ISSN 2055-0286
Advances in Social Sciences Research Journal; Vol. 13 No. 11 (2026) (410-430)
https://doi.org/10.14738/assrj.1311.12733

Fungal Pathogens as Emerging Global Threats: Review of Transmissibility, Lethality, and Pandemic Potential

Jonathan A. Coffman[1], Franklin Garcia-Godoy[2], & Peter E. Murray[3]*

1. Baptist Health Sciences University, Memphis, TN 38104, USA
2. University of Tennessee Health Science Center, College of Dentistry, Memphis, TN 38103, USA
3. Independent Scholar, 490 Post St, Ste 500 PMB 2045, San Francisco, CA 94102, USA

Abstract: Fungal pathogens pose an escalating yet historically underrecognized threat to global health, driven by expanding immunocompromised populations, environmental change, diagnostic limitations, restricted treatment options, and increasing antifungal resistance. The World Health Organization (WHO) has designated *C. auris, C. neoformans, A. fumigatus*, and *C. albicans* as critical-priority pathogens based on their clinical burden, mortality, resistance, and unmet medical needs. Among these, *C. auris* presents a distinctive threat through its capacity for persistent colonization, environmental survival, healthcare-associated transmission, invasive infection, and multidrug resistance. In contrast, *A. fumigatus* poses a substantial risk through ubiquitous airborne exposure, emerging antifungal resistance, and increasing host susceptibility. *C. neoformans* remains a leading cause of life-threatening fungal meningitis, particularly in severely immunocompromised individuals, while *C. albicans* contributes substantially to invasive fungal disease, primarily through endogenous infection. Additional pathogens, including *Mucorales, Histoplasma, Coccidioides, Fusarium*, and *Pneumocystis jirovecii*, demonstrate the diverse environmental, biological, and clinical pathways underlying severe fungal infections. This review critically evaluates major fungal threats according to transmissibility, lethality, antifungal resistance, environmental adaptability, host susceptibility, and epidemic or pandemic potential. Particular emphasis is placed on how climate-driven adaptation, emerging resistance, and shifting host vulnerability may intensify fungal disease burdens and challenge biological barriers that have historically constrained widespread human transmission. Although most fungal pathogens lack the sustained person-to-person transmissibility required for a conventional pandemic, their expanding clinical and ecological impact underscores the need for improved surveillance, diagnostics, therapeutics, and global preparedness.

Keywords: fungal pathogens, invasive fungal disease, *C. auris, Aspergillus, Cryptococcus*, antifungal resistance, mycoses, pandemic preparedness.

INTRODUCTION

Fungal pathogens represent an escalating and historically underrecognized threat to global health. Unlike many viral and bacterial pathogens capable of sustained human-to-human transmission, most medically important fungi cause disease through environmental exposure or invasion by endogenous microbiota. Consequently, their public health significance extends beyond conventional measures of contagiousness to encompass environmental prevalence, host susceptibility, invasive potential, antifungal resistance, and associated mortality.[1,2]

The global burden of fungal disease is substantial. Recent estimates suggest that approximately 6.5 million people develop life-threatening invasive fungal infections

annually, resulting in approximately 3.8 million associated deaths, of which 2.5 million are directly attributable to fungal disease.[1] Nevertheless, the true burden remains uncertain because of diagnostic limitations, inadequate surveillance, and substantial geographic disparities in access to mycological testing and treatment. Recognizing these challenges, the World Health Organization (WHO) established its first fungal priority pathogens list in 2022, identifying organisms of critical public health concern and highlighting urgent needs in surveillance, diagnostics, antifungal development, and clinical management.[2]

Several converging trends are intensifying these threats. Advances in transplantation, oncology, intensive care, and immunomodulatory therapies have expanded populations vulnerable to invasive mycoses.[3] Meanwhile, emerging antifungal resistance threatens the effectiveness of a limited therapeutic arsenal, while environmental and climatic changes may alter fungal distribution, exposure, and adaptation to mammalian temperatures.[4,5] The global emergence of *Candida auris* illustrates these intersecting risks. Its capacity for persistent colonization, environmental survival, healthcare-associated transmission, and multidrug resistance distinguishes it from most invasive fungal pathogens and demonstrates the potential for rapid international dissemination without sustained community transmission.[6,7]

Assessing fungal threats therefore requires an integrated framework that distinguishes disease burden from transmissibility and pandemic potential. This review critically examines major fungal pathogens according to environmental exposure, host susceptibility, invasive disease severity, mortality, antifungal resistance, transmission dynamics, and capacity for epidemic or pandemic spread. Particular emphasis is placed on how evolving clinical and ecological conditions may amplify fungal threats despite the biological constraints that currently limit sustained human-to-human transmission.

A FRAMEWORK FOR ASSESSING MODERN FUNGAL THREATS

Assessing fungal threats requires a framework that distinguishes population-level disease burden from transmissibility and pandemic potential. Unlike respiratory viruses, for which sustained human-to-human transmission can drive rapid epidemic expansion, most pathogenic fungi cause disease through environmental exposure or invasion by endogenous microbiota.[1,2] Their public health impact therefore depends not only on transmission dynamics but also on exposure frequency, host vulnerability, invasive potential, treatment effectiveness, and associated mortality.

Environmental exposure can generate substantial disease burdens without interpersonal transmission. Aspergillus fumigatus produces airborne conidia that are routinely inhaled, while Coccidioides and Histoplasma cause infections following inhalation of environmentally dispersed fungal propagules. Candida albicans, in contrast, commonly causes invasive disease when endogenous colonizing organisms breach anatomical barriers or enter the bloodstream through compromised mucosal surfaces or intravascular devices.[1,2] These distinct pathways demonstrate that widespread exposure and severe disease do not necessarily imply contagiousness.

Host susceptibility is a major determinant of progression from exposure or colonization to invasive infection. Neutropenia, advanced HIV infection, transplantation, malignancy, diabetes, immunosuppressive therapy, invasive medical devices, and prolonged

critical illness increase vulnerability to specific fungal pathogens.[3] Importantly, host dependence varies upon opportunistic fungi such as *Aspergillus* and *Candida* predominantly threaten medically vulnerable populations, whereas endemic dimorphic fungi can cause clinically significant disease in immunocompetent individuals. Thus, fungal pathogenicity reflects interactions among microbial virulence, inoculum, route of exposure, and host defenses rather than an intrinsic property of the organism alone.

Antifungal resistance further amplifies clinical risk. Because fungi and humans share eukaryotic cellular pathways, relatively few fungal-specific therapeutic targets are available, limiting systemic treatment to a small number of major drug classes.[4] Resistance, drug toxicity, pharmacologic interactions, and inadequate tissue penetration can further constrain effective therapy. Multidrug-resistant Candida auris and azole-resistant A. fumigatus exemplify how resistance can increase treatment complexity and worsen outcomes, particularly when diagnosis or initiation of appropriate therapy is delayed.[4,6]

Environmental persistence and transmission capacity introduce additional epidemiological dimensions. Most environmental fungi sustain human exposure independently of infected individuals, whereas *C. auris* can persist on skin and healthcare surfaces, facilitating patient-to-patient spread through direct or indirect contact.[6,7] Nevertheless, healthcare-associated outbreaks, geographically widespread environmental infections, and sustained community transmission represent distinct epidemiological phenomena and should not be conflated with pandemic potential.

Accordingly, a comprehensive assessment of modern fungal threats should integrate seven interdependent determinants: exposure, host susceptibility, invasive potential, lethality, antifungal resistance, environmental persistence, and human-to-human transmissibility. Their combined effects determine clinical severity and population-level burden, while the capacity for sustained transmission remains central to assessing conventional pandemic potential. This distinction provides a clinically and epidemiologically grounded basis for comparing fungal pathogens, identifying emerging risks, and prioritizing surveillance, prevention, and therapeutic development.

WHO CRITICAL-PRIORITY FUNGAL PATHOGENS

The World Health Organization (WHO) identifies four fungi as critical-priority pathogens: *C. auris, A. fumigatus*, *C. neoformans*, and *C. albicans*.[2] Although these organisms differ substantially in their ecology, transmission, and pathogenic mechanisms, each poses a significant threat through invasive disease, associated mortality, antifungal resistance, or limitations in diagnosis and treatment. Their classification underscores the importance of evaluating fungal threats according to both clinical severity and epidemiological characteristics rather than transmissibility alone.

C. auris: An Emerging Healthcare-Associated Transmissible Threat

C. auris represents one of the most consequential emerging fungal threats because it combines persistent human colonization, environmental survival, healthcare-associated transmission, invasive pathogenicity, and multidrug resistance. Unlike most invasive fungal pathogens, *C. auris* readily colonizes human skin, persists on contaminated surfaces, and spreads through direct or indirect contact within healthcare facilities. Asymptomatic

colonization further complicates surveillance and infection control by permitting transmission from individuals without clinically apparent disease.[6–8]

Transmission is particularly concerning in intensive care units, long-term acute-care hospitals, and skilled nursing facilities, where invasive devices, mechanical ventilation, prolonged hospitalization, and underlying illness increase susceptibility to invasive infection. These conditions facilitate both exposure and disease progression, enabling persistent institutional outbreaks.[8]

Antifungal resistance substantially magnifies this threat. Fluconazole resistance is widespread, while resistance to amphotericin B and echinocandins, including isolates resistant to all three major systemic antifungal classes, has been documented.[6,7] Importantly, resistant strains can spread between patients, allowing antifungal resistance to propagate independently of antimicrobial exposure in individual hosts.

Despite its international dissemination, *C. auris* has not demonstrated sustained community transmission comparable to major respiratory pandemic pathogens. Nevertheless, its distinctive combination of transmissibility, environmental persistence, and multidrug resistance makes it a particularly important model of fungal epidemic emergence. Its principal contemporary threat is the capacity to establish persistent, difficult-to-control outbreaks among medically vulnerable populations.

A. fumigatus: Ubiquitous Environmental Exposure and Antifungal Resistance

A. fumigatus presents a fundamentally different threat, characterized by widespread environmental exposure rather than interpersonal transmission. Its airborne conidia occur in soil, decomposing vegetation, and organic matter and are routinely inhaled. Although intact pulmonary and immune defenses generally prevent invasive infection, impaired host defenses permit pulmonary invasion and potentially fatal dissemination.[9]

Invasive *aspergillosis* disproportionately affects individuals with prolonged neutropenia, hematologic malignancies, transplantation, corticosteroid exposure, and other forms of severe immunosuppression. Mortality remains substantial, particularly with delayed diagnosis, disseminated infection, or antifungal resistance.[9] Expanding populations receiving immunosuppressive and immunomodulatory therapies consequently increase the burden of invasive aspergillosis without requiring enhanced fungal transmissibility.

Azole resistance represents a particularly important emerging concern. Resistance can develop during prolonged antifungal treatment or through environmental selection associated with agricultural azole fungicides. Consequently, patients may acquire resistant *A. fumigatus* directly from the environment despite having no previous antifungal exposure.[10] This environmental pathway complicates prevention and surveillance because resistance may emerge and spread outside clinical settings.

The convergence of ubiquitous exposure, severe opportunistic disease, and environmentally mediated antifungal resistance establishes *A. fumigatus* as a major global fungal threat. Its epidemic significance arises primarily from widespread environmental reservoirs and increasing host susceptibility rather than sustained human-to-human transmission.

C. neoformans: Neuroinvasion and High Mortality in Immunocompromised Populations

C. neoformans is an environmentally acquired fungal pathogen distinguished by its capacity for systemic dissemination and central nervous system invasion. Infection generally follows inhalation of environmental propagules and may remain asymptomatic or clinically contained in immunocompetent individuals. However, impaired cell-mediated immunity can permit hematogenous dissemination and life-threatening meningoencephalitis.[11]

Cryptococcal meningitis remains a major cause of HIV-associated mortality, particularly among individuals with advanced immunosuppression.[11,12] Clinical outcomes depend on early diagnosis, access to effective induction and consolidation antifungal therapy, management of elevated intracranial pressure, and restoration of immune function. Limited diagnostic and therapeutic resources contribute to disproportionately poor outcomes in resource-constrained settings.

Unlike *C. auris*, *C. neoformans* does not ordinarily spread between patients. Its global significance instead reflects environmental exposure, severe neuroinvasive disease, high mortality, and persistent disparities in access to effective treatment. This pattern illustrates how a minimally contagious fungal pathogen can generate substantial mortality through the interaction of microbial virulence, host immunodeficiency, and healthcare limitations.

C. albicans: Endogenous Colonization and Invasive Disease

C. albicans is a common constituent of the human gastrointestinal, oral, and genital microbiota, yet it remains a major cause of invasive fungal infection. Unlike environmentally acquired mycoses, invasive candidiasis frequently originates from endogenous colonization when mucosal disruption, impaired immunity, or invasive medical interventions permit entry into the bloodstream or normally sterile tissues.[13]

Patients at greatest risk include those undergoing major abdominal surgery, receiving broad-spectrum antibiotics or parenteral nutrition, requiring central venous catheters, or experiencing prolonged critical illness, neutropenia, or immunosuppression. Candidemia and deep-seated candidiasis are associated with substantial mortality, particularly when diagnosis, source control, or appropriate antifungal treatment is delayed.[13,14]

Although *C. albicans* can be transmitted through direct contact and healthcare-associated exposures, most invasive infections arise from endogenous sources rather than sustained interpersonal transmission. Its public health significance therefore reflects widespread colonization, frequent opportunities for invasion, and severe outcomes among vulnerable patients.

Collectively, these four critical-priority fungi illustrate distinct pathways to global disease burden: healthcare-associated transmission and multidrug resistance (*C. auris*), ubiquitous environmental exposure and acquired resistance (*A. fumigatus*), neuroinvasive disease in immunocompromised hosts (*C. neoformans*), and endogenous invasion associated with medical care (*C. albicans*). Their contrasting epidemiological characteristics reinforce the need to distinguish clinical lethality and population-level burden from the capacity for sustained epidemic or pandemic transmission.

OTHER MAJOR AND EMERGING FUNGAL THREATS

Beyond the four WHO critical-priority pathogens, several fungi pose substantial clinical and public health threats through aggressive tissue invasion, environmental exposure, antifungal resistance, or increasing host susceptibility. Although most lack sustained human-to-human transmission, their capacity to cause severe disease underscores the distinction between clinical lethality and epidemic potential.

Mucorales: Angioinvasion and Rapid Tissue Destruction

Mucormycosis, caused by fungi of the order Mucorales, is among the most rapidly progressive invasive mycoses. Its defining pathological feature is angioinvasion, which produces vascular thrombosis, tissue ischemia, and extensive necrosis. Clinical manifestations include rhino-orbital-cerebral, pulmonary, cutaneous, gastrointestinal, and disseminated disease, frequently requiring urgent intervention.[15,16]

Major risk factors include uncontrolled diabetes, particularly diabetic ketoacidosis, hematologic malignancy, neutropenia, transplantation, corticosteroid exposure, and profound immunosuppression. Mortality is substantial, especially in disseminated or central nervous system disease. Effective management generally requires prompt antifungal therapy, correction of underlying predisposing conditions, and surgical debridement when feasible.[15,16]

Despite its exceptional invasive potential, mucormycosis is predominantly acquired through environmental exposure rather than interpersonal transmission. Its threat therefore derives from rapid disease progression, high mortality, and limited therapeutic options rather than conventional contagiousness.

Histoplasma: Widespread Environmental Exposure and Disseminated Disease

Histoplasma species cause infection primarily through inhalation of airborne fungal propagules from contaminated soil or environments associated with bird or bat droppings. Although many infections are asymptomatic or self-limited, substantial inoculum exposure can produce severe pulmonary disease, while impaired cellular immunity increases the risk of progressive disseminated histoplasmosis.[17]

Disseminated disease is particularly concerning in individuals with advanced HIV infection, transplantation, or other forms of immunosuppression. Delayed diagnosis and limited access to fungal testing and antifungal therapy contribute to preventable mortality, particularly in endemic and resource-constrained regions.[17]

The epidemiological importance of histoplasmosis lies in its environmental distribution, potential for exposure-associated outbreaks, and capacity to cause severe disease without sustained human-to-human transmission.

Coccidioides: Geographic Expansion and Climate-Sensitive Exposure

Coccidioides species, the causative agents of coccidioidomycosis, inhabit soil in arid and semiarid regions. Infection occurs through inhalation of aerosolized arthroconidia, often

following soil disturbance or dust exposure. Although many infections are asymptomatic or resolve without treatment, severe pulmonary disease and extrapulmonary dissemination can occur, particularly in susceptible individuals.[18]

Environmental conditions, including temperature, precipitation, drought, and soil disturbance, influence exposure patterns and may contribute to changes in geographic distribution and disease incidence.[18,19] Climate change could further modify the ecological range of Coccidioides, although the magnitude and geographic consequences remain uncertain.

Coccidioidomycosis illustrates an important mechanism of fungal emergence: increasing population exposure through environmental and geographic change rather than enhanced interpersonal transmissibility.

Fusarium and Lomentospora prolificans: Invasive Disease and Therapeutic Resistance

Fusarium species are environmental molds capable of causing localized infection in immunocompetent individuals and severe disseminated disease in patients with profound neutropenia or other major immune deficiencies. Disseminated fusariosis may involve bloodstream infection, pulmonary disease, and characteristic cutaneous lesions. Mortality is high in persistently immunocompromised patients, and variable antifungal susceptibility complicates treatment.[20]

Lomentospora prolificans presents an especially difficult therapeutic challenge because of its extensive intrinsic resistance to available antifungal agents. Invasive infection, particularly among patients with hematologic malignancies or profound immunosuppression, is associated with poor outcomes.[21]

These pathogens demonstrate how limited treatment options can amplify clinical lethality even when environmental acquisition predominates and sustained interpersonal transmission is absent.

Pneumocystis jirovecii: Opportunistic Pneumonia and Human-Associated Transmission

Pneumocystis jirovecii causes potentially life-threatening pneumonia in individuals with impaired cellular immunity, particularly those with advanced HIV infection, hematologic malignancies, transplantation, or prolonged immunosuppressive therapy.

Although effective prophylaxis and treatment are available, delayed diagnosis and severe respiratory failure continue to contribute to mortality.[22]

Unlike most environmentally acquired fungal pathogens, P. jirovecii is closely associated with human hosts, and molecular epidemiological evidence supports airborne person-to-person transmission, including transmission from asymptomatically colonized individuals.[22,23] Healthcare-associated clusters further demonstrate its capacity for localized transmission.

Nevertheless, widespread transmission causing clinically significant disease is constrained by host susceptibility, and P. jirovecii has not demonstrated pandemic behavior comparable to highly contagious respiratory viruses. Its epidemiology highlights the

importance of distinguishing microbial transmission from the development of invasive or clinically severe disease.

Collectively, these additional pathogens illustrate that fungal threats arise through multiple mechanisms, including rapid angioinvasion, widespread environmental exposure, climate-sensitive geographic expansion, intrinsic antifungal resistance, and transmission among susceptible hosts. Their clinical impact reinforces the need for pathogen-specific risk assessment rather than reliance on contagiousness or mortality alone.

ANTIFUNGAL RESISTANCE AS A THREAT MULTIPLIER

Antifungal resistance is a major driver of emerging fungal threats because invasive mycoses are treated with a limited therapeutic arsenal. The biological similarities between fungal and human cells restrict selective drug targeting, leaving systemic therapy dependent primarily on azoles, echinocandins, and polyenes, with additional agents available for specific indications. Consequently, resistance to even one major drug class can substantially compromise treatment, while multidrug resistance may leave few effective alternatives.[4,24]

The clinical consequences extend beyond reduced drug susceptibility. Resistant infections may require less effective or more toxic therapies, prolong treatment, delay fungal clearance, and increase the risk of treatment failure and mortality. These effects are particularly consequential in critically ill and immunocompromised patients, for whom timely administration of effective antifungal therapy is essential.[24,25]

C. auris and *A. fumigatus* exemplify two distinct epidemiological pathways of resistance dissemination. Multidrug-resistant *C. auris* can spread between patients and persist within healthcare environments, enabling resistant strains to propagate through institutional transmission.[6–8] In contrast, azole-resistant *A. fumigatus* may emerge through environmental selection, including exposure to agricultural azole fungicides, and subsequently infect individuals without prior antifungal treatment.[10,26] These mechanisms demonstrate that antifungal resistance can become a population-level threat through either healthcare-associated transmission or repeated environmental acquisition.

Increasing antifungal use in clinical medicine and agriculture may intensify selective pressures, although resistance emergence varies by organism, drug class, and ecological setting.[4,26] Addressing these risks requires a One Health approach integrating clinical and environmental surveillance, susceptibility testing, antifungal stewardship, agricultural practices, and development of therapeutics with novel mechanisms of action.

Ultimately, antifungal resistance magnifies fungal pathogenic threats by increasing treatment complexity, potentially worsening clinical outcomes, and facilitating the persistence or dissemination of difficult-to-treat organisms. Its significance therefore extends beyond individual patient management to global infectious disease preparedness.

ENVIRONMENTAL CHANGE, CLIMATE, AND FUNGAL ADAPTATION

Environmental and climatic changes may increasingly influence fungal disease emergence by altering pathogen distribution, ecological selection, and human exposure. Unlike obligate human pathogens, many medically important fungi occupy extensive environmental reservoirs where temperature, precipitation, drought, land use, agricultural practices, and

extreme weather events can affect fungal survival, growth, dispersal, and opportunities for infection.[5,27]

Temperature is particularly relevant because mammalian endothermy provides a natural defense against many environmental fungi. Numerous fungal species cannot proliferate efficiently at mammalian core body temperatures, limiting their capacity to establish invasive infection.[27]

Environmental warming could theoretically select for greater fungal thermotolerance, potentially allowing previously restricted species to overcome this biological barrier. However, thermal adaptation alone does not confer the additional traits required for human pathogenicity or sustained interpersonal transmission. Although biologically plausible, the emergence of novel human fungal pathogens through climate-driven thermal selection remains an incompletely established hypothesis.[5,27]

More immediate concerns involve changes in environmental exposure. Altered precipitation, prolonged drought, soil disturbance, and extreme weather may influence fungal abundance, aerosolization, and geographic distribution. Climate-based models project potential expansion of Coccidioides-endemic regions, while environmental disturbances can increase exposure to airborne fungal propagules.[18,19,28] Such changes may increase disease incidence or expose previously unaffected populations without requiring enhanced fungal virulence or transmissibility.

Environmental change may also interact with antifungal resistance. Agricultural fungicide use can select for azole-resistant Aspergillus fumigatus, creating environmental reservoirs of resistant organisms capable of infecting individuals without prior antifungal exposure.[10,26] Although this mechanism is not necessarily driven by climate change, it illustrates how human modification of fungal ecosystems can directly influence clinical outcomes.

Collectively, these mechanisms suggest that future fungal threats may intensify through ecological expansion, increased environmental exposure, antifungal resistance, and potentially enhanced thermotolerance, even without sustained human-to-human transmission. Distinguishing established environmental effects from hypothetical evolutionary pathways is essential for scientifically grounded surveillance, risk assessment, and preparedness.

COMPARATIVE ASSESSMENT OF TRANSMISSIBILITY, LETHALITY, AND PANDEMIC POTENTIAL

Fungal pathogens differ substantially in their routes of acquisition, transmission dynamics, invasive disease severity, and antifungal resistance. These characteristics determine distinct patterns of clinical and population-level risk. Importantly, widespread environmental exposure, high case fatality, and healthcare-associated transmission represent different dimensions of pathogenic threat and should not be interpreted as equivalent indicators of pandemic potential.[2,4,26]

A comparison of the epidemiological and clinical characteristics of major fungal pathogens is shown in Table 1 below.

Table 1: Comparative epidemiological and clinical characteristics of major fungal pathogens.

Fungal pathogen	Principal acquisition	Human-to-human transmission	Severity of invasive disease	Antifungal resistance or treatment concern	Population-level threat
C. auris	Healthcare-associated contact and colonization	Established in healthcare settings	High	Frequent multidrug resistance	Persistent healthcare outbreaks and international dissemination
A. fumigatus	Environmental inhalation	Essentially absent	High	Emerging azole resistance	Widespread environmental exposure and substantial invasive disease burden
C. neoformans	Environmental Inhalation	Not ordinarily documented	High, particularly CNS infection	Treatment complexity and emerging resistance	Major mortality burden in immunocompromised populations
C. albicans	Predominantly endogenous Colonization	Possible, but not the principal route of invasive disease	High when invasive	Acquired azole & echinocandin resistance	Substantial healthcare-associated disease burden
Mucorales	Environmental inhalation or inoculation	Essentially absent	Very high in advanced or disseminated disease	Intrinsic resistance to several antifungal classes	Rapidly progressive opportunistic infections
Histoplasma spp.	Environmental Inhalation	Essentially absent	High when disseminated	Diagnostic and therapeutic limitations	Endemic disease and exposure-associated outbreaks
Coccidioides spp.	Environmental Inhalation	Essentially absent	Usually self-limited; potentially severe when disseminated	Prolonged treatment and occasional refractory disease	Regional epidemics and potential geographic expansion
Fusarium spp.	Environmental inhalation or inoculation	Not a recognized major route	High when disseminated	Variable susceptibility and frequent multidrug resistance	Severe opportunistic infections
Pneumocystis jirovecii	Human-associated airborne transmission	Established, including asymptomatic sources	High in susceptible hosts without treatment	Emerging molecular resistance markers of uncertain clinical significance	Healthcare clusters and opportunistic pneumonia
Lomentospora prolificans	Environmental inhalation or inoculation	Not a recognized major route	Very high when disseminated	Extensive intrinsic multidrug resistance	Severe, difficult-to-treat opportunistic infections

Note: Severity refers to clinically significant invasive or severe disease rather than the probability of severe outcomes following exposure. Qualitative classifications are not standardized risk scores. CNS indicates central nervous system. Comparisons reflect the epidemiological and clinical evidence discussed in references 2, 4, 6 through 26.

Interpretation of Comparative Threats

This comparison reveals three distinct dimensions of fungal pathogenic threat: transmission capacity, population exposure, and clinical lethality. *C. auris* is particularly concerning because it combines healthcare-associated transmission with persistent colonization and multidrug resistance. By contrast, *A. fumigatus, Histoplasma*, and *Coccidioides* can expose large populations through environmental reservoirs without requiring interpersonal spread. *Mucorales* and *L. prolificans* illustrate a third pattern, in which aggressive invasive disease and limited therapeutic options produce severe individual risk despite minimal transmission potential.[15,19,21]

Lethality also requires careful interpretation. This is because case fatality varies with immune status, anatomical involvement, underlying disease, diagnostic delay, and access to effective treatment. Consequently, mortality among patients with disseminated mold infections and profound neutropenia cannot be directly compared with outcomes among immunocompetent individuals experiencing uncomplicated environmental fungal

infections. Apparent differences in pathogen lethality may therefore reflect differences in host populations and clinical circumstances rather than intrinsic fungal virulence alone.[9,15,20]

A further distinction concerns epidemic potential versus pandemic potential. Environmental fungi can produce geographically extensive disease, and *C. auris* can establish persistent healthcare outbreaks across multiple countries. Neither phenomenon, however, establishes the sustained, efficient community transmission characteristic of conventional respiratory pandemics. *P. jirovecii* demonstrates that person-to-person fungal transmission is biologically possible, but clinically significant disease remains concentrated among susceptible hosts.[8,22,23]

Thus, no single fungal pathogen can be designated the greatest global threat across all dimensions. *C. auris* warrants particular attention for healthcare-associated epidemic potential, *A. fumigatus* for widespread environmental exposure and resistance, and highly invasive molds for severe outcomes in vulnerable populations. A clinically meaningful assessment must distinguish the probability of exposure, progression to invasive disease, case fatality, and capacity for sustained transmission. These determinants collectively provide a more defensible basis for evaluating fungal threats and anticipating their future public health impact (Figure 1).

PANDEMIC POTENTIAL AND THE BIOLOGICAL BARRIERS TO FUNGAL TRANSMISSION

No recognized fungal pathogen currently exhibits the combination of efficient, sustained human-to-human transmission, widespread host susceptibility, and rapid population-level spread responsible for major respiratory viral pandemics. Several biological barriers constrain this potential, including mammalian endothermy, effective innate and adaptive immune defenses, limited respiratory transmissibility, and the dependence of many invasive mycoses on substantial host immunosuppression.[5,27] These constraints help explain why fungi can cause considerable global morbidity and mortality without producing pandemics comparable to influenza or COVID-19.

Nevertheless, global disease burden, epidemic potential, and pandemic transmissibility are distinct epidemiological characteristics. Fungal pathogens can become internationally consequential through healthcare-associated transmission, widespread environmental exposure, geographic expansion, or antifungal resistance without acquiring efficient community transmission. *C. auris*, for example, combines persistent colonization, environmental survival, healthcare-associated spread, and multidrug resistance, whereas *A. fumigatus* combines thermotolerance, ubiquitous airborne exposure, invasive pathogenicity, and environmentally selected resistance.[6,7,10] Other fungi exhibit complementary characteristics: *C. neoformans* demonstrates neuroinvasive potential, Mucorales cause aggressive angioinvasive disease, and endemic dimorphic fungi can infect immunocompetent individuals following environmental inhalation.[11,15,18]

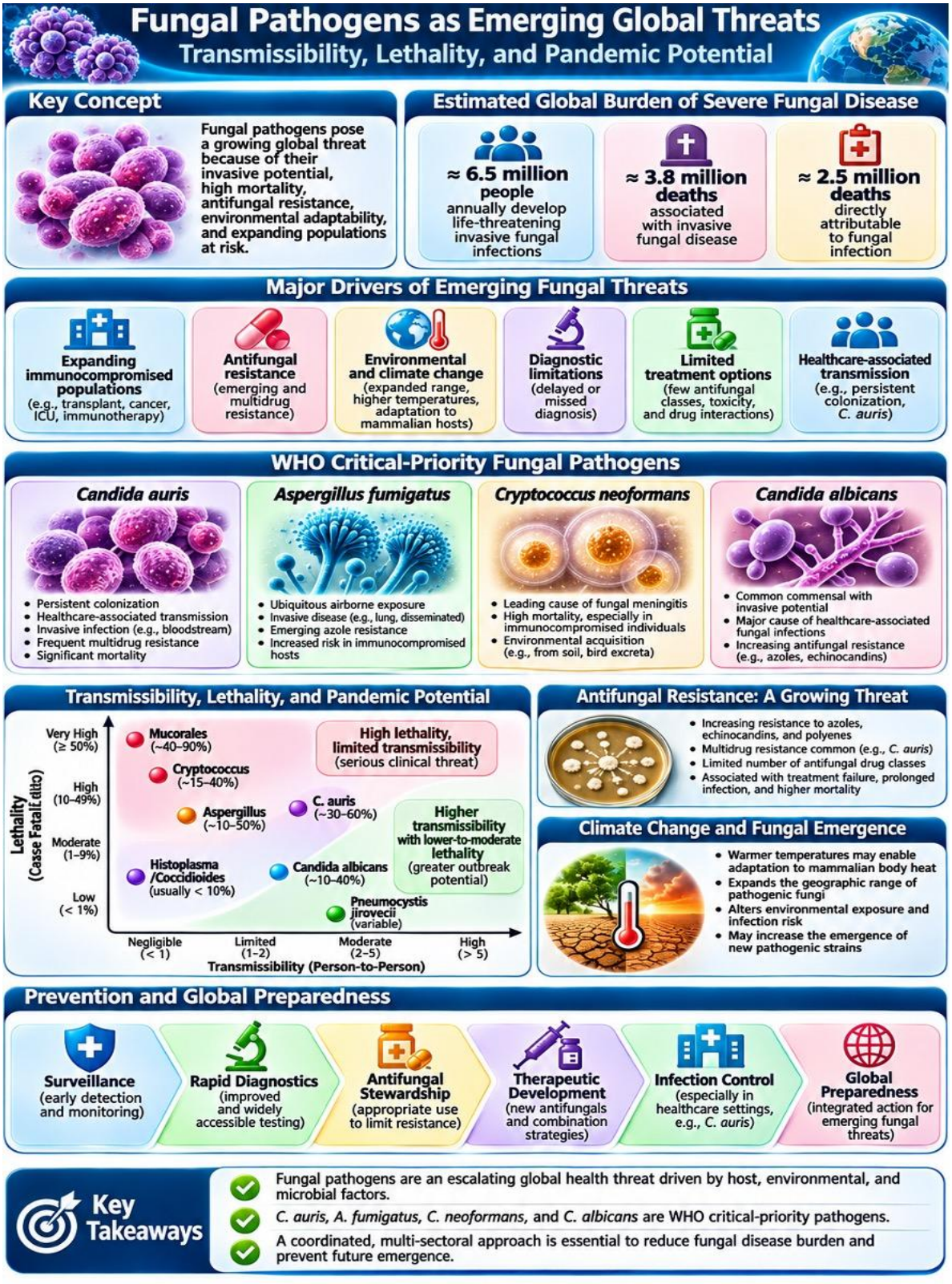


Figure 1

A hypothetical fungal pathogen combining efficient respiratory human-to-human transmission, asymptomatic shedding, mammalian thermotolerance, substantial pathogenicity in immunocompetent hosts, and multidrug resistance would pose an

exceptional pandemic threat. However, these characteristics involve distinct biological mechanisms, and their coexistence cannot be assumed. In particular, environmental aerosolization does not establish respiratory transmission between humans, while thermotolerance and invasive virulence do not necessarily confer contagiousness. The emergence of C. auris demonstrates that fungal pathogens can acquire or exhibit epidemiologically consequential combinations of colonization, persistence, resistance, and healthcare transmissibility, but it does not establish an evolutionary trajectory toward efficient community respiratory spread.[5–7]

Accordingly, the most credible near-term fungal threats involve expanding opportunistic disease burdens, persistent healthcare outbreaks, environmentally acquired resistant infections, and climate-associated changes in exposure. Although the evolution of a highly transmissible fungal pathogen remains theoretically possible, its likelihood cannot presently be quantified, and evidence does not support treating such an event as inevitable or imminent.

Pandemic preparedness should therefore prioritize established fungal threats while maintaining surveillance for changes in host range, thermotolerance, transmission dynamics, virulence, and antifungal susceptibility. This approach recognizes the potentially serious consequences of fungal adaptation without conflating biological plausibility with demonstrated pandemic risk.

THE EXPANDING POPULATION AT RISK

The future burden of invasive fungal disease will depend not only on pathogen evolution and environmental change but also on demographic trends and advances in medical care. Improved survival among patients with malignancies, organ failure, autoimmune disorders, and other serious conditions has expanded populations exposed to transplantation, chemotherapy, immunomodulatory therapies, corticosteroids, intensive care, and invasive medical devices. Although these interventions have substantially improved clinical outcomes, they can also compromise host defenses and increase susceptibility to opportunistic fungal infections.[3,9,13]

This creates an important epidemiological paradox: medical advances that prolong survival may simultaneously increase the population at risk for invasive mycoses. Consequently, fungal disease burden may rise even without changes in pathogen virulence, environmental prevalence, or transmissibility. Population aging may further amplify this trend through increasing rates of malignancy, chronic disease, hospitalization, invasive procedures, and immunosuppressive treatment.[29]

These developments are particularly consequential for *Candida*, *Aspergillus*, and *Mucorales*, whose invasive pathogenicity is closely associated with impaired immunity, disrupted anatomical barriers, and intensive medical interventions.[9,13,15] However, susceptibility is pathogen-specific: neutropenia strongly predisposes to invasive *aspergillosis*, advanced cellular immunodeficiency increases vulnerability to cryptococcosis and pneumocystosis, and uncontrolled diabetes is a major risk factor for mucormycosis.

Accordingly, future fungal disease burden will reflect the convergence of microbial, environmental, demographic, and healthcare-related determinants. Effective preparedness must extend beyond pathogen surveillance to include risk-adapted screening, antifungal

prophylaxis when indicated, rapid diagnostics, infection prevention, antimicrobial stewardship, and timely treatment among vulnerable populations. Strengthening these measures may reduce fungal morbidity and mortality even in the absence of advances in controlling environmental reservoirs or preventing fungal evolution.

RANKING THE GREATEST MODERN FUNGAL THREATS

An integrated assessment of transmissibility, lethality, antifungal resistance, environmental exposure, global disease burden, and emergence potential identifies four fungal pathogens of particular concern, consistent with the WHO critical-priority classification.[2] However, their relative importance differs according to the epidemiological and clinical dimensions evaluated.

1. ***C. auris*: Greatest Emerging Healthcare-Associated Transmission Threat.** *C. auris* presents a distinctive combination of persistent human colonization, environmental survival, healthcare-associated transmission, invasive pathogenicity, and multidrug resistance. Its international dissemination and capacity to establish persistent institutional outbreaks make it a leading concern for fungal epidemic preparedness, although sustained community transmission has not been established.[6–8]
2. ***A. fumigatus*: Major Environmental and Antifungal Resistance Threat.** Ubiquitous airborne exposure, severe invasive disease among immunocompromised patients, and emerging azole resistance make *A. fumigatus* a particularly consequential environmental pathogen. Its ability to acquire resistance through environmental selection further complicates prevention and treatment independently of human-to-human transmission.[9,10,26]
3. ***C. neoformans*: Major Neuroinvasive Mortality Threat.** *C. neoformans* causes life-threatening meningitis and disseminated infection, particularly among individuals with advanced HIV infection and other forms of impaired cellular immunity. Its substantial mortality burden, coupled with diagnostic and therapeutic disparities, makes it a persistent global public health priority.[11,12]
4. ***C. albicans*: Major Endogenous Invasive Infection Threat.** Widespread human colonization, frequent disruption of host barriers during medical care, and substantial mortality associated with invasive candidiasis sustain the clinical importance of *C. albicans*. Its global burden reflects the interaction of endogenous infection, healthcare exposure, and host vulnerability rather than exceptional interpersonal transmissibility.[13,14]

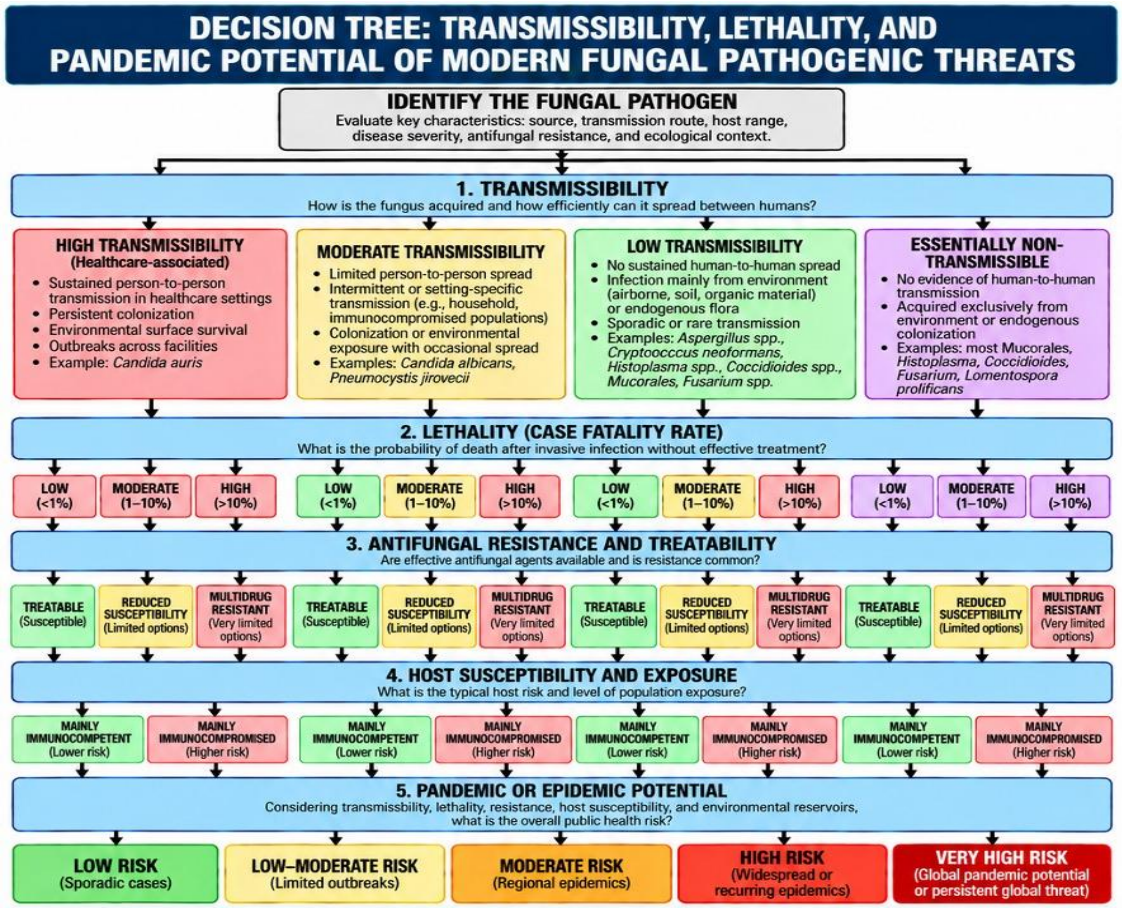
These distinctions do not establish a universal hierarchy of overall risk. *Mucorales* and *L. prolificans* may pose greater immediate threats in selected patients because of aggressive invasive disease or profound therapeutic resistance, while *Histoplasma*, *Coccidioides*, *Fusarium*, and *P. jirovecii* remain particularly consequential in specific geographic or immunocompromised populations.[15–23]

The greatest modern fungal threat is therefore context-dependent: *C. auris* is particularly concerning for healthcare-associated epidemic spread, *A. fumigatus* for environmental exposure and resistance, *C. neoformans* for neuroinvasive mortality, and *C. albicans* for its substantial burden of endogenous invasive infection. This multidimensional

assessment provides a more clinically meaningful prioritization than any ranking based solely on contagiousness, case fatality, or geographic distribution.

IMPLICATIONS FOR PANDEMIC PREPAREDNESS

Preparedness for emerging fungal threats requires a coordinated strategy that extends beyond conventional respiratory pandemic planning.



Fungal Pathogen (Examples)	Typical Source/Exposure	Relative Transmissibility	Typical Case Fatality Rate (Without Treatment)	Antifungal Resistance Concern	Current Epidemic/ Pandemic Potential	Overall Risk Category
Candida auris	Healthcare environment (contact, surfaces)	High (healthcare)	30–60% (invasive)	Very high (multi-drug resistant)	High (global spread in healthcare)	VERY HIGH
Aspergillus fumigatus	Airborne (environmental)	Low	20–50% (invasive)	High (azole resistance)	High (global environmental exposure)	HIGH
Cryptococcus neoformans	Environment (bird/bat excreta)	Low	20–40% (meningitis, disseminated)	Moderate	Moderate (global burden)	HIGH
Candida albicans	Endogenous colonization	Moderate (limited)	20–40% (invasive)	Increasing (azole/echinocandin)	Moderate–high (healthcare burden)	HIGH
Mucorales (Rhizopus, Mucor, etc.)	Environment (soil, organic material)	Very low	40–80% (invasive)	Intrinsic resistance/ limited options	Low (opportunistic)	HIGH
Histoplasma spp.	Soil (bird/bat droppings)	Very low	10–30% (disseminated)	Moderate	Low–moderate (regional/geographic)	MODERATE
Coccidioides spp.	Soil (arid regions)	Very low	<5% (most cases)	Lower	Low–moderate (geographic expansion)	MODERATE
Fusarium spp.	Soil, water, plants	Low	30–70% (invasive)	High	Low (opportunistic)	HIGH
Pneumocystis jirovecii	Respiratory (human-associated)	Moderate (limited)	20–60% (untreated)	Emerging concern	Moderate (clusters in vulnerable populations)	MODERATE–HIGH
Lomentospora prolificans	Environment	Very low	50–90% (invasive)	Very high (multi-drug resistant)	Low (sporadic, opportunistic)	HIGH

Figure 2

Because fungal disease can emerge through environmental exposure, endogenous infection, healthcare-associated transmission, and antifungal resistance, effective preparedness must integrate epidemiological surveillance, early diagnosis, infection prevention, therapeutic innovation, and protection of vulnerable populations.[2,4]

A decision-tree for the transmissibility, lethality and pandemic potential of modern pandemic threats is shown in Figure 2.

Surveillance must encompass invasive infections, asymptomatic colonization, antifungal susceptibility, healthcare-associated outbreaks, and changes in the geographic distribution of environmental fungi. Integrating clinical, laboratory, and environmental data would improve detection of emerging resistance, identify changing exposure patterns, and strengthen responses to geographically expanding fungal threats.[2,26]

Rapid diagnosis and timely treatment are equally critical. Invasive fungal infections frequently present with nonspecific manifestations, while conventional diagnostic methods may lack sensitivity, require specialized expertise, or produce delayed results. Expanding access to fungal biomarkers, molecular diagnostics, species identification, and susceptibility testing is essential for improving clinical outcomes and reducing inappropriate antimicrobial exposure.[2,9,13]

Antifungal stewardship must become an integral component of antimicrobial resistance policy. Appropriate prescribing, susceptibility-guided treatment, and resistance surveillance should be complemented by environmental monitoring and responsible agricultural fungicide practices. A One Health framework is particularly important for addressing resistance mechanisms that emerge outside healthcare settings and subsequently affect human infections.[4,10,26]

Healthcare infection prevention requires particular emphasis for *C. auris*. Early identification of colonized or infected patients, appropriate screening of exposed individuals, effective environmental disinfection, transmission-based precautions, and communication during interfacility transfers are essential for limiting institutional spread.[6–8] Prevention strategies for other invasive mycoses should be tailored to pathogen-specific exposure pathways and patient risk factors.

Therapeutic innovation remains indispensable. The limited number of systemic antifungal drug classes, increasing resistance, treatment-related toxicity, and persistent diagnostic gaps underscore the need for new antifungal agents, improved drug delivery, rapid diagnostics, and research into vaccines and host-directed immunotherapies.[4,24,25] These investments are particularly consequential because transplantation, oncology, intensive care, and immunomodulatory medicine depend on effective prevention and treatment of opportunistic fungal infections.

Ultimately, fungal preparedness should prioritize reducing preventable mortality, containing healthcare-associated transmission, detecting emerging resistance, and anticipating environmental and demographic changes in disease risk. Strengthening these capabilities would address established fungal threats while improving readiness for potentially novel pathogenic or transmission characteristics. Unlike conventional pandemic preparedness, success should be measured not only by the prevention of widespread transmission but also by reductions in invasive disease, treatment failure, and mortality among vulnerable populations.

A PRACTICAL CLINICAL FRAMEWORK

Understanding fungal pathogens requires more than memorizing organisms, clinical manifestations, and antifungal agents. Medical students should develop a systematic approach that connects fungal ecology, routes of acquisition, host susceptibility, clinical syndromes, diagnostic testing, and therapeutic decisions. Unlike many bacterial infections, invasive fungal disease frequently develops through environmental exposure or endogenous colonization rather than direct human-to-human transmission. Accordingly, clinical reasoning should begin with the patient's immune status, anatomical site of infection, epidemiological exposures, and healthcare history. Recognizing these relationships helps distinguish colonization from invasive disease, identify patients requiring urgent evaluation, and guide appropriate antifungal therapy.[2,9,13]

From Host Susceptibility to Pathogen Probability

The initial assessment should identify the clinical syndrome and determine which host factors increase the likelihood of fungal infection. Neutropenia, advanced HIV infection, transplantation, corticosteroid exposure, uncontrolled diabetes, prolonged intensive care, and invasive medical devices suggest different fungal pathogens and disease patterns.

For example, prolonged neutropenia raises concern for invasive aspergillosis; advanced HIV infection suggests cryptococcal meningitis or Pneumocystis pneumonia; diabetic ketoacidosis increases the risk of mucormycosis; and central venous catheterization or recent abdominal surgery increases the probability of invasive candidiasis. Healthcare exposure and prolonged institutional care should also prompt consideration of *C. auris*, particularly when colonization or transmission has been documented.[8,9,11,13,15]

The central principle is that host susceptibility and clinical presentation should guide pathogen probability rather than reliance on isolated organism associations.

From Clinical Presentation to Diagnostic Confirmation

Fungal infections frequently present with nonspecific manifestations, including fever, pulmonary infiltrates, respiratory failure, meningitis, bloodstream infection, or progressive tissue necrosis. Diagnostic evaluation should therefore integrate clinical findings with appropriate microbiological, histopathological, antigen-based, and molecular testing.

Blood cultures are important in candidemia but have limited sensitivity for several invasive fungal infections. Serum or cerebrospinal fluid cryptococcal antigen testing supports the diagnosis of cryptococcosis, while galactomannan testing and respiratory sampling may assist in diagnosing invasive aspergillosis. Tissue histopathology and culture are particularly important when mucormycosis is suspected.[9,11,13,15]

Importantly, detecting a fungus does not necessarily establish invasive infection. Respiratory isolation of *Aspergillus* may represent colonization, while detection of *Candida* in nonsterile specimens frequently reflects colonization rather than tissue invasion. Diagnostic interpretation must account for specimen source, host risk factors, compatible clinical findings, and evidence of invasive disease.

From Pathogen Identification to Effective Treatment

Antifungal treatment requires integration of organism identification, susceptibility, anatomical involvement, host characteristics, and infection severity. Echinocandins are generally preferred for initial treatment of candidemia in many adults, whereas invasive aspergillosis commonly requires mold-active triazole therapy. Cryptococcal meningitis requires combination induction therapy followed by prolonged consolidation and maintenance treatment, while mucormycosis frequently necessitates liposomal amphotericin B and urgent surgical debridement.[9,11,13,15]

Antifungal selection must also consider resistance, tissue penetration, drug interactions, organ dysfunction, and toxicity. Source control, including removal of infected intravascular devices when appropriate or debridement of necrotic tissue, may be essential. Clinical reassessment should determine whether therapy is effective, complications are developing, and treatment requires modification.

The essential lesson is that correct pathogen identification does not automatically establish the optimal antifungal regimen. An integrated clinical decision-making framework is shown below.

An Integrated Clinical Decision-Making Framework

The fungal disease assessment can be organized into eight sequential questions:

1. **Identify the clinical syndrome.** Is the infection pulmonary, bloodstream, central nervous system, cutaneous, or disseminated?
2. **Assess host susceptibility.** Is the patient neutropenic, immunosuppressed, diabetic, critically ill, or exposed to invasive medical devices?
3. **Determine the likely acquisition pathway.** Is infection environmentally acquired, endogenous, or healthcare-associated?
4. **Prioritize probable fungal pathogens.** Which organisms best explain the clinical syndrome and epidemiological context?
5. **Select appropriate diagnostic tests.** Which cultures, antigens, biomarkers, molecular assays, or tissue examinations can establish the diagnosis?
6. **Initiate appropriate treatment.** Which antifungal agents provide effective activity and adequate tissue exposure, and how urgently must therapy begin?
7. **Evaluate resistance and source control.** Is antifungal resistance likely, and are catheter removal, drainage, or surgical debridement necessary?
8. **Reassess clinical response.** Should therapy be modified according to organism identification, susceptibility, treatment response, and complications?

The clinical sequence to memorize is: HOST → SITE → EXPOSURE → FUNGUS → TEST → DRUG → RESISTANCE/SOURCE CONTROL → REASSESS

This framework emphasizes transferable clinical reasoning while providing a foundation for understanding the epidemiology, diagnosis, and management of major fungal infections.

Educational and Clinical Implications

The central educational objective is to replace isolated memorization with an integrated understanding of fungal pathogenesis, epidemiology, and clinical management. Students should recognize that the probability and severity of fungal infection depend on the interaction of environmental exposure, host defenses, microbial virulence, and treatment availability. Applying a consistent diagnostic and therapeutic framework allows students to distinguish colonization from infection, prioritize clinically important pathogens, interpret laboratory findings, and select appropriate treatment strategies.

Ultimately, medical mycology is not simply the study of fungi, but the application of fungal biology to clinical diagnosis, patient management, and infectious disease prevention. Understanding why a fungus causes disease in a particular host, how it is acquired, and which interventions improve outcomes provides a durable foundation for clinical practice and preparedness against emerging fungal threats.

CONCLUSION

Fungal pathogens represent an escalating global health threat driven primarily by environmental exposure, host susceptibility, invasive disease, and increasing antifungal resistance rather than efficient human-to-human transmission. Their epidemiological diversity underscores the need to distinguish clinical lethality and population-level disease burden from epidemic and pandemic potential.

Among contemporary pathogens, *C. auris* presents the most distinctive emerging healthcare-associated transmission threat, combining persistent colonization, environmental survival, invasive pathogenicity, and multidrug resistance. *A. fumigatus* poses a major environmental threat through ubiquitous airborne exposure, severe opportunistic infection, and emerging azole resistance. *C neoformans* remains a significant cause of fatal neuroinvasive disease, while *C. albicans* contributes substantially to invasive infections arising from endogenous colonization. Other pathogenic fungi further illustrate the diverse mechanisms underlying severe mycoses.

Future fungal disease burdens will likely reflect the convergence of expanding immunocompromised populations, antifungal resistance, environmental and climatic change, and evolving fungal adaptation. Although increased thermotolerance could potentially broaden the range of fungi capable of infecting mammals, its implications for human transmissibility remain uncertain. No recognized fungal pathogen currently combines efficient sustained community transmission, substantial pathogenicity in immunocompetent hosts, and multidrug resistance at a level comparable to major respiratory pandemic threats.

The greatest foreseeable fungal danger may therefore arise not from a conventional pandemic but from the cumulative consequences of increasingly prevalent, invasive, and difficult-to-treat infections. Preparedness must prioritize integrated surveillance, rapid diagnostics, antifungal stewardship, healthcare infection prevention, environmental monitoring, and development of novel therapeutics. Addressing these established threats while monitoring emerging biological and epidemiological changes offers the most scientifically grounded strategy for reducing fungal morbidity and mortality and strengthening global infectious disease preparedness.

Disclosure: The authors did not report any disclosures.

REFERENCES

1. Denning DW. Global incidence and mortality of severe fungal disease. Lancet Infect Dis. 2024;24(7):e428-e438. doi:10.1016/S1473-3099(23)00692-8
2. World Health Organization. WHO Fungal Priority Pathogens List to Guide Research, Development and Public Health Action. World Health Organization; 2022. https://www.who.int/publications/i/item/9789240060241
3. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases: estimate precision. J Fungi (Basel). 2017;3(4):57. doi:10.3390/jof3040057
4. Lockhart SR, Chowdhary A, Gold JAW. The rapid emergence of antifungal-resistant human-pathogenic fungi. Nat Rev Microbiol. 2023;21(12):818-832. doi:10.1038/s41579-023-00960-9
5. Casadevall A. Global warming could drive the emergence of new fungal pathogens. Nat Microbiol. 2023;8:2217-2219. doi:10.1038/s41564-023-01512-w
6. Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous emergence of multidrug-resistant Candida auris on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis. 2017;64(2):134-140. doi:10.1093/cid/ciw691
7. Chowdhary A, Jain K, Chauhan N. Candida auris genetics and emergence. Annu Rev Microbiol. 2023;77:583-602. doi:10.1146/annurev-micro-032521-015858
8. Forsberg K, Woodworth K, Walters M, et al. Candida auris: the recent emergence of a multidrug-resistant fungal pathogen. Med Mycol. 2019;57(1):1-12. doi:10.1093/mmy/myy054
9. Latgé JP, Chamilos G. Aspergillus fumigatus and aspergillosis in 2019. Clin Microbiol Rev. 2019;33(1):e00140-18. doi:10.1128/CMR.00140-18
10. Verweij PE, Snelders E, Kema GHJ, Mellado E, Melchers WJG. Azole resistance in Aspergillus fumigatus: a side-effect of environmental fungicide use? Lancet Infect Dis. 2009;9(12):789-795. doi:10.1016/S1473-3099(09)70265-8
11. Rajasingham R, Smith RM, Park BJ, et al. Global burden of disease of HIV-associated cryptococcal meningitis: an updated analysis. Lancet Infect Dis. 2017;17(8):873-881. doi:10.1016/S1473-3099(17)30243-8
12. Rajasingham R, Govender NP, Jordan A, et al. The global burden of HIV-associated cryptococcal infection in adults in 2020: a modelling analysis. Lancet Infect Dis. 2022;22(12):1748-1755. doi:10.1016/S1473-3099(22)00499-6
13. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1-e50. doi:10.1093/cid/civ933
14. Kullberg BJ, Arendrup MC. Invasive candidiasis. N Engl J Med. 2015;373(15):1445-1456. doi:10.1056/NEJMra1315399
15. Cornely OA, Alastruey-Izquierdo A, Arenz D, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. Lancet Infect Dis. 2019;19(12):e405-e421. doi:10.1016/S1473-3099(19)30312-3
16. Roden MM, Zaoutis TE, Buchanan WL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis. 2005;41(5):634-653. doi:10.1086/432579
17. Azar MM, Hage CA. Clinical perspectives in the diagnosis and management of histoplasmosis. Clin Chest Med. 2017;38(3):403-415. doi:10.1016/j.ccm.2017.04.004

18. McCotter OZ, Benedict K, Engelthaler DM, et al. Update on the epidemiology of coccidioidomycosis in the United States. Med Mycol. 2019;57(suppl 1):S30-S40. doi:10.1093/mmy/myy095

19. Gorris ME, Treseder KK, Zender CS, Randerson JT. Expansion of coccidioidomycosis endemic regions in the United States in response to climate change. GeoHealth. 2019;3(10):308-327. doi:10.1029/2019GH000209

20. Nucci M, Anaissie E. Fusarium infections in immunocompromised patients. Clin Microbiol Rev. 2007;20(4):695-704. doi:10.1128/CMR.00014-07

21. Seidel D, Meißner A, Lackner M, et al. Prognostic factors in 264 adults with invasive Scedosporium spp. and Lomentospora prolificans infection reported in the literature and FungiScope®. Crit Rev Microbiol. 2019;45(1):1-21. doi:10.1080/1040841X.2018.1514366

22. Thomas CF Jr, Limper AH. Pneumocystis pneumonia. N Engl J Med. 2004;350(24):2487-2498. doi:10.1056/NEJMra032588

23. Choukri F, Menotti J, Sarfati C, et al. Quantification and spread of Pneumocystis jirovecii in the surrounding air of patients with Pneumocystis pneumonia. Clin Infect Dis. 2010;51(3):259-265. doi:10.1086/653933

24. Perfect JR. The antifungal pipeline: a reality check. Nat Rev Drug Discov. 2017;16(9):603-616. doi:10.1038/nrd.2017.46

25. Berman J, Krysan DJ. Drug resistance and tolerance in fungi. Nat Rev Microbiol. 2020;18(6):319-331. doi:10.1038/s41579-019-0322-2

26. Fisher MC, Hawkins NJ, Sanglard D, Gurr SJ. Worldwide emergence of resistance to antifungal drugs challenges human health and food security. Science. 2018;360(6390):739-742. doi:10.1126/science.aap7999

27. Robert VA, Casadevall A. Vertebrate endothermy restricts most fungi as potential pathogens. J Infect Dis. 2009;200(10):1623-1626. doi:10.1086/644642

28. Gorris ME, Cat LA, Zender CS, Treseder KK, Randerson JT. Coccidioidomycosis dynamics in relation to climate in the southwestern United States. GeoHealth. 2018;2(1):6-24. doi:10.1002/2017GH000095

29. Brown GD, Denning DW, Gow NAR, Levitz SM, Netea MG, White TC. Hidden killers: human fungal infections. Sci Transl Med. 2012;4(165):165rv13. doi:10.1126/scitranslmed.3004404