

at 2 mg/ml (wheal of 1.5 times). Because the patient required 5-HT<sub>3</sub> receptor antagonists, we challenged him the same day with granisetron. He received intravenously at 30-min intervals and under strict hospital surveillance increasing doses of granisetron, starting with 1 mg up to the therapeutic dose of 100 mg. He consequently failed to experience any hypersensitivity reaction and could thereafter complete his chemotherapy trial.

The 5HT<sub>3</sub>-induced anaphylaxis has been described several times (1–6) and considered as a class effect (6) until a recent report (5) where the authors described an IgE-mediated allergy to granisetron and safe use of ondansetron. Both ondansetron and tropisetron share an indole heterocycle, however ondansetron and granisetron do not and this may possibly explain the absence of cross-reactivity between the latter two drugs. Considering the positive skin tests in our patient, the negative skin tests in seven controls and negative histamine release test in one case report (5), ondansetron does not appear to be a nonspecific histamine-releaser. Our case report underlines the importance of a thorough drug allergy work up.

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## References

1. Ross AK, Ferrero-Conover D. Anaphylactoid reaction due to the administration of ondansetron in a pediatric neurosurgical patient. *Anesth Analg* 1998;**87**:779–780.
2. Kossey JL, Kwok KK. Anaphylactoid reactions associated with ondansetron. *Ann Pharmacother* 1994;**28**:1029–1030.
3. Weiss KS. Anaphylactic reaction to ondansetron. *Arch Intern Med* 2001;**161**:2263.
4. Chen M, Tanner A, Gallo-Torres H. Anaphylactic reactions associated with ondansetron. *Ann Intern Med* 1993;**119**:862.
5. Kanny G, Beaudouin E, Moneret-Vautrin DA. IgE-mediated allergy to granisetron and safe use of ondansetron. *J Allergy Clin Immunol* 2001;**108**:1059–1060.
6. Kataja V, de Bruijn KM. Hypersensitivity reactions associated with 5-hydroxytryptamine(3) receptor antagonists: a class effect? *Lancet* 1996;**347**:584–585.
7. Levine BB. Immunologic mechanisms of penicillin allergy. A haptenic model system for the study of allergic diseases of man. *N Engl J Med* 1966;**275**:1115–1125.

## Allergy to pholcodine: first case documented by oral challenge

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**Key words:** intradermal test; oral challenge; pholcodine.

Pholcodine (morpholinyl-ethyl-3 morphine) is an anti-tussive opiate indicated for the symptomatic treatment of cough. This substance is a component of many medicinal products. We report the first documented case of allergy to pholcodine proved by positive oral challenge.

In 1992, a female, 33 years old, presented with facial angio-edema 8 h after taking Respilène® (Coopération Pharmaceutique Française, Melun, France), syrup containing pholcodine associated with domperidone, tixocortol and bacitracine, for a sore throat. Symptoms resolved after i.v. administration of corticosteroids.

She had a history of facial angio-edema related to a β-lactam for 8 years.

Prick tests to routine airborne allergens were negative. Intradermal test (IDT) to

5 µg/ml pholcodine (Coopération Pharmaceutique Française) was positive: the diameter of the papula was 3 mm after injection and the diameter of the wheal at 15 min was 7 mm, surrounded by erythema. The patch test (20% in vaseline) was negative at 48 h. Skin tests with domperidone, tixocortol, bacitracine and β-lactams were negative (1, 2).

The basophil activation test and leukotriene release test were negative to pholcodine and to amoxicillin.

Open oral challenge with pholcodine was performed with 5 and 15 mg, 1 h apart. Results were positive with the total 20-mg dose: laryngeal angio-edema occurred 9 h after the second dose, disappearing a few hours after corticosteroid i.v. injection. An oral challenge to amoxicillin, 500 mg, was negative.

No case of allergy to pholcodine was found either in the literature or in the French pharmacovigilance database. One case of recurring eosinophilic cellulitis (Wells' syndrome) has been reported, involving other drugs including pholcodine (3). The diagnosis was confirmed by histology. Circulating immune complexes and a peri-vascular deposit of IgG and C3 were detected by direct immunofluorescence. An immunological mechanism mediated by drug-induced immune complexes was postulated. Pholcodine was not formally involved.

This case report documents allergy to pholcodine demonstrated by clinical history, positive skin test and oral challenge at a total 20-mg dose. This reactogenic dose is compatible with the presumed intake: two spoonfuls of Respilène® contain 12 mg of pholcodine. The allergic mechanism involved in this reaction was not formally established: the positive intradermal test indicates an IgE-mediated allergy, but the delay before the reaction is unusual. During the interview, the patient mentioned history of suspected allergy to β-lactams. However, this incident reported might be related to a concomitant intake of pholcodine.

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## References

1. Brockow K, Romano A, Blanca M, Ring J, Pichler W, Demoly P. General considerations for skin test procedures in the diagnosis of drug hypersensitivity. *Allergy* 2002;**57**:45–51.
2. Torres MJ, Blanca M, Fernandez J, Romano A, De Weck A, Aberer W et al. Diagnosis of immediate allergic reactions to beta-lactam antibiotics. *Allergy* 2003;**58**:961–972.
3. Ferrier MC, Janin-Mercier A, Souteyrand P, Bourges M, Hermier C. Eosinophilic cellulitis (Wells' Syndrome): ultrastructural study of a case with circulating immune complexes. *Dermatologica* 1998;**176**:299–304.

## Anaphylaxis after the ingestion of lamb meat

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**Key words:** anaphylaxis; food allergy; ovine serum albumin (OSA); lamb meat.

Food anaphylaxis is one of the most common causes of anaphylactic reactions in industrialized countries. Meat allergy represents, with an incidence of 8.2%, a rather small proportion of all food allergies (1).

Amongst those, about 10% are caused by lamb meat (1).

A 32-year-old Turkish female patient repeatedly developed generalized urticaria and angioedema after eating beef and lamb meat without food additives or spices simultaneously. Since then, the patient has consumed beef, milk products and milk without any complications.

**An immediate-type allergy to lamb meat is important to diagnose to prevent cross-reactivity.**

Because of her religious background, she was not exposed to pork.

Total IgE and antigen-specific IgE (kU/l) were determined by the CAP System (Pharmacia, Freiburg, Germany). An allergen-specific immunoblot was performed in order to identify ovine serum albumin (OSA) as the major allergen or to detect so far unknown antigens.

Specific IgE was detected against lamb, beef, pork, casein and beef lactoferrin. Several lamb-specific IgE-binding protein bands between 18 and 200 kDa with strongest signalling between 22 and 50 kDa could be detected. In a control group with pooled sera of six healthy volunteers, no lamb-specific IgE-reactive bands were found. Skin-prick tests for milk, milk products and whole egg were negative. Skin-prick tests for boiled lamb meat showed a positive reaction with a wheal of > 3 mm. After the ingestion of 9 g of boiled lamb meat, an anaphylactic reaction with generalized pruritus, erythema on the chest and dyspnoea occurred within 30 min.

Interestingly, in this case, using immunoblotting with the serum of the patient, we could not detect specific IgE for the 67 kDa OSA protein, but for several other so far not characterized bands, which may represent previously unknown proteins responsible for lamb meat allergy. However, further identification of the antigens of the positively tested bands and the causal role of these proteins in the anaphylactic reaction remains to be investigated. In 50% of beef allergies, a cross-reactivity is described between serum albumin of beef and lamb (2). Ayuso et al. (3) showed that patients with a suspected beef allergy have an IgE reactivity directed against meat proteins. This reactivity is mainly directed against a protein of 160 kDa, which was identified as bovine IgG. A cross-reactivity between lamb and beef exists, indicating similar epitopes in beef and lamb IgG antibodies. The specific IgE against common milk allergens such as beef lactoferrin and casein, have no clinical relevance, if milk and milk products can be tolerated. In our case, specific IgE was detected against lamb, beef and pork. Interestingly, only the ingestion of lamb meat caused anaphylactic reactions,

beef was well tolerated and pork avoided by the patient because of her religion.

For patients with a history of anaphylactic reaction to meat, one should first rule out an allergy or intolerance to penicillin, papain, nitrates or nitrite salts, as they may be associated with angioedema and anaphylaxis (4, 5). It is noteworthy that some cases of anaphylactic reactions, upon meat ingestion, have been observed without positive skin-prick tests or any detectable specific IgE (6). Therefore, after exclusion of allergy to penicillin or an intolerance of preservatives, the diagnosis of a given meat allergy has to be confirmed by oral provocation test.

Taken together, an immediate-type allergy to meat, especially lamb meat, is rare, but it is important to diagnose this to prevent cross-reactivity.

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## References

1. Wuthrich B. Allergy to meat proteins in adults. *Allergologie* 1996;**19**:130–134.
2. Restani P, Fiocchi A, Beretta B, Velina T, Giovannini M, Galli CL. Meat allergy: III – Proteins involved and cross-reactivity between different animal species. *J Am Coll Nutr* 1997;**16**:383–389.
3. Ayuso R, Lehrer SB, Lopez M, Reese G. Identification of bovine IgG as a major cross-reactive vertebrate meat allergen. *Allergy* 2000;**55**:348–354.
4. Hawkins CA, Katelaris CH. Nitrate anaphylaxis. *Ann Allergy Asthma Immunol* 2000;**85**:74–76.
5. Jäger L, Wüthrich B. Nahrungsmittelallergien und –intoleranzen. München: Urban & Fischer, 2002.
6. Chua YY, Bremner K, Llobet JL, Kokubu HL, Collins-Williams C. Diagnosis of food allergy by the radioallergosorbent test. *J Allergy Clin Immunol* 1976;**58**:477–482.