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No Escape Indoors and Outdoors: The Underestimated Risk of Mold Allergies

I. Introduction

The prevalence of allergic diseases has continued to rise over the past two to three decades, becoming a major challenge for global public health. According to data from the Global Burden of Disease study, since 1990, the total number of cases of asthma and atopic dermatitis has steadily increased, with the number of asthma patients exceeding 260 million by 2021 (GBD 2021 Chronic Respiratory Diseases Collaborators, 2023). Although age-standardized prevalence has declined slightly in some regions, the overall case numbers and healthcare burden continue to rise. This trend is particularly evident in children—multiple international studies have shown that sensitization rates to common allergens in children reach as high as 40–50%, with urbanization and prolonged indoor living identified as key background factors driving the risk.

Among these highly sensitized populations, house dust mites, pollen, animal dander, and molds are the most common inhalant triggers. In particular, molds are widely present in damp indoor environments and can release large amounts of tiny spores and cell wall fragments into the air, with clear biological potential to aggravate respiratory allergies and asthma. According to WHO/IUIS statistics, about 9% of currently recognized allergens originate from molds. This proportion suggests that in clinical practice, roughly 1 in 10 allergy patients may have a disease course associated with molds—yet in most diagnostic and treatment processes, such risks are often overlooked. Compared to dust mites or pollen, molds receive significantly less attention in clinical testing, public awareness, and policy planning. This underestimation, however, is quietly undermining the respiratory health of millions of people through long-term exposure and chronic allergy.

This article aims to integrate existing epidemiological data, clinical study findings, and experimental reports to explore the types of fungi as allergens and their associations with respiratory diseases, thereby addressing the insufficient attention to fungal exposure risks in current discussions on allergy prevention and management.

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II. Literature Review

(i) The Major Allergen Source in Fungi: Spores

Among the various structures of fungi, spores are the most frequently identified as the primary cause of sensitization. As the reproductive units of fungi, spores are small, easily airborne, and capable of being produced in large quantities. Their size ranges from 2 to 30 micrometers, small enough to penetrate the upper respiratory tract and even reach the bronchioles and alveoli. Numerous studies have shown a clear association between exposure to high concentrations of fungal spores in the air and the onset of allergic rhinitis, acute asthma exacerbations, and seasonal conjunctivitis (Mendell et al., 2011; Zureik et al., 2002). These spores often float unnoticed in everyday air. In particular, during hot and humid conditions from late spring to autumn, both outdoor and indoor spore concentrations can rise sharply, becoming a major trigger for peak incidence in certain populations. A closer look at the fungal allergens formally registered by the WHO/IUIS Allergen Nomenclature Sub-Committee reveals that they encompass more than 30 protein families, primarily derived from several fungal genera with high allergenic potential. The following will introduce the most common and clinically relevant species, which show the highest sensitization rates in both clinical and environmental studies:

- ***Aspergillus fumigatus***: Widely present in compost, dust, and damp indoor building materials, its spores carry multiple named allergenic proteins, such as Asp f 1, Asp f 2, Asp f 4, and Asp f 6 (Banerjee et al., 2010). It is closely associated with allergic bronchopulmonary aspergillosis (ABPA) and asthma exacerbations. When gardening soil is disturbed, compost bins are cleaned, or damp walls are repaired, A. fumigatus spores can be released in large amounts instantly.
- ***Alternaria alternata***: One of the most common fungal spores found in outdoor air, particularly originating from dried plant debris and soil. Its major allergen, Alt a 1, is strongly associated with acute asthma attacks in children. The risk of exposure increases during farming seasons, after lawn mowing in yards, or when unmaintained potted plants are placed indoors.
- ***Cladosporium herbarum***: The concentration of its spores in the air often exceeds that of other fungi, with large

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releases occurring during spring and summer. Some cases are also associated with cross-reactivity to pollen. Spores of *C. herbarum* may be inhaled when opening uncleaned curtains, hanging laundry outdoors, or sweeping fallen leaves.

- ***Penicillium chrysogenum**:* Commonly found in indoor storage rooms, food factories, and air-conditioning filters, with certain sensitization reactions cross-linked to *Aspergillus.* In old air-conditioning systems and damp storage rooms, it may continuously release spores over extended periods.
- ***Epicoccum nigrum, Fusarium spp.*, and *Trichoderma spp.***: Although sensitization rates are relatively low in the general population, they pose potential allergenic risks in high-exposure groups such as those involved in agriculture, compost handling, and food production. Activities such as grain storage handling, compost turning, or raw material processing may lead to significant spore inhalation.

The allergens found on fungal spores are mostly high-molecular-weight glycoproteins or enzymatic substances, characterized by structural stability and strong binding affinity to IgE antibodies. Similar phenomena can also be observed in other allergen domains—for example, the major proteins responsible for peanut allergy retain their allergenic capacity even after roasting or long-term storage. Likewise, fungal spore allergens can remain active in the air for extended periods. Once inhaled, they may rapidly trigger immediate-type allergic reactions, while long-term low-dose exposure can lead to persistent airway inflammation and structural remodeling. Some spores also possess protease activity, similar to certain pollen allergens, enabling them to damage the epithelial barrier of the respiratory tract, thereby allowing more allergenic substances to penetrate and exacerbating the course of asthma and allergies.

(ii) Fungal Allergens: The Allergenic Potential of Hyphae

Discussions on fungal-induced allergies have long focused on airborne spores, but recent studies further reveal that fungal hyphae and their fragments also possess high allergenic potential and, under certain conditions, may serve as important antigen sources closely associated with respiratory allergies. Hyphae are filamentous structures

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produced during the vegetative growth phase of fungi. When they break due to aging, mechanical disturbance, or desiccation, they release fine fragments, typically smaller than 5 micrometers. These particles can remain suspended in the air for long periods and, because of their tiny size, penetrate deep into the alveoli to trigger immune responses.

Multiple studies have confirmed that fungal hyphae express and secrete various proteins and enzymes with allergenic properties during growth (Krüger et al., 2015). For example, in *Aspergillus fumigatus*, hyphal-stage expression includes Asp f 3 (a peroxiredoxin-like antioxidant enzyme) and Asp f 9/16 (β-1,3-glucanase), both of which are recognized as major allergens. Asp f 3 has attracted particular attention because it shows IgE binding rates as high as 70% in diagnostic studies, making it one of the clinically important markers of sensitization (Dellière & Aimanianda, 2023). In addition, Asp f 5, a secreted protease, can disrupt the respiratory epithelial barrier and further promote sensitization responses. These proteins can be recognized by dendritic cells and promote T_H2-skewed immune responses, while also exacerbating existing asthma and allergic rhinitis symptoms.

Studies on airborne particles have also shown that in environments with high fungal activity or humidity, hyphal fragments account for 3–5% of fungal particles in the air, with some originating from *Cladosporium* or *Penicillium*specie s. Although the concentration of hyphal fragments is generally lower than that of spores, their deep penetration capacity and carried antigenic structures pose a threat to highly sensitive individuals, much like invisible indoor smoke—imperceptible to the eye, yet sufficient to ignite the spark of an allergic reaction within the body.

(iii) Indoor and Outdoor Fungal Spore Concentrations and Seasonal Influence

Clinical manifestations of mold allergies often show clear seasonality, with the transitional period between spring and summer representing a particularly high-risk season for allergic outbreaks. This phenomenon is strongly correlated with changes in airborne fungal spore concentrations, especially in regions with active agriculture and warm, dry climates, where both the dispersal capacity and concentrations of spores rise significantly. The most

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common allergenic fungi under such conditions are *Alternaria* and *Cladosporium*. These are considered "dry-air molds," with optimal growth and dispersal occurring in the afternoon under high temperatures, low humidity, and increasing wind speed. This also explains the clinical observation of peak allergic symptoms in the afternoons and evenings between May and August each year. During farming seasons, lawn mowing, leaf pile clearing, or handling long-stored potted soil, spores may be released in large quantities due to disturbance, posing high risks to outdoor workers and gardening populations. According to integrated European observational data, median peak concentrations of *Cladosporium* can reach 18,800 spores/m³ during midsummer, while *Alternaria* reaches 665 spores/m³—both well above the clinical threshold levels that typically trigger allergic symptoms.

Compared with the outdoor environment, indoor mold allergens are mainly dominated by ***Penicillium*** and ***Aspergillus*** species. These genera of molds show strong environmental adaptability: they are not only common in damp homes in tropical and subtropical regions, but can also grow stably indoors under cold-climate conditions (Adams et al., 2013). Studies have shown that in places such as Austria and Northern Europe during winter, the indoor concentration of *Aspergillus/Penicillium* spores can reach 1.5–2 times that of the outdoors, reflecting the hidden risk of mold exposure faced by residents in cold regions. Contributing factors include long periods of heating without ventilation, the use of outdated air-conditioning systems, and water leakage or dampness in kitchen and bathroom corners. These conditions create fertile grounds for mold growth, leaving people who spend extended hours in offices, schools, or sealed homes under continuous exposure.

The tropics likewise face significant indoor mold problems. In regions with tropical, rainy climates, year-round high humidity combined with prolonged use of air conditioning keeps indoor *Aspergillus* and *Penicillium* spore concentrations consistently elevated, sometimes 1.5–3 times higher than outdoors. Surveys from Singapore and Malaysia have shown that air-conditioning and sealed residential settings promote the accumulation of

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mold allergens in indoor air. This leads to prolonged exposure for occupants to sensitizing environments; even without direct contact with visibly moldy surfaces, inhaling spore levels sufficient to trigger allergic reactions remains a constant risk.

(iv) Clinical Studies on Mold Allergy

Although the sensitization rate to molds in the general healthy population is generally lower than that of common inhalant allergens such as dust mites and pollen (about 2–5%), the proportion rises to 5–20% among patients with allergic diseases, and can even exceed 30% in certain high-risk groups (Shalev et al., 2015). These figures indicate that while mold allergy is not the most prevalent in terms of overall prevalence, it plays a critical role in specific populations, with a particularly notable impact on asthma control and disease severity.

Children represent a group that requires special attention. Studies have shown that mold-sensitized children exhibit significantly lower lung function (e.g., FEV_1) compared with non-sensitized peers, markedly increased airway hyperresponsiveness (AHR), and are often associated with higher IgE levels and more frequent asthma exacerbations (Lee, Lee, & Kim, 2017). *Alternaria alternata* and *Aspergillus fumigatus* are the most common mold allergens, with *Alternaria* exposure being strongly associated with acute asthma attacks in children. In a multi-city study conducted in the United States, emergency visits were significantly higher among mold-allergic children compared with non-sensitized groups (JACI In Practice, 2016), underscoring the clinical importance of mold allergy management.

This phenomenon is not limited to Western countries. An epidemiological survey of school-aged children in Jeju Island, Korea, further demonstrated the presence of mold allergy within the general pediatric population. Using skin prick testing for common allergens, the study found that up to 7.3% of children exhibited sensitization to *Alternaria* (Lee & Hong, 2023). This suggests that even children without clear symptoms may still be at risk, with their conditions often overlooked due to mild or subtle signs. Results from the European ISAAC project and the German Environmental Health Survey likewise confirmed that damp housing conditions and mold allergy contribute significantly to childhood asthma exacerbations,

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highlighting the cross-regional consistency of this phenomenon.

III. Conclusion

In daily life, we may be inhaling mold allergens every single day without realizing it. As airborne allergens, molds exert a much deeper impact on human health than previously recognized. Both highly dispersible spores and tiny, deeply penetrating hyphal fragments have been shown to trigger a wide range of immune responses, including allergic rhinitis, asthma, and conjunctivitis, with especially pronounced effects in children and highly sensitive populations. Studies indicate that under specific environmental conditions—such as hot, dry agricultural seasons or enclosed, damp indoor spaces—mold spore concentrations are strongly associated with the onset of allergic symptoms, and the allergenic activity of their proteins is further modulated by climatic factors.

What is even more alarming is that an estimated 4.8 million asthma patients worldwide suffer from allergic bronchopulmonary aspergillosis (ABPA), a condition caused by mold allergy. These represent only the most severe cases that have been clinically diagnosed and recorded, a number equivalent to the population of a medium-sized country. Beneath this “tip of the iceberg” lies a vast number of patients with mild to moderate mold allergies, who remain chronically exposed in daily and occupational environments without recognition or diagnosis.

This highlights that despite substantial epidemiological and clinical evidence confirming the seriousness of mold allergy, it remains underestimated in clinical practice, air quality management, and public health education. Compared with dust mites and pollen, molds are more difficult to detect visually, show extreme fluctuations in concentration, and lack standardized diagnostic reagents—factors that often lead to their omission in allergy assessment processes. Moreover, the general public tends to associate molds merely with “dampness, musty odors, and visible stains,” without realizing that they may be hidden culprits behind asthma exacerbations and childhood respiratory illnesses.

In today’s world—shaped by climate change, increasingly airtight urban buildings, and a steadily rising allergic population—it is imperative to re-examine the close relationship between

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molds and allergy, and to integrate them into comprehensive strategies for air quality monitoring, clinical diagnosis, and environmental control. Future research and policy should place greater emphasis on mold allergy screening, risk identification in vulnerable populations, and prevention science. Only by granting this long-neglected health issue the proper attention and resources, and translating knowledge into concrete actions, can we mitigate the long-term threat of mold allergy to public health.

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