

# Occupational Contact Dermatitis From Carbapenems

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To the Editor:

Contact sensitivity to drugs that are systemically administered can occur among health care workers.<sup>1</sup> We report the case of a 28-year-old nurse who developed eczema on the dorsal aspect of the hand (Figure 1A) and the face (Figure 1B) in the workplace. The nurse was working in the hematology department where she usually handled and administered antibiotics such as imipenem, ertapenem, piperacillin, vancomycin, anidulafungin, teicoplanin, and ciprofloxacin. She was moved to a different department where she did not have contact with the suspicious drugs and the dermatitis completely resolved.

One month after the resolution of the eczema she was referred to our allergy department for an allergological evaluation. A dermatologic evaluation was made and a skin biopsy was performed from a lesional area of the left hand. The patient underwent delayed skin test and patch tests with many  $\beta$ -lactam compounds including penicilloyl polylysine, minor determinant mixture, penicillin G, penicillin V, ampicillin, amoxicillin, bacampicillin, piperacillin, mezlocillin and ticarcillin, imipenem-cilastatin, aztreonam, meropenem, ertapenem, and cephalosporins (eg, cephalexin, cefaclor, cefalotin, cefadroxil,

cephradine, cefuroxime, ceftriaxone, cefixime, cefoperazone, cefamandole, ceftazidime, cefotaxime). Undiluted solutions of commercial drugs (parenteral



**Figure 1.** Patient with eczema on the dorsal aspect of the hand (A) and the face (B).

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The authors report no conflict of interest.

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drugs when available were used) were used for skin prick test, and if negative, they were tested intradermally as described by Schiavino et al.<sup>2</sup> The concentrations used for the skin test and for the patch test are reported in the Table. Histamine (10 mg/mL) and saline were employed as positive and negative controls, respectively. Immediate reactions of at least 3 mm greater in diameter compared to the control for the skin prick test and 5 mm greater for intradermal tests were considered positive. Immediate-type skin tests were read after 20 minutes and also after 48 hours should any delayed reaction occur. An infiltrated erythema with a diameter greater than 5 mm was considered a delayed positive reaction.

Patch tests were applied to the interscapular region using acrylate adhesive strips with small plates. They were evaluated at 48 and 72 hours. Positivity was assessed according to the indications of the European Network for Drug Allergy.<sup>3</sup> Patch tests were carried out using the same drugs as the skin test. All drugs were mixed in petrolatum at

25% wt/wt for ampicillin and amoxicillin, 5% for penicillin G, and 20% for the other drugs as recommended by Schiavino et al.<sup>2</sup> We also performed patch tests with ertapenem in 20 healthy controls.

A skin biopsy from lesional skin showed a perivascular infiltrate of the upper dermis with spongiosis of the lesional area similar to eczema. Patch tests and intradermal tests were positive for ertapenem after 48 hours (Figure 2). Imipenem-cilastatin, ampicillin, piperacillin, mezlocillin, and meropenem showed a positive reaction for patch tests. We concluded that the patient had delayed hypersensitivity to carbapenems (ertapenem, imipenem-cilastatin, and meropenem) and semisynthetic penicillins (piperacillin, mezlocillin, and ampicillin).

Drug sensitization in nurses and in health care workers can occur. Natural and semisynthetic penicillin can cause allergic contact dermatitis in health care workers. We report a case of occupational allergy to ertapenem, which is a 1- $\beta$ -methyl-carbapenem that is administered as a single agent. It is highly active

### Concentration of Drug Used for Skin and Patch Tests

Drug	Skin Test Concentration	Patch Test Concentrations (In Petrolatum)
Amoxicillin	2–20 mg/mL	25%
Ampicillin	2–20 mg/mL	25%
Aztreonam	0.2–2 mg/mL	20%
Cefalotin	0.2–2 mg/mL	20%
Cefamandole	0.2–2 mg/mL	20%
Cefepime	0.2–2 mg/mL	20%
Cefoperazone	0.2–2 mg/mL	20%
Cefotaxime	0.2–2 mg/mL	20%
Ceftazidime	0.2–2 mg/mL	20%
Ceftriaxone	0.2–2 mg/mL	20%
Cefuroxime	0.2–2 mg/mL	20%
Ertapenem	0.2–2 mg/mL	20%
Imipenem-cilastatin	0.1–1 mg/mL	20%
Meropenem	0.1–1 mg/mL	20%
Mezlocillin	2–20 mg/mL	20%
Penicillin G	100–10000 U/mL	5%
Piperacillin	2–20 mg/mL	20%
Ticarcillin	2–20 mg/mL	20%



**Figure 2.** Positivity of patch test for ertapenem.

in vitro against bacteria that are generally associated with community-acquired and mixed aerobic and anaerobic infections.<sup>4</sup> Occupational contact allergy to other carbapenems such as meropenem also was reported.<sup>5</sup> The contact sensitization potential of imipenem has been confirmed in the guinea pig.<sup>6</sup> Carbapenems have a bicyclic nucleus composed by a  $\beta$ -lactam ring with an associated 5-membered ring. In our patient, patch tests for ertapenem, imipenem, and meropenem were positive. Although the cross-reactivity between imipenem and penicillin has been demonstrated,<sup>2</sup> data on the cross-reactivity between the carbapenems are not strong. Bauer et al<sup>7</sup> reported a case of an allergy to imipenem-cilastatin that tolerated treatment with meropenem, but our case showed a complete cross-reactivity between carbapenems. Patch tests for ampicillin, mezlocillin, and piperacillin also were positive; therefore, it can

be hypothesized that in our patient, the  $\beta$ -lactam ring was the main epitope recognized by T lymphocytes. Gielen and Goossens<sup>1</sup> reported in a study on work-related dermatitis that the most common sensitizers were antibiotics such as penicillins, cephalosporins, and aminoglycosides.

Health care workers should protect their hands with gloves during the preparation of drugs because they have the risk for developing an occupational contact allergy. Detailed allergological and dermatological evaluation is mandatory to confirm or exclude occupational contact allergy.

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