

LETTER TO THE EDITOR

Edible mushroom allergy: a clinically heterogeneous and under-recognized condition

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To the Editor,

Edible mushrooms are consumed globally and include commonly cultivated species such as *Agaricus bisporus* (button mushroom), *Lentinula edodes* (shiitake mushroom), *Pleurotus ostreatus* (oyster mushroom), *Flammulina velutipes* (enoki mushroom), and *Hypsizygus marmoreus* (beech mushroom). Although mushroom ingestion is usually well tolerated, clinically important adverse reactions are increasingly recognised. These reactions are often grouped together as “mushroom allergy,” despite involving distinct immunological and toxic mechanisms. This distinction matters: IgE-mediated food allergy, occupational respiratory allergy, contact dermatitis, hypersensitivity pneumonitis, shiitake flagellate dermatitis, and poisoning require different diagnostic pathways, preventive measures, and patient counselling. The evidence base remains primarily limited to case reports, small case series, and occupational observations, so prevalence and predictors of severe reactions are uncertain [1,2]. Earlier review estimated food-allergic reactions to mushrooms at approximately 1%, but this figure was not derived from robust population-based studies and should be interpreted cautiously [1].

IgE-mediated reactions after mushroom ingestion appear uncommon but can range from oral pruritus and urticaria to angioedema, respiratory compromise, and anaphylaxis. *Agaricus bisporus* (button mushroom) is most frequently reported, with sensitisation supported in individual cases by skin testing, mushroom-specific IgE, basophil activation, or immunoblotting [2-4]. Severe reactions have also been reported following the ingestion of *Tricholoma matsutake* (matsutake mushroom), *Hypsizygus marmoreus* (beech mushroom), *Boletus edulis* (porcini mushroom), and other edible mushrooms [5,6]. Importantly, a positive test should not be equated with clinical allergy. Commercial mushroom extracts are poorly standardised, and fungal cross-reactivity may yield sensitisation in individuals who tolerate ingestion. The diagnosis therefore rests primarily on a reproducible exposure-reaction history, supported rather than replaced by allergy testing.

A clinically useful concept is the potential link between respiratory sensitisation to airborne moulds and food reactions to mushrooms. Patients with mould-associated rhinitis or asthma have developed oral allergy syndrome-like symptoms or anaphylaxis after raw *Agaricus bisporus* (button mushroom)

ingestion, while tolerating cooked or canned preparations [3,4]. Inhibition studies and immunoblotting have suggested cross-reactivity between mushroom proteins and mould allergens, and similar observations have been made with *Macrolepiota procera* (parasol mushroom) and *Hypsizygus marmoreus* (beech mushroom) in mould-sensitised patients [4-6]. Heat-labile proteins may explain why some reactions are restricted to raw or lightly cooked mushrooms; in contrast, a digestion-stable allergen has been described in *Boletus edulis* (porcini mushroom), which may be relevant to systemic food allergy [7]. These reports support two non-mutually exclusive pathways: primary sensitisation through dietary or occupational exposure, and secondary food reactions in patients already sensitised to airborne fungi. However, most candidate allergens have been identified in single patients, recombinant validation is uncommon, and their clinical relevance remains uncertain and patient-specific (Table 1).

The route of exposure is particularly relevant in occupational settings. Mushroom cultivation, harvesting, packaging, and drying can generate spores, fragments of fruiting bodies and compost-associated organic dust. Spore allergy and fruiting-body allergy should be distinguished: spores are predominantly inhaled and may drive rhinitis, asthma, or hypersensitivity pneumonitis, whereas contact with or ingestion of fruiting-body proteins may cause contact dermatitis or IgE-mediated food reactions. Occupational rhinitis and asthma have been reported in shiitake handlers and workers exposed to white mushroom or *Boletus edulis* (porcini mushroom) [8,9]. Symptoms may improve away from work, and respiratory sensitisation may occur despite continued tolerance of mushroom ingestion. Risk of developing mushroom allergy is likely modified by atopy, pre-existing mould allergy, asthma, exposure intensity and duration, ventilation and respiratory protection, and possibly genetic susceptibility, although robust predictive data are lacking. A focused occupational history should therefore document work tasks, timing of symptoms across shifts, use of protective equipment, and improvement during weekends or holidays. Early recognition and exposure reduction are important, since occupational asthma may persist or progress with ongoing exposure [10].

Mushroom-associated skin disease also requires careful classification. Protein contact dermatitis produces recurrent hand eczema with immediate flares after protein contact and has been described in shiitake workers with evidence of *Lentinula edodes* (shiitake)-specific IgE [9]. Allergic contact dermatitis may occur in food handlers and growers, but it should be separated from shiitake flagellate dermatitis. The latter is a striking, intensely pruritic linear eruption after ingestion of raw or insufficiently cooked shiitake and is generally regarded as a toxic, non-IgE-mediated reaction related to the thermolabile polysaccharide lentinan. Misclassification as IgE-mediated food allergy may result in unnecessary broad dietary restriction and obscure the simple preventive message of adequate cooking.

Another distinct occupational entity is hypersensitivity pneumonitis (HP), sometimes termed mushroom worker's lung. Repeated occupational inhalation of fungal spores, mushroom material, and compost-associated organic dust may trigger an immune-mediated interstitial lung disease. Bunashimeji mushroom has been implicated in provocation-confirmed disease, and cases have been reported among *Pleurotus* growers [11,12]. Acute HP may present several hours after exposure with fever, malaise, dry cough, chest tightness, and dyspnoea; chronic exposure can lead to progressive exertional breathlessness and fibrotic lung disease. Serum IgG indicates exposure or sensitisation rather than diagnosis in isolation. Diagnosis should integrate credible exposure, high-resolution CT, bronchoalveolar lavage where appropriate, and multidisciplinary assessment in line with HP guidance [11].

For suspected immediate mushroom allergy, an allergy-focused history should establish the species, preparation method, quantity, route of exposure, latency, reproducibility, co-factors, and response to avoidance. Exercise, alcohol, non-steroidal anti-inflammatory drugs, intercurrent infection, and concurrent mould exposure may modify the threshold for reactions. Clarifying tolerance to cooked

versus raw products is particularly informative. Skin prick testing and serum-specific IgE could demonstrate sensitisation, but commercial extracts and assays are limited by poor standardisation, variable allergen content, and uncertain sensitivity and specificity. Prick-to-prick testing and ELISA using in-house extracts where available, may provide greater diagnostic value. Immunoblotting and immunoblot-inhibition can identify IgE-binding bands and support cross-reactivity, although these techniques remain mainly research tools. Basophil activation testing may offer functional evidence of clinically relevant IgE reactivity when history and conventional testing are discordant, but mushroom-specific protocols and diagnostic thresholds are not validated. Testing for mould sensitisation is reasonable when symptoms resemble pollen-food allergy syndrome or the patient has respiratory mould allergy. A medically supervised open oral food challenge is suitable in most equivocal clinical cases; a double-blind placebo-controlled food challenge should be reserved for selected equivocal cases or research and remains the most rigorous reference standard. A phenotype-based diagnostic pathway is summarised in Table 2.

Management should be proportionate to the confirmed phenotype. Patients with IgE-mediated reactions should avoid the culprit species while continuing to consume mushroom species that have already been tolerated. Routine avoidance of all mushrooms, fermented foods, or all fungus-derived products is not evidence based. In particular, mushroom allergy does not establish allergy to mycoprotein products derived from *Fusarium venenatum* (microfungus); individual assessment is preferable where prior severe reactions, mould sensitisation, or symptoms after fungal foods raise concern [12]. Patient education should include recognition of symptoms, emergency treatment, and practical avoidance advice. Because mushrooms may be concealed in soups, sauces, stocks, seasoning powders, meat substitutes, vegetarian dishes, supplements, and restaurant foods, patients should be counselled to check ingredient lists, ask about mixed dishes, and consider cross-contamination during preparation. Labelling requirements vary by jurisdiction and mushrooms are not universally designated priority allergens; therefore, direct communication with food providers may be necessary. Those with previous anaphylaxis, respiratory compromise, hypotension, or relevant asthma should have adrenaline autoinjectors, training in their use, and a written emergency plan. Intramuscular adrenaline remains first-line treatment for anaphylaxis; antihistamines must not delay adrenaline for airway, breathing, circulatory, or rapidly evolving multisystem symptoms. Occupational management should prioritise source control, ventilation, task modification, appropriate respiratory and skin protection, occupational-health assessment, and early removal from exposure when occupational asthma or HP is confirmed.

The current literature leaves important unanswered questions. Prospective registries and multicentre cohorts are needed to define prevalence, natural history, reaction thresholds, and factors associated with severe outcomes. Future laboratory studies should identify and validate clinically relevant mushroom allergens, clarify cross-reactive fungal protein families, and determine how cooking, canning, drying, and fermentation change allergenicity. Standardised diagnostic extracts, component-resolved tests, and validated challenge protocols would improve diagnostic certainty. For occupational disease, exposure measurement and intervention studies are needed to identify effective controls. Until these data are available, clinicians should resist both under-recognition and over-diagnosis: a structured history, phenotype-specific investigation, and targeted avoidance offer the most defensible approach.

In summary, adverse reactions to edible mushrooms encompass several conditions rather than a single disease. IgE-mediated food allergy can cause anaphylaxis and may be linked to mould sensitisation in selected patients, particularly when raw mushrooms provoke symptoms, but cooked products are tolerated. Occupational exposure may produce rhinitis, asthma, dermatitis, or HP, whereas shiitake flagellate dermatitis is usually toxic and non-IgE-mediated. Recognition of this distinct pathogenic

mechanism is essential to avoid inappropriate restriction, detect potentially serious workplace lung disease, and provide effective prevention and emergency care.

Declarations

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Species (common name)	Protein or family	Approximate molecular mass	Stability or cross-reactivity	Evidence and limitations
<i>Agaricus bisporus</i> (button mushroom)	Manganese-dependent superoxide dismutase (MnSOD)	24 kDa	Cross-reactive with fungal MnSOD, particularly <i>Aspergillus fumigatus</i> Asp f 6; thermal stability not directly established in the identifying study	Identified by two-dimensional IgE immunoblotting and mass spectrometry in a single mould-sensitised patient. Inhibition assays confirmed cross-reactivity between the <i>A. bisporus</i> extract and recombinant Asp f 6 [3].
<i>Agaricus bisporus</i> (button mushroom)	NADP-dependent mannitol dehydrogenase	27 kDa	Sequence homology with the mould allergens Alt a 8 and Cla h 8; direct IgE cross-inhibition was not demonstrated	Identified together with MnSOD by two-dimensional IgE immunoblotting and mass spectrometry in one patient; clinical relevance requires validation [3].
<i>Agaricus bisporus</i> (button mushroom)	Porin-family protein	Approximately 36 kDa	Reported to be heat-stable and cross-reactive with a protein of similar mass from <i>Alternaria alternata</i>	Identified in a single patient by IgE immunoblotting, inhibition studies, and proteomic analysis; not available for routine component-resolved testing [14].
<i>Lentinula edodes</i> (shiitake mushroom) and <i>Pleurotus eryngii</i> (king oyster mushroom)	Ribosomal proteins S8 and S15a	Approximately 15 kDa IgE-reactive band	Cross-reactivity demonstrated between the two mushroom species; no established homology with recognised fungal aeroallergens	Identified by immunoblotting, inhibition experiments, and mass spectrometry in one patient; broader clinical relevance is unknown [13].

<i>Boletus edulis</i> (porcini mushroom)	Uncharacterised digestion-resistant protein	75 kDa	Retained IgE binding after simulated gastric digestion	Detected in the serum of one patient with recurrent anaphylaxis but not in a patient with oral allergy syndrome or controls; molecular identity remains unknown [7].
<i>Pleurotus ostreatus</i> (oyster mushroom)	Trehalose phosphorylase	IgE-reactive band approximately 150–250 kDa	Band detected only in cooked mushroom extract, suggesting heat stability, heat-induced aggregation, or increased extractability after cooking	Identified by IgE immunoblotting and mass spectrometry in one challenge-confirmed case. The native molecular form, recombinant IgE reactivity, and population relevance have not been established [15].
Multiple fungal and edible-mushroom species	Candidate conserved fungal proteins, including enolase, heat-shock proteins, aldolase, and other metabolic or ribosomal proteins	Variable	Potential cross-reactivity based on conservation across fungal species	These families are recognised fungal allergens or plausible cross-reactive proteins, but mushroom-specific IgE binding and clinical relevance remain incompletely characterised [12].

Table 1. Reported IgE-binding proteins and candidate allergens in edible mushrooms. Evidence is derived largely from individual case reports using immunoblotting, inhibition assays, mass spectrometry, or related experimental methods; therefore, the listed proteins should not be regarded as fully validated diagnostic allergens.

Phenotype	Key history	Initial assessment	Specialist or complementary investigations	Diagnostic confirmation and management implications
Immediate food reaction	Implicated mushroom species and preparation; quantity and route; onset, usually within minutes to 2 hours; reproducibility; cofactors; and tolerance of raw, cooked, canned, or dried preparations	Allergy-focused history; skin prick testing or prick-to-prick testing with the implicated mushroom; serum-specific IgE where available; assessment of mould sensitisation when clinically relevant	BAT, ELISA using in-house extracts, immunoblotting, and inhibition studies may be considered in specialist or research centres, although mushroom-specific methods and thresholds are not validated	A medically supervised open oral food challenge is appropriate in most equivocal clinical cases when risk is acceptable. A double-blind placebo-controlled food challenge may be considered when an open challenge is indeterminate, when subjective symptoms predominate, or in research. Confirmed cases require species- and preparation-specific avoidance, education, and an emergency plan proportionate to reaction risk
Delayed or contact-associated cutaneous reaction	Timing and morphology of the eruption; direct handling versus ingestion; immediate flares superimposed on chronic eczema; occupational exposure; and ingestion of raw or insufficiently cooked shiitake	Dermatological examination and detailed exposure assessment	Patch testing when allergic contact dermatitis is suspected; prick or prick-to-prick testing and serum-specific IgE when protein contact dermatitis or contact urticaria is suspected; skin biopsy only when needed to clarify an uncertain diagnosis	Distinguish allergic contact dermatitis, protein contact dermatitis, contact urticaria, and toxic shiitake flagellate dermatitis. Management may include allergen avoidance, reduction of skin exposure, protective measures, treatment of dermatitis, or adequate cooking of shiitake

Occupational rhinitis or asthma	Mushroom species and materials handled; exposure to spores, fruiting bodies, compost, or organic dust; specific tasks; temporal relationship with work; and improvement during rest days or holidays	Confirmation of rhinitis or asthma using appropriate objective testing; spirometry with bronchodilator reversibility; sensitisation testing directed towards relevant mushroom or mould material where available; serial peak expiratory flow measurements during periods at and away from work	Serial assessment of nonspecific bronchial responsiveness, fractional exhaled nitric oxide, or airway inflammation may provide supportive evidence. Specific inhalation or workplace challenge may be considered in an experienced occupational respiratory centre when the diagnosis remains uncertain	Establish an objective relationship between exposure and disease rather than relying on history or sensitisation alone. Management should prioritise elimination or reduction of exposure, engineering controls, task modification, appropriate respiratory and skin protection, pharmacological treatment, and occupational-health follow-up
Hypersensitivity pneumonitis	Nature, intensity, frequency, and duration of exposure to mushroom spores, fungal material, compost, or organic dust; delayed respiratory or systemic symptoms after exposure; and improvement away from the exposure	Comprehensive exposure assessment; high-resolution computed tomography performed using an appropriate HP protocol; pulmonary function testing to assess physiological impairment; and serum IgG testing or precipitins as supportive markers of exposure	Bronchoalveolar lavage with lymphocyte analysis, multidisciplinary discussion involving respiratory, radiological, and pathological expertise, and tissue sampling when diagnostic uncertainty remains and the result would alter management. Specific inhalation challenge may be considered only in selected expert centres	Diagnosis should integrate exposure evidence, HRCT pattern, BAL findings, and, where necessary, histopathology; serum IgG alone is not diagnostic. Management centres on identification and avoidance or substantial reduction of the inciting exposure, with treatment guided by whether disease is non-fibrotic or fibrotic

Table 2. Proposed phenotype-based diagnostic approach to mushroom-associated reactions. *The algorithm is based on general guidelines for food allergy, contact dermatitis, occupational asthma, and hypersensitivity pneumonitis, supplemented by the limited mushroom-specific literature. It has not*

been prospectively validated for mushroom-associated disease. Positive skin testing, serum-specific IgE, or serum IgG indicates sensitisation or exposure and should be interpreted in conjunction with the clinical history and, where appropriate, challenge testing. BAT, basophil activation test; BAL, bronchoalveolar lavage; ELISA, enzyme-linked immunosorbent assay; HP, hypersensitivity pneumonitis; HRCT, high-resolution computed tomography; IgE, immunoglobulin E; IgG, immunoglobulin G.