

Case report

Ingestive and inhalative allergy to the mushroom *Boletus edulis*

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This is the first report on inhalative and ingestive allergy to the common edible mushroom *Boletus edulis* (*Be*) (English, *edible boletus*; German, *Steinpilz*; French, *bolet*; Italian, *porcino* or *boletto*) belonging to the class Basidiomycetes. Four cases observed in our allergy unit are presented, showing different clinical manifestations of this rare allergy: as an occupational problem or life-threatening anaphylactic reactions after eating *Be*. In all cases, skin prick-to-prick tests with raw *Be* were strongly positive; in three cases, specific IgE against *Be* could be found. The symptoms were reproducible after an inhalation challenge test. It is noteworthy that not only can Basidiomycetes cause airborne allergy but also that edible mushrooms from this class can cause inhalative and intestinal allergy. The two patients with strong anaphylactic reactions demonstrate that *Be* may have great allergenic potential.

There are from 250 000 to 1 500 000 species of fungi depending on the authority, but only 70 000 have been fully described (1). Fungi taxonomy is based on various systems and undergoes constant revision. The word “mushroom” denotes macrofungi with edible fruiting bodies, while “toadstool” refers to those with poisonous fruiting bodies. These fungi, with boletus and agarics as major groups, mostly belong to the Basidiomycotina: fungi producing basidiospores. Consequently, mushrooms and macrofungi are often called Basidiomycetes: but this is just the name of a class. However, edible mushrooms are not limited to this class: morels, for example, belong to the class Ascomycetes (fungi producing ascospores) (2). *Boletus edulis* (*Be*) (English, *edible boletus*; German, *Steinpilz*; French, *bolet*; Italian, *porcino* or *boletto*; Swedish, *stensopp*), belonging to the class Basidiomycetes, is a very common edible mushroom. It grows in temperate climates in woods, mainly in late summer and autumn, and is one of the gastronomically most important mushrooms. However, to our knowledge, IgE-mediated inhalant or food allergies to *Be* have not yet been reported. In our allergy unit, in the past 10 years, we have observed four cases of allergy to *Be*: two patients developed inhalative

and ingestive occupational allergy; the other two had anaphylactic reactions after eating *Be*. We present these four cases and discuss the inherent problems.

Material and methods

Skin testing

Our usual range of commercial aeroallergens and food extracts (Alyostal, Stallergènes Laboratories, France) was used to perform skin prick tests (SPT) with a standardized prick test needle (Stallerpoint). Our atopy-screening included extracts of *Dermaphagoides pteronyssinus* and *D. farinae*; grass mix, rye, mugwort, birch, alder, and hazel pollen; cat, dog, and horse epithelia; and cow's milk and egg proteins. Our mold screening included extracts of *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*, *Candida*, *Botrytis*, *Chaetomium*, *Epicoccum*, *Fusarium*, *Helminthosporium*, *Mucor*, *Merulius*, *Pullularia*, *Rhodotorula*, *Neurospora*, *Hormodendrum*, *Rhizopus*, *Stemphylium*, *Trichotecium*, and yeast mixture. The prick-to-prick tests and scratch tests with the different mushrooms were done with native, dried, and steamed mushroom

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material. Reactions were considered positive if a wheal diameter at least 3 mm greater than that produced by the negative control (glycerol diluent) occurred (3). To exclude the possibility of a non-specific irritative reaction, five atopic patients without history of mushroom allergy were additionally skin tested in the same procedure. No reactions were observed. Three healthy volunteers were tested by bronchial and another three by nasal challenges with *Be* in the way stated above, and no reactions were observed (negative controls).

Serologic testing

Allergen-specific IgE antibodies and total IgE in serum were measured with Pharmacia CAP (ImmunoCAP FEIA System, a fluoroenzyme-immunoassay), according to the directions for use (Pharmacia Diagnostics AB, Uppsala, Sweden). The solid-phase allergens of the mushrooms *B. edulis*, *Coprinus comatus*, and *Agaricus bisporus* were coupled to disks and tested by RAST. Immunoelectrophoresis to demonstrate precipitating IgG antibody against various mushroom components and bacteria causing allergic alveolitis was performed in the Immunologic Laboratory, University Hospital of Geneva, Switzerland. The measurement of tumor necrosis factor- α (TNF- α) (TNF- α ELISA, Endogen, Boston MA, USA), interleukin (IL)-1, IL-2, IL-4, and IL-6 (ELISA-Quantikin human, RD Research Diagnostics System, Minneapolis, MN, USA) was performed as ELISA technique in the Immunologic Laboratory, Department of Internal Medicine, University Hospital of Zurich, Switzerland, according to the manufacturers' instructions.

Case reports and Results

Case 1

Personal history. A 50-year-old office worker, in good general health and with no history of atopy, had experienced severe asthma attacks over the past 2–3 years only while he was at work. During the weekend and in the holidays, he never had attacks. He also experienced symptoms of oral allergy syndrome (OAS) with oropharyngeal itching, tingling, and swelling of the lips a few minutes after eating *Be*, but the ingestion of *Be* never elicited systemic symptoms. The food import company he worked for specialized in packing dried mushrooms, but he never had direct contact with the items.

Results. The physical examination and the laboratory tests (routine hematology and chemistry) were

normal. The dynamic lung volumes were normal. The methacholine challenge test showed strong bronchial hyperreactivity: 35% fall in the FEV₁ value after cumulative inhalation of 300 μ g of methacholine.

Skin tests. Atopy and mold screening was negative. Scratch tests with house dusts were negative. The scratch test with dust from the work office was strongly positive. Prick-to-prick tests with native and dried *Be* were strongly positive. Prick and scratch tests with other dried mushrooms (morel, *Pleurotus*, *Lactarius*, shiitake (*Lentidus edones*), and champignon were negative.

Serologic tests for IgE. The test for *Be* showed 2.0 PRU/ml (RAST class 2); tests for *A. bisporus* and *C. comatus* were negative.

Nasal challenge test. The patient inhaled once and briefly through his nose the dust of dried *Be* by the Insuffler Intal[®] Nasal (Fisons Ltd); the exact amount of material was not measured. He developed rhinoconjunctivitis and bronchoconstriction after 15 min, leading to a 28% fall in the FEV₁. Inhalation of flour dusts did not elicit symptoms (negative control).

Case 2

Personal history. A 35-year-old cook, in good general health and with no history of atopy, had had rhinoconjunctivitis and asthma over the past 2 years only while he was at work. His restaurant specialized in mushroom recipes, so that in autumn he often cooked a large amount of *Be*. The frequency of the asthma attacks increased dramatically when he was in contact with *Be*. After eating these mushrooms, he also had several anaphylactic reactions with severe gastrointestinal cramps and diarrhea, generalized urticaria, and asthma attacks with dizziness.

Results. The physical examination and the laboratory tests (routine hematology and chemistry) were normal. The static and dynamic lung volumes were normal.

Skin tests. Atopy and mold screening tests were negative. Prick-to-prick tests with native, dried, and steamed *Be* were strongly positive. Prick and scratch tests with other common dried mushrooms (morel, *Pleurotus*, *Lactarius*, shiitake, and champignon) were negative.

Serologic tests for IgE. The total IgE level was 165 kU/l. CAP tests with mx1 (mold mix), m11

(*Rhizopus*), fx5 (food mix), fx70 (spice mix), fx71 (spice mix), and fx72 (spice mix) were negative. The test with *B. edulis* was 4.9 PRU/ml (RAST class 3); tests with *A. bisporus* and *C. comatus* were negative.

Serologic tests for precipitating IgG. The tests were negative for several fungal allergens (*Aspergillus fumigatus*, *A. niger*, *A. nidulans*, *A. flavus*, *A. terreus*, *Allescheria boydii*, *Fusarium*, *Aureobasidium pullulans*, *Cladosporium*, and *Penicillium casei*).

Bronchial challenge test. To demonstrate a cause-and-effect relationship between *Be* and asthma, the patient cooked a normal portion of *Be* (about 50 g) with water and inhaled the steam for 5 min. A strong bronchoconstriction response 15–30 min afterward led to a 60% fall in FEV₁. IL-6 significantly increased at 2–8 h after exposure occurred (Fig. 1), whereas no changes were observed after 2, 6, and 24 h in axillary temperature, blood cell counts, eosinophil cationic protein (ECP), histamine, tryptase, C-reactive protein, TNF- α , IL-1, IL-2, and IL-4 levels. Radiographs of the chest before and 6 and 24 h after exposure detected no changes, excluding allergic alveolitis. Inhalation of steam (no *Be* having been boiled in the water)

alone for 5 min did not lead to a change of FEV₁ (negative control).

Case 3

Personal history. A 42-year-old housewife in good general health, but with a history of rhinoconjunctivitis and bronchial asthma due to allergy to grass pollen, experienced four anaphylactic episodes after eating mushrooms, with severe diarrhea, generalized urticaria, and asthma attacks with dizziness. In two episodes, hypotension and tachycardia were observed, leading to hospitalization. The patient never experienced other episodes of food intolerance.

Results. The physical examination and the laboratory tests (routine hematology and chemistry) were normal.

Skin tests. Atopy screening tests were only strongly positive with grass pollens. Mold screening was not done. Prick and intracutaneous tests with cow's milk, cheese, casein, nuts, celery, and cereal flours were negative. Scratch tests with several native spices (aniseed, cumin, fennel, curry, pepper, and paprika) were negative. Prick-to-prick tests

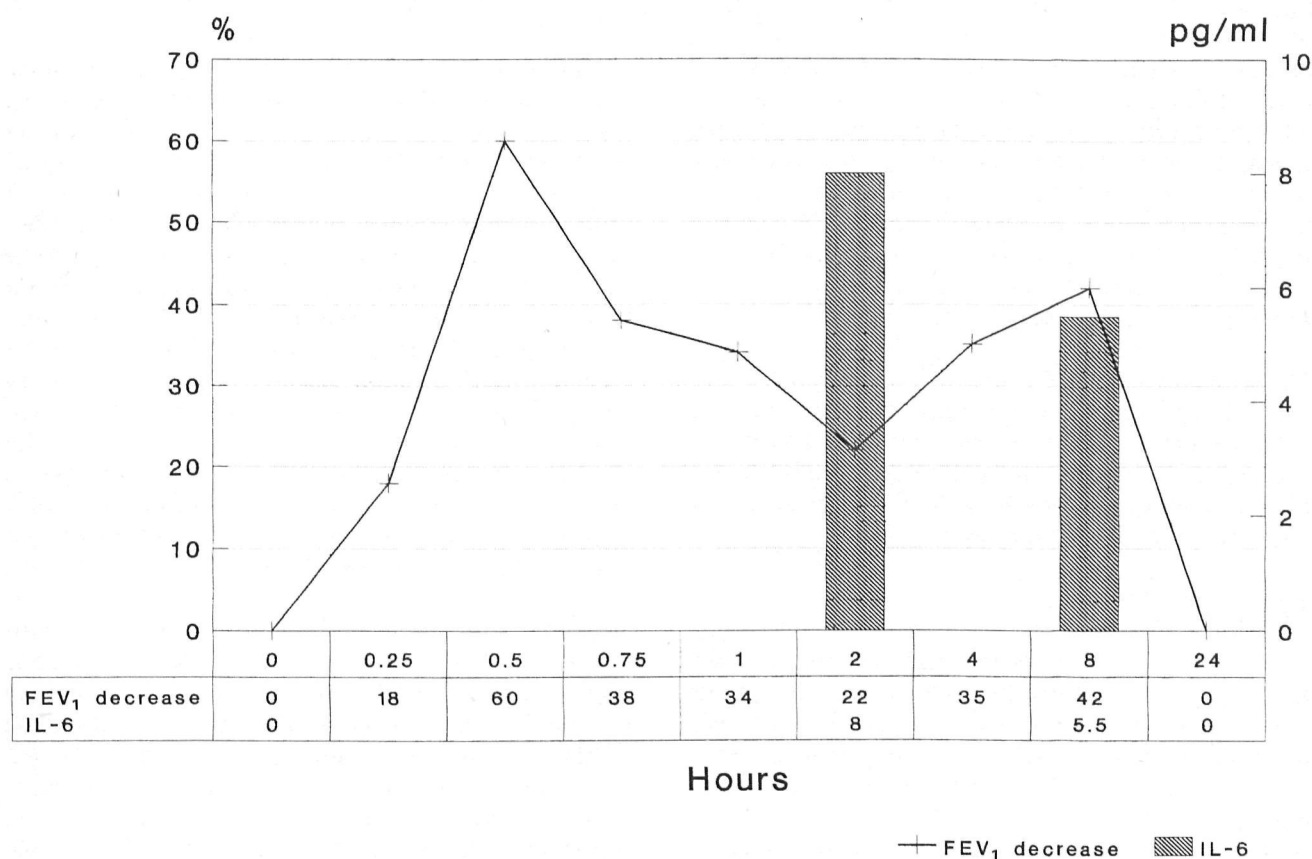


Fig. 1. Bronchial challenge test with values of FEV₁ and IL-6.

with native and dried *Be* were strongly positive. Prick and scratch tests with other mushrooms (morel, shiitake, and champignon) were negative.

Serologic tests for IgE. The test with *B. edulis* was 0.6 PRU/ml (RAST class 1); *A. bisporus* and *C. comatus* were not tested.

Case 4

Personal history. A 65-year-old hotel manager, in good general health, but with a history of hay fever in childhood and sensitivity to acetylsalicylic acid and pyrazolones, had an anaphylactic reaction after eating mushroom on toast: 2 h after ingestion, he developed generalized urticaria and a fall of blood pressure with preshock symptoms, leading to hospitalization in an intensive care unit. Previously, ingestion of *Be*, champignons, and other mushrooms had not elicited symptoms.

Results. The physical examination and the laboratory tests (routine hematology, chemistry, and immunologic parameters) were normal.

Skin tests. Atopy screening was negative. Mold screening was not done. Prick tests with several spices (aniseed, cumin, fennel, curry, pepper, and paprika), fruits (banana, lemon, strawberry, kiwi, olive, melon, orange, and peach), vegetables and grain (bean, pea, carrot, potato, garlic, parsley, rice, celery, soya, spinach, tomato, and onion), and nuts were negative. Prick-to-prick tests with native and dried *Be* were strongly positive. In prick and scratch tests with other common mushrooms (morel, *Pleurotus*, *Lactarius*, shiitake, *Portabella*, chanterelle, and champignon), champignon was positive and all others negative. Three healthy volunteers failed to react to champignon.

Serologic tests for IgE. The total serum IgE level was 110 kU/l; the test for Sx1 (aeroallergen mix) was 5.2 CAP kU/l. CAP tests with fx5 (food mix), f13 (peanut), f31 (carrot), f47 (garlic), f49 (apple), and f85 (celery) were negative. RAST with *B. edulis*, *A. bisporus*, and *C. comatus* was negative.

Discussion

Basidiomycetes comprises approximately 25 000 species including mushrooms, puffballs, smuts, rusts, and jelly and bracket fungi. Their spores constitute a major portion of the airborne spores in many areas of the world. Davies et al., for example, reported that basidiospores and ascospores comprised 54% and 29%, respectively, of the total spore counts in Liverpool and London (4).

Spore counts in the same country show that basidiospores of Agaricales are in the air from June to November with peaks in August and September, in quantities comparable to pollen and mold spores. The Finnish data from 1976 to 1986 (2, 5) show that the easily identifiable spores of Boletaceae always occur from July to September and can reach values of 9000/m³ (2). Gregory & Hirst (1952) were the first to suggest that high atmospheric concentrations of basidiospores might cause seasonal asthma (6), but the allergenicity and the clinical relevance of Basidiomycetes have been confirmed only recently (7).

Mushroom antigens are known to produce allergic reactions of all the Gell and Coombs types I–IV, but the overall prevalence and incidence of mushroom allergy are unknown (2). It may be very small (food allergy) but could be very important, like pollen or mold allergy (inhalative allergy due to the fungi spores). Reports of food allergy to edible mushrooms are practically nonexistent, although many people have reported symptoms after eating mushrooms. Since mushrooms spoil quickly, these reactions probably occur on a pseudo-allergic (nonallergic hypersensitivity means non-immune-mediated intolerance) or toxic basis. Only one case of peroral exposure to *Ramaria flava* which led to anaphylaxis and death (Tony Foucard, personal communication in Reference 2) is known. The *Paxillus* syndrome, named after *Paxillus involutus*, is a complement-mediated immunohemolytic reaction caused by peroral antigen exposure to *P. involutus*, *Suillus luteus*, and probably *Gyromitra esculenta* (8).

Edible Basidiomycetes have also been rarely reported to elicit allergies: a case of occupational inhalative allergic rhinitis caused, for example, by puffballs (*Lycoperdon maximum*) (9) and contact dermatitis cases due to *Suillus luteus* (8, 10) have been published. Japanese authors have observed several cases of toxicodermia caused by shiitake (*L. edones*) (11). Bringham et al. described mushroom worker's lung, in analogy to farmer's lung, in 1959 (12); afterward it was discovered that thermophilic actinomycetes play a definite role in the etiology of this disorder (13). Mushroom spores and mycelium should indeed be considered etiologically important factors (14, 15), although the exact etiology of mushroom worker's lung remains obscure.

In Switzerland and several other European countries, *Boletus* species (there are 13 different edible species, e.g., *B. edulis* [Fig. 2]) are gastronomically famous and very common. They belong to the class Basidiomycetes, the order Boletales/Agaricales (in revision), and the family Boletaceae. Allergic reactions are indeed unknown. We found no case reports of allergic reactions to *Be* or other edible mushrooms of this family in the literature. In our

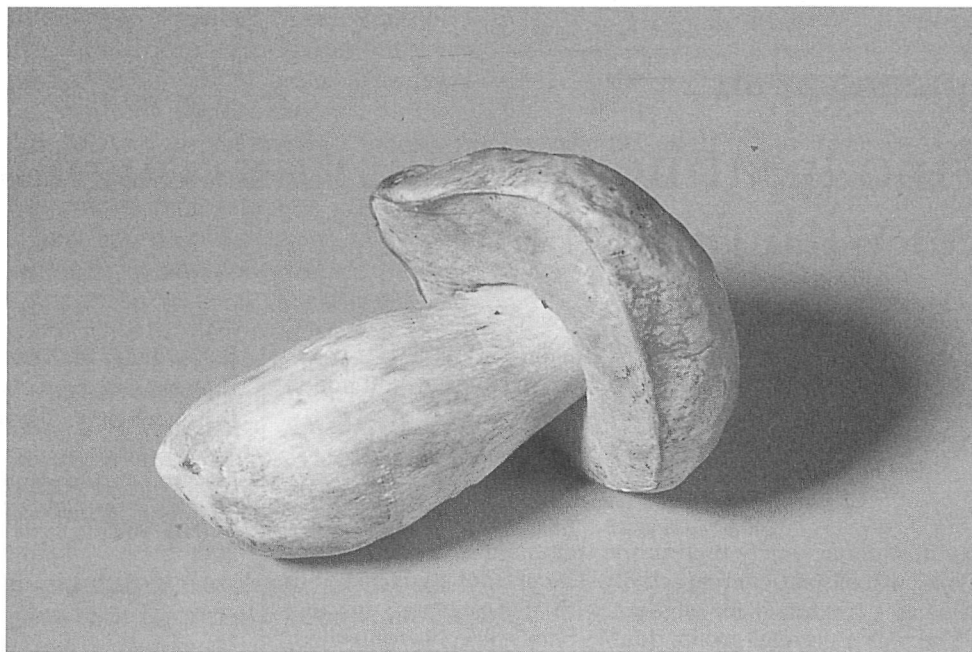


Fig. 2. Specimen of *Boletus edulis*.

allergy unit, we have observed only four cases of allergy to this mushroom in the past 20 years. These cases, however, especially the very well-documented case 2, illustrate an extensive clinical spectrum of allergy to *B. edulis*: a combination of inhalative allergy and OAS, or inhalative and ingestive allergy, as an occupational problem with life-threatening anaphylactic reactions. Interestingly, the first patient was not directly exposed to the dust of dried *Be* while working in his office away from the packing area. The first two patients had both positive skin tests and specific IgE against *Be*, and the symptoms were reproducible after a challenge test. In the second case, a dual asthmatic response with a significant increase of IL-6 at 2–8 h after exposure occurred, whereas no changes in the value of other markers of allergic inflammation, such as ECP, histamine, or tryptase, after challenge were observed. IL-6 is a multifunctional cytokine that is produced by a range of cells and is a marker for acute-phase reactions.

It is important to realize not only that Basidiomycetes can cause the allergy to airborne spores, as suggested in the 1950s and confirmed in the 1980s, but also that edible mushrooms from this class can elicit inhalative and intestinal allergy, although the thermostable causal allergen has not been identified. The two patients with strong anaphylactic reactions demonstrate that *B. edulis* may have great allergenic potential.

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