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ENVIRONMENTAL MOLDS AND MYCOTOXINS: SYSTEMATIC REVIEW OF MULTISYSTEMATIC HEALTH IMPACTS, PATHOPHYSIOLOGICAL MECHANISMS, AND CHRONIC DISEASE

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ABSTRACT
Environmental molds and mycotoxins are a growing global health concern, contributing to over 1.5 million annual fatalities worldwide despite widespread underdiagnosis. Climate change and increased exposure further amplify these risks. Following PRISMA 2020 guidelines, literature was retrieved from PubMed, Google Scholar, SciSpace and BASE (Bielefeld Academic Search Engine). Key species (*Alternaria alternata, Aspergillus spp., Mucorales*) and mycotoxins (e.g., T-2 toxin) were linked to respiratory, neurological, dermatological, and systemic conditions. Mechanisms include IgE-mediated sensitization, angioinvasive damage, and immune dysregulation. Up to 80% of asthmatic children show Alternaria sensitization, and invasive infections carry 30–90% mortality. Climate change expands fungal rates and enhances thermotolerance. Molds and mycotoxins exert significant multisystemic impacts on global health. Integrated strategies for environmental control, early diagnosis, and targeted treatment are needed, alongside research to clarify long-term effects and standardize clinical management.

Keywords:
Environmental molds; Mycotoxins; Human health; Pathophysiology; Chronic diseases; Systematic review; PRISMA

INTRODUCTION
Fungi represent a vast and diverse kingdom of organisms, with an estimated six million species widely distributed across natural and built environments (Firacative, 2020). These organisms are ubiquitously present in atmospheric environments, on human surface, and in settings ranging from natural ecosystems to damp homes. While most fungal species do not cause harm to humans, several hundred are known to disrupt health through three primary mechanisms which are causing infections(mycoses), triggering allergic reactions, or producing toxins(mycotoxicosis). Human fungal pathogens have been characterized as "hidden killers," presenting an unprecedented and growing threat to global public health that results in more than 1.5 million annual fatalities (Thambugala et al., 2024).
The multisystem impacts of environmental molds and fungal pathogens are increasingly recognized as a major global health burden. In the respiratory system, species including Alternaria and Cladosporium are prominent outdoor allergens that contribute to morbidity in patients with asthma or allergic rhinitis (Michaels, 2017; Novembre et al., 2025). Inhalation of fungal spores can progress to severe conditions such as Allergic Bronchopulmonary Aspergillosis (ABPA) or Severe Asthma with Fungal Sensitization (SAFS), which induce persistent inflammation and impair lung function (Baxi et al., 2016; Oliveira et al., 2023). Beyond allergic manifestations, certain molds and fungi are capable of invasive infection, with Invasive Mold Disease (IMDs) involving dissemination into the bloodstream and organs. While historically associated with severely immunocompromised populations, IMD incidence is rising among patients with diabetes mellitus, chronic obstructive pulmonary disease (COPD), and severe viral infection including COVID-19 and influenza. These invasive

pathogens often exhibit angioinvasive properties, leading to vascular thrombosis and tissue necrosis (Lee, 2023; Stanzani et al., 2015)

Health impacts are further compounded by mycotoxins, secondary metabolites that cause toxic damage to the liver, kidneys, and other vital organs following ingestion or inhalation (Ratnaseelan et al., 2018). Additionally, anthropogenic factors such as climate change are altering patterns of fungal disease by expanding the geographic range of endemic mycoses and selecting for enhanced pathogenic traits like thermal tolerance. Rising temperatures and increased frequency of extreme weather events contribute to expanded pathogen distributions and heightened virulence, including severe skin infections following traumatic injuries (Michaels, 2017; van Rhijin & Bromley, 2021).
Despite these significant impacts, mold-related and fungal illnesses remain underdiagnosed and underappreciated. Key contributing factors include the absence of universal diagnostic methods, variability in fungal extracts used for testing, and the non-reportable status of most fungal infections (Lee, 2023). This systematic review synthesizes current knowledge on the epidemiology, immunopathogenesis, and clinical implications of environmental fungi to provide a comprehensive overview of their multisystem effects on human health.

OBJECTIVES

The main objective of this study is to provide an extensive analysis of environmental fungi and their multisystematic impacts in human health. To specify, it seeks to summarize by identifying major fungal or mold species associated with allergic, infectious, and mycotoxin-related diseases. Also, to discuss the diseases produced by these molds and their corresponding symptoms in affected individuals. Moreover, the study aims to examine modern diagnostic methods such as imaging, laboratory tests, and histology techniques for detecting fungal-related diseases. In addition, to explore trends and contributing factors such as environmental exposure and climate change influencing the incidence of fungal diseases. Lastly, the purpose of the study is to provide a solid overview of fungal health implications by synthesising findings from recent studies and reviews.

METHODOLOGY

This systematic review was conducted to synthesize current knowledge on the epidemiology, immunopathogenesis, and clinical implications of environmental molds and mycotoxins on human health. The methodology followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure high transparency and reproducibility.

1. Research Design and Approach

This study employed a systematic review design to provide a comprehensive and unbiased overview of the multisystemic impacts of environmental molds and mycotoxins on human health. This approach was chosen to systematically identify, evaluate, and synthesize existing evidence, ensuring a thorough summary of current knowledge, pathophysiological mechanisms, and chronic disease associations.

2. Search Strategy (Data Collection)

The literature search was conducted using multiple databases, search engines such as Google Scholar, PubMed, SciSpace and BASE (Bielefeld Academic Search Engine). The search terms utilized were "mold AND human health AND mycotoxins". The search was limited to articles published within a ten-year timeframe, specifically between 2015 and 2025, to ensure the inclusion of the most recent research.

Inclusion Criteria:

- Studies focusing on the human health impacts of environmental molds and mycotoxins.
- Articles published between 2015 and 2025.
- Studies reporting clinical, environmental, or mechanistic findings.

Exclusion Criteria:

- Studies not directly related to human health impacts.
- Articles published outside the specified timeframe.

3. Selection and Screening Process

The selection process involved an initial screening of titles and abstracts, followed by a full-text review of potentially relevant articles.

- Initial Screening: A total of 34 out of 50 articles were initially identified through the search strategy. These

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articles underwent an initial screening based on their titles and abstracts to assess their relevance to the review's objectives.

- Full-Text Review: All 14 articles that met the initial screening criteria were then subjected to a full-text review to confirm their adherence to the defined inclusion and exclusion criteria.
- Inter-rater Reliability: The screening process was conducted by a single reviewer.

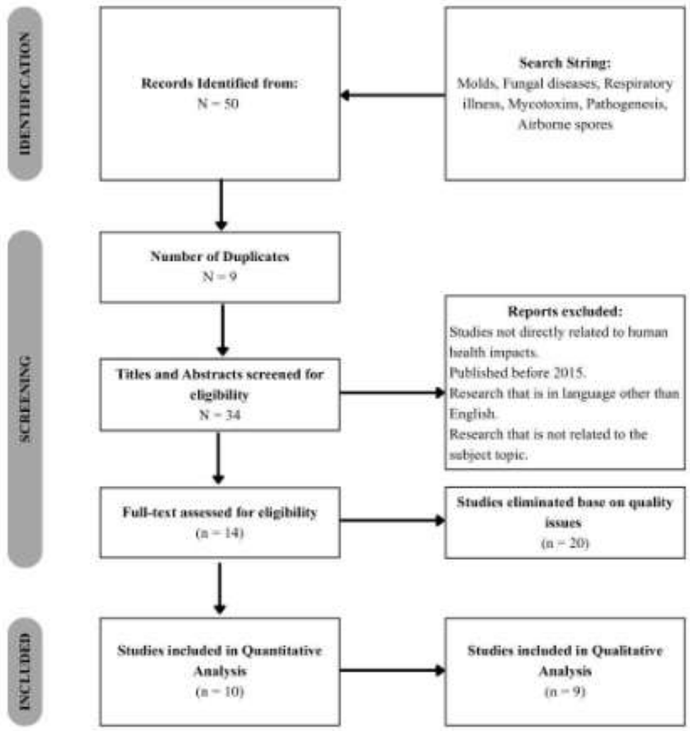

Fig 1. Flow Chart of Study Selection Process using PRISMA Method

4. Data Extraction

Data from the selected articles were extracted into a structured summary table. This table allowed for the systematic collection of key information from each study to ensure consistency and facilitate analysis. The specific data points extracted included:

- Species (Mold/Fungi): Identification of the specific mold or fungal species.
- Driven Diseases: Diseases associated with the identified mold/fungi.
- Symptoms: Clinical manifestations or symptoms of the associated diseases.
- Diagnosis and Possible Cures: Methods used for diagnosis and available treatment or management strategies.
- Analysis: Key findings or interpretations from the original study.
- Author and Year: Reference information for each study.

5. Data Synthesis and Analysis

The collected data were synthesized and analyzed primarily through thematic analysis and narrative synthesis.

- Thematic Analysis: Key themes, patterns, and trends across the included studies were identified. This involved categorizing the information from the data extraction table to highlight common mold species, prevalent diseases, diagnostic approaches, and treatment modalities.
- Narrative Synthesis: The findings from the individual studies were summarized in a descriptive manner,

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comparing and contrasting the evidence to identify consistencies and inconsistencies in the literature regarding the multisystemic impacts of environmental molds and mycotoxins.

- Methodological Appraisal: Due to the scope of this review, a formal risk of bias assessment for individual studies was not performed. The synthesis primarily focused on interpreting the reported findings and mechanisms.

6. Limitations

This systematic review acknowledges several potential limitations, including:

- While multiple search engines were utilized, the primary focus on Google Scholar and limited scope of other platforms might affect the overall comprehensiveness of the retrieved literature.
- The search terms were specific, potentially overlooking other relevant studies using different terminology.
- The screening and data extraction process was conducted by a single reviewer, which could introduce bias.

RESULTS AND DISCUSSION

The diversity of organisms in Kingdom Fungi includes yeasts, mushrooms, and molds, which serves as a critical component of human environmental exposure. While some of the fungi may pose no harm in human health, several hundred species act as opportunistic pathogens (Novembre et al., 2025). The summary table organizes distinct diseases and conditions to illustrate the broad spectrum of these impacts.

Species (Mold/Fungi)	Driven Diseases	Symptoms	Diagnosis and Possible Cures	Analysis	Author and Year
Alternaria alternata (specifically major allergen Alt a 1)	Allergic Rhinitis (AR) and Pediatric Asthma	Sneezing, nasal congestion, wheezing, and chronic cough	Diagnosis: Skin-prick tests (SPT), specific IgE measurement, and component-resolved diagnostics; Cures: Environmental control, intranasal corticosteroids, and Allergen Immunotherapy (AIT)	Review of epidemiology and treatment for Alternaria sensitization in children	Novembre et al., 2025
Aspergillus spp.	Invasive Aspergillosis	Cough, chest pain, hemoptysis, and dyspnea	Diagnosis: Histopathologic tissue invasion, galactomannan (GM) assay, and CT identifying the "halo sign"; Cures: Voriconazole, isavuconazole,	Review of epidemiology and diagnosis in cancer and transplant patients	Sang-Oh Lee, 2023

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			or lipid formulations of amphotericin B		
Invasive molds such as Aspergillus	Invasive Pulmonary Mold Disease (Radiographic Focus)	Non-specific clinical signs in patients with hematological malignancies	Diagnosis: CT Pulmonary Angiography (CTPA) identifying the "vessel occlusion sign"; Cures: Antifungal therapy; negative CTPA allows earlier cessation of treatment	Prospective comparison of diagnostic performance between CTPA and standard CT imaging findings	Stanzani et al., 2015
Aspergillus spp. (e.g., A. fumigatus)	Allergic Bronchopulmonary Aspergillosis (ABPA)	Dry cough, wheezing, and severe respiratory allergy	Diagnosis: Total serum IgE measurement and component-resolved diagnostics; Cures: Environmental control and multifaceted pharmacological management	Meta-analysis of manifestations including severe asthma with fungal sensitization	Oliveira et al., 2023
Aspergillus (A. fumigatus, A. flavus)	Aspergillosis (Allergic, Chronic, Invasive)	Allergic reactions, chronic pulmonary issues, invasive systemic infection	Diagnosis: Histology and culture; Cures: Azoles (first-line); Amphotericin B (salvage therapy)	Rising temperatures and CO_2 increase susceptible populations (COPD/TB). Climate change accelerates drug resistance via agricultural fungicide use and favors A. fumigatus due to thermotolerance	van Rhijn and Bromley, 2021
Aspergillus	Severe allergic	Elevated	Diagnosis:	Pro-allergenic	Kraft,

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fumigatus	asthma	total IgE, broncho-obstructio n (FEV1/FV C), and increased asthma severity	Positive skin prick test, CAP test, elevated total serum IgE, FEV1/FVC ratio	Th2 response; acts as a sensitizer associated with increased allergic asthma severity	2021
Aspergillus and Penicillium genera	Aflatoxicosis; respiratory and toxic effects	Liver damage, acute poisoning, and respiratory distress	LC/MS, LC/MS/MS, ELISA, and PCR for mycotoxin identification; Cures: Not specified	Fungi produce harmful mycotoxins during grain storage; production influenced by temperature and water activity	Mannaa, 2017
Lichtheimia spp. and Scedosporiu m spp.	Complex soft tissue coinfection and invasive mold infection	Non-healing wound, invasive hyaline paucisepta te fungal hyphae, and aggressive tissue involveme nt	Diagnosis: Histopathologic review, culture, and biopsy; Cures: Liposomal amphotericin B, isavuconazoniu m sulfate, and surgical debridement or amputation	Associated with trauma (rooster spur puncture) in immunosuppre ssed patients; Scedosporium may be wholly resistant to amphotericin B, requiring multiple antifungal modalities	B Puello Yocum & J Lavik, 2022
Mycotoxins (e.g., T2) Trichoderma , Fusarium, and Stachybotrys	Autism Spectrum Disorder (ASD)	Pathogene sis linked to pro-inflammat ory cytokine secretion	Diagnosis: Detection of T2 mycotoxins in patient sera; Cures: Reducing environmental exposure to moisture and contaminated sources	Systematic review of mycotoxins' relationship to neuropsychiatr ic effects	Ratnaseel an et al., 2018
Trichophyto n, Microsporu m, and Epidermoph yton	Dermatophytos is (Tinea)	Localized skin lesions, inflammati on, and brittle,	Diagnosis: Clinical examination, microscopy, and culture of skin samples;	Comprehensiv e overview of fungal pathogens extracted from over 850	Thambug ala et al., 2024

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		discolored nails	Cures: Topical or oral antifungal agents such as azoles and polyenes	recent case reports	
Penicillium and Aspergillus	Asthma, allergic rhinitis, tonsillitis, adenoid hypertrophy, and impaired lung function	Pulmonary inflammation, airway sensitization, and oxidative stress	Diagnosis: Comprehensive literature search; Cures: Chemical and physical control measures for environmental prevention	Building deterioration is a major source; spores (1–10 µm) remain suspended and enter the respiratory tract via inhalation	Hai Xiao et al., 2025
Mucorales (Mucor, Rhizopus, Lichtheimia)	Mucormycosis (Rhinocerebral, Cutaneous)	Tissue infarction, vessel thrombosis, necrosis, angioinvasion	Diagnosis: Clinical suspicion/histology; Cures: Aggressive debridement or amputation, antifungal therapy, and correction of underlying conditions (diabetes)	Highly thermotolerant. Prevalence is linked to extreme weather (tornadoes, tsunamis) and risk factors like diabetes. Climate change increases disaster frequency, driving cutaneous cases	Carolina Firacative, 2020

Table 1. Summary of Allergic, Infectious, and Mycotoxin-Driven Diseases Linked to Environmental Fungi

The findings summarized in Table 1 demonstrate that environmental molds and their associated mycotoxins exert multisystemic impacts on human health, primarily affecting the respiratory, integumentary, immune, and nervous systems. Across reviewed studies, fungal species such as *Alternaria alternata, Aspergillus spp., Penicillium, Mucorales,* and dermatophytes were consistently linked to a wide spectrum of diseases ranging from mild allergic reactions to severe invasive infections and chronic systemic conditions. However, their impacts vary significantly depending on fungal species, exposure pathway, and host condition. Rather than producing uniform outcomes, fungi exhibit distinct pathogenic behaviors ranging from allergenic responses to invasive and systemic diseases.

Respiratory diseases were the most frequently reported outcomes, particularly allergic rhinitis, asthma, hypersensitivity pneumonitis, and chronic pulmonary conditions. Studies showed that exposure to airborne fungal spores, especially those measuring 1–10 µm facilitates deep inhalation into the lower respiratory tract, triggering inflammation, airway sensitization, and oxidative stress. In this case, a **comparison** of studies reveals that respiratory disorders are the most often reported adverse effects, while their severity varies. For example, *Alternaria alternata* is strongly linked to allergic rhinitis and pediatric asthma via IgE-mediated sensitization, whereas Aspergillus species can induce both allergy disorders (e.g., ABPA) and severe invasive infections in immunocompromised people. This difference shows the importance of the host's immunological state in illness progression.

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Invasive aspergillosis and mucormycosis infections which develop from mold contamination create dangerous health risks that rank among the most critical extreme forms of fungal diseases because the fungi demonstrate aggressive "angioinvasive" behavior. The process starts when fungal hyphae enter blood vessels through their walls and continues until they grow inside the vessel which results in thrombosis and tissue death known as necrosis and causes a high death rate which occurs when doctors fail to treat the infection during its early stage (Stanzani et al., 2015).

Allergic and invasive mechanisms differ substantially. Allergic conditions are driven by repeated exposure to airborne spores that trigger chronic inflammation, while invasive infections involve direct tissue and vascular invasion, resulting in thrombosis and necrosis. Studies such as Stanzani et al. (2015) demonstrate that improved diagnostic tools, such as High-Resolution Computed Tomography Angiography (CTPA), serves as a diagnostic indicator to show blood flow disruption from fungal invasion and it achieves better detection accuracy than standard imaging methods .

Dermatophytosis, which are dermatological fungal diseases that affect human skin, continue to stand as major medical problems which affect most of the world's population. The tinea infections which impact skin and hair and nail areas show high recurrence rates while spreading easily through direct contact and through environmental surfaces which have been contaminated (Thambugala et al., 2024).

In contrast to respiratory and invasive diseases, dermatological infections such as dermatophytosis are highly prevalent but less severe. Their persistence is linked to environmental contamination and reinfection cycles rather than immune suppression. This indicates that disease burden is influenced not only by severity but also by prevalence and transmission dynamics.

From typical single-pathogen infections, the coinfection with *Lichtheimia* (a Mucorales mold) and *Scedosporium* can complicate diagnosis and cure due to varying antifungal susceptibilities. While mucormycosis typically requires aggressive surgical intervention and amphotericin B therapy, *Scedosporium* species may exhibit resistance to this treatment, necessitating alternative antifungal agents. This contrast highlights how crucial it is to combine culture data with histopathology findings in order to precisely identify all causal organisms (Puello & Lavik, 2022).

Through a variety of processes, such as damage to epithelial barriers, modification of inflammatory pathways, and modification of immune cell responses, mycotoxins can impair immunological function. The significance of environmental exposure as a contributing element to disease progression rather than a direct cause, in contrast to research that only focuses on infection. The results highlight the need for additional mechanistic and epidemiological study to elucidate causative links while also suggesting that mold and mycotoxins operate as substantial modifiers of disease severity, particularly in susceptible populations (Kraft et al., 2021).

The ongoing existence of these conditions demonstrates how important proper environmental hygiene practices and effective moisture management systems are for stopping the spread of fungal infections. The global incidence of both invasive and dermatological mold diseases will increase because climate change causes fungi to develop better thermotolerance while expanding their geographic reach thus requiring healthcare systems to adopt more unified methods for environmental protection and patient care (van Rhijn & Bromley, 2021).

The researchers discovered that mycotoxins which include T-2 toxin and gliotoxin as secondary metabolites from environmental molds show substantial effects on both the whole body and brain functions of humans. The substances function as strong immune system modulators because they disrupt normal immune system operations and start inflammatory processes at the cell level. The toxins cause cells to produce pro-inflammatory cytokines which, together with mast cell activation, create a state of continuous immune system dysfunction that affects the entire human body.

The central nervous system sustains extensive harm from chronic inflammatory responses which result from prolonged exposure to these toxins. The biological processes identified here function as main contributors which worsen Multiple Sclerosis (MS) symptoms and initiate neuropsychiatric disorders specific to Autism Spectrum Disorder (ASD). The presence of these toxins in biological samples such as serum functions as essential proof that they enter the bloodstream to disrupt cellular functions thus contributing to the development of complex chronic diseases.

The persistence of these conditions shows how crucial good environmental hygiene procedures and efficient moisture management systems are to halting the spread of fungal infections. The global incidence of both invasive and dermatological mold diseases will increase because climate change causes fungi to develop better thermotolerance while expanding their geographic reach thus requiring healthcare systems to adopt more unified methods for environmental protection and patient care (van Rhijn & Bromley, 2021).

Environmental conditions play a significant role in the distribution and impact of molds. Factors such as temperature, humidity, and indoor dampness influence fungal growth and spore dispersal. Climate change has been identified as a driver

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of increased fungal thermotolerance and geographic spread, which affects disease patterns and antifungal resistance (van Rhijn & Bromley, 2021). Therefore, successful mitigation needs an integrated approach which combines advanced medical treatments like azoles and amphotericin B with environmental controls that maintain indoor air quality and moisture levels.

The qualitative analysis presented in this table shows that the health impacts of environmental molds are driven by distinct but interconnected mechanisms.

Table 2: Qualitative Analysis of Pathophysiological Mechanisms, Sources of Exposure, and Resulting Health Outcomes of Environmental Molds and Mycotoxins

Category	Description	Health Outcomes	References
Allergic Sensitization	Immune response to fungal allergens through IgE pathways	Asthma, allergic rhinitis, ABPA	Novembre et al., 2025; Kraft, 2021;
Derma Infection	Tinea infections caused by contaminated surfaces or direct contact	Dermatophytosis (Tinea)	Thambugala, 2024
Invasive Infection	Tissue and vascular invasion by fungal hyphae	Aspergillosis, mucormycosis, *Lichtheimia* spp. and *Scedosporium* spp.	Lee, 2023; Puello & Lavik, 2022
Toxin Exposure	Cellular damage caused by mycotoxins	Liver toxicity, systemic effects	Mannaa & Kim, 2017
Neuroinflammation	Cytokine release and immune dysregulation	ASD, MS exacerbation	Ratnaseelan et al., 2018;
Environmental Exposure	Inhalation or contact with spores in damp environments	Respiratory and chronic diseases	Xiao et al., 2025;
Climate Influence	Environmental changes enhancing fungal survival and spread	Increased disease incidence	van Rhijn & Bromley, 2021;

Allergic sensitization is a major pathway in respiratory diseases, where repeated exposure to fungal allergen leads to immune activation and chronic inflammation. This mechanism explains the high prevalence of asthma and allergic conditions associated with indoor mold exposure (Novembre et al., 2025). However, while highly prevalent, these conditions are generally less severe compared to invasive infections.

Invasive infection represents a more severe mechanism, involving direct tissue invasion and vascular damage. This process is observed in diseases such as aspergillosis and mucormycosis, where fungal growth within host tissues leads to necrosis and systemic complications (Lee, 2023; Firacative, 2020). Early detection and antifungal treatment are critical in managing these conditions.

In contrast, invasive infections represent a more critical mechanism due to their ability to penetrate tissues and blood vessels, resulting in severe complications such as necrosis and systemic spread. Although less common, their high mortality rate underscores the importance of early detection and treatment.

Toxin-mediated effects highlight the systemic impact of molds beyond localized infections. Mycotoxins interfere with cellular processes and immune regulation, contributing to organ damage and chronic disease development. Neuroinflammatory responses linked to these toxins provide insight into their role in neurological disorders (Ratnaseelan et al., 2018).

Toxin-mediated effects provide a different perspective, as they operate at the cellular level and contribute to long- term

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systemic and neurological conditions. Unlike allergic and invasive mechanisms, these effects are less immediately visible but may lead to chronic health outcomes, emphasizing the need for broader environmental monitoring.

Environmental exposure remains a central factor connecting all mechanisms. Indoor dampness, poor ventilation, and contaminated materials increase the concentration of airborne spores, leading to higher exposure levels. Climate- related changes intensify these risks by creating favorable conditions for fungal growth and adaptation (van Rhijn & Bromley, 2021).

> Systemic and Neurological Effects of Mycotoxins

Mycotoxins produced by environmental molds exert systemic effects that extend beyond localized infections. Compounds such as T-2 toxin and gliotoxin disrupt immune regulation and induce inflammatory responses at the cellular level. These toxins stimulate cytokine release and activate mast cells, which contributes to persistent immune dysregulation (Ratnaseelan et al., 2018; Kraft et al., 2021).

Neurological implications include associations with autism spectrum disorder and exacerbation of multiple sclerosis. These conditions are linked to neuroinflammation and demyelination processes triggered by prolonged exposure to mycotoxins. Detection of mycotoxins in biological samples such as serum supports their role in disease pathogenesis. Reduction of exposure to contaminated environments has been identified as a key intervention strategy.

A key similarity across all mechanisms is their dependence on environmental exposure. Indoor dampness, poor ventilation, and contaminated materials significantly increase the risk of fungal proliferation. Climate change further intensifies these conditions by promoting fungal growth and expanding their geographic range.

> Environmental and Ecological Determinants

Environmental factors influence the growth, distribution, and pathogenicity of molds. Temperature, humidity, and water activity are critical variables that regulate fungal proliferation and mycotoxin production. Conditions within indoor environments, including dampness and poor ventilation, increase the concentration of airborne spores and exposure risk (Xiao et al., 2025).

Climate change alters fungal ecology by increasing thermotolerance and expanding the geographic range of pathogenic species. Extreme weather events contribute to environmental contamination and increased incidence of fungal infections (van Rhijn & Bromley, 2021; Firacative, 2020).

The growth and pathogenicity of environmental molds are primarily governed by specific physical parameters, where optimal toxin production in species like *Fusarium* and *Aspergillus flavus* occurs at temperatures between 28°C and 37°C and water activity levels exceeding 0.95. (Mannaa & Kim, 2017). Indoor environments create conditions which enable spores measuring 1–10 µm to become airborne because structural damage and insufficient air circulation maintain these spores in the atmosphere where they can be easily inhaled into the lower respiratory tract.

Climate change amplifies this problem by allowing fungi to survive in human body temperatures, while extreme weather events such as floods and storms promote the spread of disease-causing organisms. Human activities produce antifungal resistance in Aspergillus species by the prevalent practice of applying agricultural fungicides, making medical treatment more difficult.

> Integrated Interpretation of Findings

The synthesis of findings from the reviewed studies indicates that environmental molds and mycotoxins affect multiple physiological systems through diverse mechanisms. Respiratory diseases represent the most common outcome, while invasive infections and toxin-mediated effects contribute to severe and chronic conditions.

The interaction between environmental exposure, host susceptibility, and fungal adaptability explains the complexity of mold-related diseases. Ecological changes influence fungal behavior, while individual health status determines disease severity. This relationship highlights the importance of integrating environmental and clinical perspectives in understanding disease progression.

The evidence supports the need for strategies that address both environmental control and medical management. Measures that reduce exposure to molds, improve indoor air quality, and enhance early diagnosis can contribute to better health outcomes. Continued research is necessary to further clarify the long-term effects of mold exposure and to develop effective prevention strategies.

The quantitative analysis presented in this table shows that environmental mold exposure is associated with measurable variations in disease prevalence, severity, and risk, influenced by exposure pathways, host susceptibility, and environmental conditions.

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Table 3: Quantitative Analysis of Mold Exposure, Biological Mechanisms, Health Outcomes, and Reported Statistical Measures

Factors	Exposure or Pathway Mechanism	Health Outcome	Quantitative Measure	Mediation or Interaction Effect	References
Alternaria alternata (indoor/outdoor spores)	Inhalation → IgE-mediated sensitization	Allergic rhinitis, pediatric asthma	Up to 80% of asthmatic children show fungal sensitization; elevated IgE levels correlate with severity	IgE-mediated hypersensitivity amplifies airway inflammation	Novembre et al., 2025
Aspergillus spp. (clinical exposure)	Inhalation → tissue invasion in immunocompromised hosts	Invasive aspergillosis	Mortality rates range from 30–90% depending on immune status and treatment timing	Immunosuppression increases fungal invasion and reduces clearance	Lee, 2023
Pulmonary mold infection (radiographic detection)	Angioinvasion detected via CT imaging	Invasive pulmonary mold disease	CT pulmonary angiography shows ~100% sensitivity for vessel occlusion sign	Early imaging detection reduces mortality risk through early intervention	Stanzani et al., 2015
Indoor airborne fungi (Penicillium, Aspergillus)	Continuous inhalation of spores (1–10 µm)	Asthma, reduced lung function	Indoor mold exposure linked to 30–50% increase in respiratory symptoms in damp buildings	Indoor air quality mediates exposure-response relationship	Xiao et al., 2025
Dermatophytes (Trichophyton, Microsporum)	Direct contact with contaminated surfaces	Dermatophytosis (Tinea)	Affects 20–25% of global population; high recurrence rates TNF-α elevation)	Environmental persistence and reinfection sustain disease cycle	Thambugala et al., 2024
Mycotoxins (T-2 toxin, gliotoxin)	Inhalation/ingestion → immune and neural disruption	ASD, neuroinflammation	Detectable toxin levels in serum associated with increased cytokine activity (e.g., IL-6, TNF-α elevation)	Cytokine-mediated inflammation affects neurological function	Ratnaseelan et al., 2018; Kraft et al., 2021
Grain molds	Food contamination	Mycotoxicoses,	Optimal toxin	Environmental	Mannaa &

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(Fusarium, Aspergillus flavus)	under high moisture	liver damage	production at 28–37°C and water activity >0.95	conditions directly regulate toxin gene expression	Kim, 2017
Mucorales (environmental exposure)	Entry via wounds or inhalation	Mucormycosis	Mortality rates range from 40–80% depending on infection site	Diabetes and trauma increase susceptibility and severity	Firacative, 2020
Mixed fungal exposure (clinical cases)	Inhalation, ingestion, or skin contact	Respiratory, cutaneous, systematic infections	Respiratory manifestations account for majority (>50%) of reported cases	Exposure route determines organ system involvement	Oliveira et al., 2023

The quantitative findings demonstrate that environmental mold exposure is strongly associated with measurable increases in disease incidence; however, the magnitude of risk varies across exposure type and host condition. Respiratory diseases show the most consistent association, with studies indicating that up to 80% of asthmatic children exhibit sensitization to fungal allergens such as *Alternaria alternata*. This strong correlation is primarily driven by the small size of fungal spores (1–10 µm), which allows deep penetration into the lower respiratory tract and promotes chronic inflammation (Novembre et al., 2025). Through IgE- mediated immune responses these may occur, where repeated exposure triggers chronic inflammation and airway reactivity. These symptoms or effects are most frequently seen indoors, especially in wet, poorly ventilated buildings where mould development is persistent and airborne concentrations are still significant. (Xiao et al., 2025)

Respiratory manifestations account for a substantial proportion of fungal-related diseases, with more than half of reported cases involving the respiratory system. This pattern reflects the dominance of inhalation as the primary exposure pathway, given the airborne nature of fungal spores and their ability to reach the lower respiratory tract. Cutaneous and systemic manifestations are also observed depending on exposure route and duration, indicating that multiple pathways contribute to disease development (Oliveira et al., 2023).

Invasive fungal infections are associated with high mortality rates, particularly among immunocompromised populations. Reported mortality ranges for invasive aspergillosis and mucormycosis highlight the severity of these conditions and the importance of early diagnosis and treatment (Lee, 2023; Firacative, 2020).

In contrast, invasive fungal infections, although less frequent, present significantly higher mortality rates ranging from 30% to 90%, particularly among immunocompromised individuals. This highlights a critical distinction between prevalence and severity, where less common diseases may pose greater clinical risk. Advances in diagnostic techniques, such as CT pulmonary angiography, demonstrate near-complete sensitivity in detecting vascular invasion, reinforcing the importance of early detection in improving patient outcomes. (Stanzani et al., 2015). These findings show that both biological mechanisms and diagnostic capabilities influence disease outcomes.

With studies reporting a 30–50% rise in affected individuals in damp environments. This suggests that environmental conditions, particularly moisture and ventilation, play a crucial role in determining exposure levels and disease progression (Xiao et al., 2025).

Dermatological infections remain highly prevalent globally, affecting a significant portion of the population and showing frequent recurrence due to environmental persistence of fungal organisms (Thambugala et al., 2024). These findings indicate that both environmental exposure and host factors influence disease progression and recurrence.

Quantitative evidence also highlights the role of mycotoxins and environmental conditions in disease development. Detection of mycotoxins in biological samples is associated with increased inflammatory markers and immune dysregulation, which contributes to neurological and systemic conditions (Ratnaseelan et al., 2018; Kraft et al., 2021). For example, individuals with chronic conditions such as COPD show a 1.5–2× higher risk of adverse outcomes when exposed to molds, demonstrating the role of host susceptibility. Similarly, dermatological infections affect approximately 20–25% of the global population, emphasizing their widespread but less severe nature (Thambugala, 2024). Environmental

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parameters such as temperature and moisture strongly influence fungal growth and toxin production, with optimal conditions identified at 28–37°C and high water activity (Mannaa & Kim, 2017).

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CONCLUSION

The systematic review indicates that environmental molds and mycotoxins represent significant contributors to human disease, affecting multiple physiological systems through diverse mechanisms. These include allergic sensitization, invasive infection, and toxin-mediated effects, with outcomes ranging from mild respiratory conditions to severe systemic and neurological disorders. The findings highlight that the impact of fungal exposure is influenced by the interaction between environmental conditions, fungal characteristics, and host susceptibility.

Airborne fungal spores, particularly those within the 1–10 µm size range, facilitate deep respiratory exposure and are strongly associated with chronic inflammation and asthma. In contrast, mycotoxins such as T-2 toxin and gliotoxin contribute to immune dysregulation and neuroinflammatory processes, demonstrating that the effects of molds extend beyond localized infections. Additionally, invasive fungal pathogens such as *Aspergillus fumigatus* and members of the Mucorales group are associated with severe clinical outcomes, particularly among immunocompromised individuals.

Through complex and interconnected pathways, environmental molds and mycotoxins impact numerous physiological systems, making them major contributors to the worldwide illness burden. The review's conclusions emphasize how crucial host vulnerability and environmental exposure are in influencing disease outcomes.

However, the need for more thorough and extensive research is indicated by the limits of the current research, such as the absence of established procedures and the diversity in study design. Improving diagnostic consistency, measuring exposure levels, and determining causal links should be the primary objectives of future study.

An integrated approach integrating environmental control, clinical management, and public health policies is still required to reduce the health risks associated with mold exposure.

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