

False tolerant food challenges in children with food protein-induced enterocolitis syndrome



To the Editor:

We were interested to read Argiz et al.¹ description of false-negative resolution challenges for food protein-induced enterocolitis syndrome (FPIES) leading to reactions at home on subsequent exposure. We report 2 further cases from our own practice and our 5-year experience of undertaking 2 sequential hospital-based challenges for this indication.

The first child was male, who presented with a history of recurrent vomiting within an hour of eating chicken at 6 months. He was challenged at 43 months to chicken, receiving 0.38 g/kg of protein. He tolerated this challenge, and home reintroduction was advised. On further reintroduction at home, 2 weeks later he developed vomiting, diarrhea, and pallor 3 hours after ingesting chicken and required hospital admission. A subsequent challenge 2 years later produced a similar reaction requiring intravenous fluids and ondansetron.

This case prompted the introduction of a dual challenge protocol, to ensure that subsequent unexpected reactions occurred under supervision. If there was no reaction at the first challenge, we undertook a second challenge 2 to 6 weeks later with administration of an age appropriate portion size and 4 to 6 hours of observation. Over 5 years, 24 patients had 30 first (several patients had several foods tested) and 20 second challenges—a total of 50 resolution challenges. Twenty challenges had a second challenge. There was 1 further false tolerant challenge. In addition to these 2 cases of false tolerant challenge, 3 active FPIES cases were detected at the first challenge.

The second child was a female who presented at 10 months with profuse vomiting 3 hours after scrambled egg, becoming pale and floppy with loose stool the next day. At 33 months, she had a skin prick test (SPT) to a raw hen egg of 4 mm, baked egg slurry 0 mm. She tolerated a baked egg challenge, receiving 0.12 g/kg of egg protein. Three weeks later she vomited 3 hours after a second baked egg challenge of 0.06 g/kg of protein and was treated with intravenous fluids. Three years later her SPT was 0 mm to a raw egg. She vomited 4 hours after 0.12 g/kg of baked egg protein and was treated with intravenous ondansetron and fluids.

These 2 cases are in addition to those described by Argiz et al.¹ Another case has been described in a study of 26 FPIES resolution challenges to 15 patients at John Hopkins Paediatric Food Allergy Clinic.² Their challenge to 0.6 g/kg of chicken/turkey was concluded to be falsely negative when the patient reacted 1 month later during home reintroduction 2 hours after ingesting turkey, requiring hospital treatment. There may be other early cases of this phenomenon to cow's milk, but the description is not as clear cut.^{3,4}

False tolerant FPIES challenges after a period of abstinence occur infrequently but are seen across different countries. It is possible that the allergen exposure at the first challenge acts as a boost to waning immunity, leading to a return of symptoms on subsequent exposure. In practice, clinicians should be aware of this possibility and counsel families accordingly.

Gabriella Weisz, BM, BS^a
Stephanie Cross, MRCPCH, MSc^b
Kate Grimshaw, PhD^{b,c,d}
Michel Erlewyn-Lajeunesse, FRCPCH, DM^{a,b}

^aFaculty of Medicine, University of Southampton, Southampton, United Kingdom

^bPaediatric Allergy & Immunology, Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

^cSalford Royal NHS Foundation Trust, Manchester, United Kingdom

^dManchester Institute of Biotechnology, University of Manchester, Manchester, United Kingdom.

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Corresponding author: Michel Erlewyn-Lajeunesse, FRCPCH, DM, Paediatric Allergy & Immunology, Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton SO16 6YD, United Kingdom. E-mail: Mich.Lajeunesse@soton.ac.uk.

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Penilloate and penicilloate concentrations in practical guidance recommendations



To the Editor:

Concerning the recently released "Practical Guidance for the Evaluation and Management of Drug Hypersensitivity: Specific Drugs,"¹ I would like to let you know that referred concentrations of penilloate and penicilloate (see Table I in the article) are in misalignment with those featured in several sources²⁻⁴; these sources point to a recommended concentration of benzyl penilloate of 1.5×10^{-3} mol/L.

Furthermore, penilloate concentrations featured in Table I of the article do not match those of the only fully validated and commercialized penilloate determinant diagnostic, included in the DAP Penicillin Test Kit.⁵ Validated common practice with the kit involves prick testing with reagents at a concentration of 1.5×10^{-3} mol/L (with an occasional previous prick test conducted using a 1.5×10^{-4} mol/L solution). Prick testing is followed by intradermal testing at 1.5×10^{-4} mol/L and, subsequently, 1.5×10^{-3} mol/L.

Thus, Table I in the referred article establishes a higher penilloate diagnostic concentration (10×10^{-3} mol/L to 20×10^{-3}

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.

Enric Maroto, PhD

Diater Laboratorios, Marketing Department, Madrid, Spain.

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Corresponding author: Enric Maroto, PhD, Diater Laboratorios, Av. Gregorio Peces-Barba, 2, Parque Tecnológico de Leganés, 280918 Leganés, Madrid, Spain. E-mail: e.maroto@diater.com.

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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.

Antonino Romano, MD^{a,b}

Ana Dioun Broyles, MD^c

Aleena Banerji, MD^d

Timothy Lax, MD^e

Maria Jose Torres, MD, PhD^f

Mariana Castells, MD, PhD^g

^aIRCCS Oasi Maria S.S., Troina, Italy

^bFondazione Mediterranea G.B. Morgagni, Catania, Italy

^cDivision of Allergy/Immunology, Boston Children's Hospital, Boston, Mass

^dDivision of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Boston, Mass

^eDivision of Allergy and Inflammation, Beth Israel Deaconess Medical Center, Boston, Mass

^fAllergy Unit and Research Group, Hospital Regional Universitario de Málaga, UMA-IBIMA-BIONAND, ARADyAL, Málaga, Spain

^gDrug Hypersensitivity and Desensitization Center, Brigham and Women's Hospital, Boston, Mass.

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Corresponding author: Ana Dioun Broyles, MD, Division of Allergy/Immunology, Boston Children's Hospital, 300 Longwood Ave., Boston, MA 02115. E-mail: ana.broyles@childrens.harvard.edu.

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