

TABLE I. Concentrations for penicillin skin testing reagent

Reagent	Epicutaneous	Intradermal
Penicilloyl-polylysine (PRE-PEN)	6×10^{-5} M	6×10^{-5} M
Penicillin G	10,000 units/mL	100 units/mL* 1000 units/mL* 10,000 units/mL
Penicilloate	0.01 M to 0.02 M	0.01 M to 0.02 M
Penilloate	1.5×10^{-4} M*	1.5×10^{-4} M
	1.5×10^{-3} M	1.5×10^{-3} M

M, mole.

*Optional, based on physician discretion.

mol/L) than that featured in the only validated and commercialized kit. To supply a concentration in alignment with existing practice, we suggest featuring concentrations of 1.5×10^{-4} mol/L and 1.5×10^{-3} mol/L. See Table I to view the suggested table contents.

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REFERENCES

1. Broyles A, Banerji A, Barmettler S, Benhamu M, Biggs C, Blumenthal K. Practical guidelines for the evaluation and management of drug hypersensitivity: specific drugs. *J Allergy Clin Immunol Pract* 2020;8:S16-116.
2. Romano A, Atanaskovic-Markovic M, Barbaud A, Bircher AJ, Brockow K, Caubet JC, et al. Towards a more precise diagnosis of hypersensitivity to beta-lactams—an EAACI position paper. *Allergy* 2020;75:1300-15.
3. Brockow K, Aberer W, Bircher A, Przybilla B. Correction to: Guideline for the diagnosis of drug hypersensitivity reactions. *Allergo J Int* 2018;27:40-2.
4. Wurpts G, Aberer W, Heinrich D, Brehler R, Jakob T, Kreft B, et al. Guideline on diagnostic procedures for suspected hypersensitivity to beta-lactam antibiotics: Guideline of the German Society for Allergology and Clinical Immunology (DGAKI) in collaboration with the German Society of Allergology (AeDA), German Society for Pediatric Allergology and Environmental Medicine (GPA), the German Contact Dermatitis Research Group (DKG), the Austrian Society for Allergology and Immunology (ÖGAI), and the Paul-Ehrlich Society for Chemotherapy (PEG). *Allergo J Int* 2019;28:121-51.
5. Laboratorios Diater SA. Zusammenfassung der merkmale des arzneimittels: DAP Penicillin Test Kit1-13.

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Reply to “Penilloate and penicilloate concentrations in practical guidance recommendations”



To the Editor:

We read with great interest Dr Maroto's observations¹ regarding our article² and specifically his concern that the concentrations of 2 minor determinants of benzylpenicillin (ie, penilloate and penicilloate) for skin testing shown in Table I differ from those indicated in some articles published in European journals.^{3,4} In particular, he points out that the maximum concentration of penilloate to be used for penicillin skin tests shown in Table I

(ie, 0.02 M = 20×10^{-3} mol/L) is higher than that (1.5×10^{-3} mol/L) recommended for the only fully validated and commercially available penilloate diagnostic reagent, which is included in the DAP Penicillin Test Kit (Diater, Leganés, Spain).

We acknowledge that Dr. Maroto's observations are pertinent. The concentrations of the penicillin reagents shown in Table I of our article² are consistent with those indicated in the 2010 practice parameter.⁵ In fact, this document⁵ states that penicilloate and penilloate are used for skin testing at 0.01 M (ie, 10×10^{-3} mol/L) even though they have never been commercially available in the United States. Therefore, the maximum concentration of penilloate shown in Table I of our article² and that indicated in the 2010 practice parameter⁵ are higher than that (1.5×10^{-3} mol/L) recommended in the aforementioned articles,^{3,4} one of which⁴ is a European Academy of Allergy and Clinical Immunology position paper regarding the diagnosis of hypersensitivity to β -lactams.

Actually, Table I of our article² refers to penicillin reagents marketed (penicilloyl-polylysine, PPL [PRE-PEN; AllerQuest LLC, West Hartford, Conn]) or otherwise used (penilloate and penicilloate) in the United States. In fact, benzylpenicilloyl-octa-L-lysine (BP-OL), which is marketed in Europe by Diater and is mentioned in the text together with penilloate, is not included in Table I. However, considering that our article² is a practical guide for the evaluation of drug hypersensitivity and that readers are not only from the United States, we totally agree with Dr. Maroto that it is advisable to also provide information on the maximum concentrations of benzylpenicillin reagents marketed outside the United States and currently used in clinical practice.

In this regard, the recommended final concentrations of BP-OL and penilloate are 8.64×10^{-5} mol/L and 1.5×10^{-3} mol/L, respectively.

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REFERENCES

1. Maroto E. Penilloate and penicilloate concentrations in practical guidance recommendations. *J Allergy Clin Immunol Pract* 2021;9:1418-9.

2. Broyles AD, Banerji A, Barmettler S, Biggs CM, Blumenthal K, Brennan PJ, et al. Practical guidance for the evaluation and management of drug hypersensitivity: specific drugs. *J Allergy Clin Immunol Pract* 2020;8(S):S16-116.
3. Torres MJ, Romano A, Celik G, Demoly P, Khan DA, Macy E, et al. Approach to the diagnosis of drug hypersensitivity reactions: similarities and differences between Europe and North America. *Clin Transl Allergy* 2017;7:7.
4. Romano A, Atanaskovic-Markovic M, Barbaud A, Bircher AJ, Brockow K, Caubet JC, et al. Towards a more precise diagnosis of hypersensitivity to beta-lactams—an EAACI position paper. *Allergy* 2020;75:1300-15.
5. 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.

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New aspects of fundamental pathology and environmental control: Important issues in allergic bronchopulmonary mycosis



To the Editor:

We read with interest the paper by Okada et al in a recent issue of *J Allergy Clin Immunol Pract*.¹ This case report of allergic bronchopulmonary mycosis (ABPM) suggested the importance of identifying and controlling environmental antigen exposure, but we have some questions.

The fundamental pathology of allergic bronchopulmonary aspergillosis is recognized as an eosinophilic mucus plug.² Applied to ABPM caused by *Schizophyllum commune*, the acute clinical manifestations would be difficult to explain. Based on our previous data using bronchoprovocation examination of *S. commune* crude antigens and environmental exposure, the essential condition underlying this disease is not the mucus plug itself, which would be produced subsequently, but eosinophilic airway inflammation, which spreads from the bronchi to alveoli evoked by inhaled antigens.³

Although an inflammatory reaction occurs at the time of acute exacerbation, a mucus plug would not be formed suddenly. In this case, did the authors immediately notice mucus plug formation at the next onset occurring 9 months after the first episode? Did the reported patient have a fever immediately after discharge from the first hospitalization?

On the basis of the basic pathophysiology of ABPM associated with *S. commune*, we proposed the following 4 treatment methods previously:³

1. Removal of fungi from the airway with antifungal drugs
2. Inhaled or oral steroids for eosinophilic bronchitis caused by fungal colonization
3. Bronchoscopic suctioning of mucus plugs
4. Environmental management from the perspective of *S. commune* ecology.

In this case, it was emphasized that improvement of symptoms was achieved by only environmental management without drug therapy. Cleaning at the time of examination with bronchoscopy might be a potent treatment leading to symptom improvement.

It is described that fungal culture of the air conditioner filter was not performed, but the presence of *S. commune* remaining in the indoor environment can be investigated, even after the air conditioner has been removed. *S. commune* and *Aspergillus fumigatus* are included in the same filamentous fungus group.

However, *A. fumigatus* is commonly detected on the filters of air conditioning systems, whereas *S. commune* is usually not detected. If accurate knowledge of the ecology of the *S. commune* is provided, the patient would not have to quit his job around air conditioning systems.

Further discussion and sharing of clinical practice regarding this case will be useful for establishing the pathophysiology and disease management of ABPM.

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REFERENCES

1. Okada N, Oguma T, Shiraishi Y, Nishimura T, Hattori S, Tanaka J, et al. Repeated exacerbation by environmental exposure and spontaneous resolution of allergic bronchopulmonary mycosis. *J Allergy Clin Immunol Pract* 2021;9:558-60.e1.
2. Tamura A, Hebisawa A, Kurashima A, Kawabe Y, Machida K, Yotsumoto H, et al. The use of bronchofiberscopy for diagnosis of allergic bronchopulmonary aspergillosis. *Intern Med* 1997;36:865-9.
3. Ogawa H, Fujimura M, Takeuchi Y, Makimura K, Satoh K. The definitive diagnostic process and successful treatment for ABPM caused by *Schizophyllum commune*: a report of two cases. *Allergol Int* 2012;61:163-9.

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Reply to "New aspects of fundamental pathology and environmental control: Important issues in allergic bronchopulmonary mycosis"



To the Editor:

Ohkura et al¹ offered interesting insights and raised several questions in their correspondence regarding our report on a case with repeated exacerbation by environmental exposure and spontaneous resolution of allergic bronchopulmonary mycosis (ABPM).²

First, they raised the question of how quickly mucus plugs can be formed during acute exacerbation of ABPM. We could not demonstrate direct evidence that mucus plug formation occurred during the acute episode in the present case due to the lack of radiographic data before the first visit to our hospital. There have been no studies examining the time required for mucus plug formation after allergen exposure in ABPM. The history of transient exposure to a moldy air conditioner, acute symptoms including high fever and elevated serum C-reactive protein levels in the presented case suggested that the patient was exposed to higher levels of fungal allergen than usual for ABPM cases or