumin conjugate IgE
Park <i>et al.</i> ²⁷	2011	Delayed	MP rash with eosinophilia	1	Not done	Yes	
Cabanas <i>et al.</i> ²⁸	2014	Delayed	DRESS	8	3 positive for PT 1 negative PT 4 not done	No	8 Positive LTT to PT 1 positive patch test to PT
Tomida <i>et al.</i> ²⁹	2016	Delayed	LABD	1	1 not done	No	Positive LTT to PT
Rutkowski <i>et al.</i> ³²	2016	Delayed	DRESS	6	5 positive for PT, 1 not documented	No	
Gaspar-Marques <i>et al.</i> ³⁰	2018	Immediate	Anaphylaxis	1	1 positive to PT penicillin G, major & minor determinants	No	
Kornmehl <i>et al.</i> ³¹	2018	Delayed	FDE	1	Not done	Yes	
Li <i>et al.</i> ²	2019	Both		6	6 negative	Yes	

PT, piperacillin-tazobactam; SPT, skin prick tests; IDT, intradermal tests; DPT, drug provocation tests; slgE, specific immunoglobulin E; DRESS, drug rash with eosinophilia and systemic symptoms; AGEP, acute generalized exanthematous pustulosis; LTT, lymphocyte transformation tests; MP, maculopapular; LABD, linear IgA bullous dermatosis; FDE, fixed drug eruption.

either positive DPT (7: 4 immediate-type and 3 delayed-type) or lymphocyte transformation tests/patch test (1 patient). If all patients with positive ST were genuinely PT-allergic, the false-negative rate (“miss rate”) would to 44.4%.

DISCUSSION

Previously, PT “allergies” have mostly been reported in sporadic case reports only and many without proper allergy workup. In this study, we present the largest published cohort of patients with suspected PT allergy who underwent allergological investigations. Our study is unique as only patients who had undergone complete PT allergy workup (*i.e.* either positive ST or completed DPT) were included. We identified a growing trend of PT utilization which corresponded with an increase in the number of reported PT allergies. Around one-third of patients with suspected PT allergy were diagnosed as being allergic either by ST or DPT and the NPV for ST was only 71.9%. In contrast, only 10%–20% of all suspected β -lactam allergies were genuine after workup.^{2,3,33,34} In comparison, the NPV for penicillin ST is greater than 90%.^{2,3,35} A literature review of all existing reports on PT allergy since 2000 also reflected the high rate of false-negative ST. In view of the low NPV, we caution the interpretation of ST results and to always consider a cautious DPT if STs are negative.

In the era of increasing antimicrobial resistance, PT ranked the highest in terms of usage and expenditure among intravenous broad-spectrum antibiotics since 2004.³⁶ Between 2015 and 2019, we identified a greater than 150% increase in patients prescribed with PT. Almost 60,000 patients received PT in 2019 alone. In Hong Kong, PT is usually reserved for inpatients as a second-line antibiotic or used empirically in those with co-morbidities, such as bronchiectasis with *P. aeruginosa* colonization as 92% of isolates remain susceptible to PT.¹⁶ These prescription practices are reflected in this current cohort, with more than 90% of patients with suspected PT allergy having at least 1 medical co-morbidity or were on concurrent immunosuppressants leading to increased risk of infections. We postulate that

these at-risk patients were exposed to repeated courses of PT, increasing their likelihood for sensitization and subsequent development of allergy. This also explains the corresponding increase in the number of newly reported PT allergies during the study period.

Incomplete workup for those with allergy labels in this particularly vulnerable cohort can lead to detrimental clinical outcomes. It severely restricts the choice of antibiotics to suboptimal alternatives and increases the likelihood for bacterial resistance.^{9,41} This was evidenced by 2 patients in our study who unfortunately died from *A. baumannii* and *Enterobacter spp.* pneumonia (both susceptible to PT) before an appointment could be arranged for DPT. Arguably, their clinical outcomes may have been different if access to earlier allergy appointment were available. Given the lack of allergists in Hong Kong, the waiting time for a supervised DPT usually takes many weeks to months.³⁷ This highlights the urgent need for the expansion of allergy services to de-label incorrect PT allergies or identify safe alternatives for these patients.

Finally, PT allergies were more likely to have an index reaction consistent with delayed-type reactions and less likely to have an unknown or forgotten history. In fact, all patients who were confirmed PT-allergic were able to recall details of their index reactions. This finding is similar to that of a previous study in the UK where a history of an unknown index β -lactam was one of the criteria to predict a “low risk” β -lactam allergy.³ We suggest to physicians that they clarify these important details during history taking to help assess the pre-test probability of PT allergy prior to allergy testing.

There are several limitations to our study. First, we have a relatively small cohort, and arguably patients with severe delayed-type reactions (such as SCARs) reported in previous case reports were under-represented. However, we feel this pragmatic study reflected the everyday practice of an allergist with a general low rate for these severe reactions. As illustrated in the literature review, previous publications likely reflected a reporting bias for more severe cases. It may be possible that the performance of ST improves with the severity of the index reaction. Given the relatively small number of “true positive” cases, we calculated the NPV of ST for both immediate- and delayed-type reactions. Future prospective and collaborative studies are required to study the full spectrum of PT allergies as well as the predictive value of ST for immediate-type and delayed-type reactions separately. We advocate for further international collaboration, especially among Asian countries, to combine existing registries and form prospective databases.³⁸⁻⁴² Secondly, we were unable to fully study the cross-reactivity of PT allergy as only 2 patients had positive ST and we did not perform DPT with other non-PT penicillins in confirmed allergies. Cross-reactivity between other penicillins likely exists as evidenced by 1 patient who was sensitized to MD and BP as well as PT (*i.e.* non-selective reactor). Thirdly, although generally deemed less useful in penicillin allergy testing, we did not have the facilities to study the utility of *in vitro* test.⁴³ Associations of HLA B62 and drug rash with eosinophilia and systemic symptoms caused by PT had also been previously reported.³² Finally, it is possible that the low NPV could be explained by the lack of validated ST concentrations for PT. However, in comparison to previous reports, we had already used higher drug concentrations of 225 mg/mL (neat concentration) for SPT and 22.5 mg/mL (1:10 dilution) for IDT.^{23,28,30} Furthermore, we did not have testing available for standalone piperacillin or tazobactam and therefore unable to exclude or further study the possibility of an allergy to the β -lactamase inhibitor, tazobactam. Allergy to another β -lactamase inhibitor, clavulanic acid, accounted for around 30% of immediate reactions to amoxicillin-clavulanate, and testing for clavulanic-acid allergy has been recommended

when conventional ST are negative.⁴⁴ Differentiating between a piperacillin and tazobactam allergy would be important for broadening the choices of antibiotics, especially as the novel combination of cephalosporin and β -lactamase inhibitor, ceftolozane-tazobactam, becomes more widely available. To date, there has been no reported allergy against ceftolozane or the combination drug and it would be interesting to explore the tolerance of ceftolozane-tazobactam in PT allergic patients in the future.

In conclusion, we identified a growing trend in PT allergy and report the largest cohort of suspected PT-allergic patients to date. As an exception to usual penicillin allergies, around one-third of patients with suspected PT allergy were confirmed as allergic and the NPV of ST was only around 70%. The growing utilization of PT corresponded to the increase in reported cases of suspected PT allergies. The majority of patients with PT allergy had underlying medical comorbidities and at increased risk for recurrent infections. Without proper drug allergy evaluation, allergy labels can lead to detrimental consequences. To tackle the growing and difficult PT allergy, a dedicated penicillin allergy clinic has been established in Hong Kong and prospective studies into their efficacy are underway.

Future studies are warranted to assess validity and to compare with other populations because of differences in ethnicity, antibiotic practices, spectrum of bacteria, resistance trends and patterns. The increasing trend of PT allergy is unlikely only restricted to Hong Kong and we urge other investigators to study the burden of PT allergy in their populations as well.

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