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**Review Article**

# Review On Fungal Infection and Its Pathogenesis

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## ABSTRACT

Due to the rising prevalence of drug-resistant strains, fungal infections—which are caused by a wide variety of eukaryotic organisms—pose serious threats to world health. Particularly in immunocompromised people, these infections can vary from superficial to potentially fatal systemic illnesses. The need for innovative antifungal treatments has increased due to the rise of drug-resistant bacteria. The pathophysiology of numerous fungal diseases, the state of antifungal medications today, and the processes driving treatment resistance are all covered in this thorough overview. We highlight the significance of improving diagnostic methods to fight these tenacious organisms and go over the most recent developments in antifungal medication development, including novel medicines in clinical trials. By covering both treatment problems and opportunities in this quickly developing field, the study seeks to offer insights into potential future pathways for successful antifungal interventions.

## INTRODUCTION

Fungal infections represent a significant public health concern worldwide, affecting millions of individuals each year. They range from superficial infections involving the skin, hair, and nails to more severe systemic infections that may become life-threatening in immunocompromised individuals. Among these, superficial mycoses of the scalp and skin are particularly common in tropical and subtropical regions where heat and humidity provide favorable conditions for fungal growth. Poor hygiene, excessive sweating, prolonged antibiotic use, and immunosuppressive conditions further contribute to the rising incidence of fungal infections. These infections not only cause physical discomfort but also lead to cosmetic and psychological distress, emphasizing the need for safe and effective antifungal therapies.[1]

The fungi are a group of eukaryotic microorganisms, some of which are capable of causing superficial, cutaneous, subcutaneous, or systemic disease. Fungi are heterotrophic and essentially aerobic, with limited anaerobic

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capabilities, and can synthesize lysine by the L-α-adipic acid biosynthetic pathway. Fungi are eukaryotic microorganisms. Fungi can occur as yeasts, molds, or as a combination of both forms. Some fungi are capable of causing superficial, cutaneous, subcutaneous, systemic or allergic diseases. Yeasts are microscopic fungi consisting of solitary cells that reproduce by budding. Molds, in contrast, occur in long filaments known as hyphae, which grow by apical extension. Hyphae can be sparsely septate to regularly septate and possess a variable number of nuclei. Regardless of their shape or size, fungi are all heterotrophic and digest their food externally by releasing hydrolytic enzymes into their immediate surroundings (absorptive nutrition). Other characteristics of fungi are the ability to synthesize lysine by the L-α-adipic acid biosynthetic pathway and possession of a chitinous cell wall, plasma membranes containing the sterol ergosterol, 80S rRNA, and microtubules composed of tubulin.[2]

Fungi can use a number of different carbon sources to meet their carbon needs for the synthesis of carbohydrates, lipids, nucleic acids, and proteins. Oxidation of sugars, alcohols, proteins, lipids, and polysaccharides provides them with a source of energy. Differences in their ability to utilize different carbon sources, such as simple sugars, sugar acids, and sugar alcohols, are used, along with morphology, to differentiate the various yeasts. Fungi require a source of nitrogen for synthesis of amino acids for proteins, purines and pyrimidines for nucleic acids, glucosamine for chitin, and various vitamins. Depending on the fungus, nitrogen may be obtained in the form of nitrate, nitrite, ammonium, or organic nitrogen; no fungus can fix nitrogen. Most fungi use nitrate, which is reduced first to nitrite (with the aid of nitrate reductase) and then to ammonia. Nonfungal organisms, including bacteria, synthesize the amino acid lysine by the meso-α,ε diaminopimelic acid pathway (DAP pathway), whereas fungi synthesize lysine by only the L-α adipic acid pathway (AAA pathway). Use of the DAP pathway is one of the reasons microorganisms previously considered to be fungi, such as the myxomycetes, oomycetes, and hyphochytrids, are no longer classified as fungi. The DAP and AAA biosynthetic pathways for lysine synthesis represent dichotomous evolution. Fungal infections are of serious public health concern. The incidence of fungal infections in patients with other diseases including Covid-19 is associated with life-threatening mycoses and mortality.

Fungal infections can include superficial, cutaneous, sub-cutaneous, mucosal and systemic infections with varying degree of severity. Organisms such as Candida spp. are part of human microbiota that can cause opportunistic infections in individuals and life threatening infections (invasive candidiasis) in immuno-compromised patients such as HIV patients, cancer patients receiving chemotherapy, and patients receiving immuno-suppressive drugs. Besides, opportunistic and systemic infections, fungal pathogens such as Candida, Aspergillus, Fusarium, Mucorales and molds can cause healthcare-associated infections (HAI) in patients with underlying diseases (Perlroth et al., 2007). In certain geographical areas, fungal pathogens cause prevalent life-threatening endemic mycoses such as Blastomycosis, Coccidiodomycosis, Histoplasmosis, Talaromycosis, Paracoccidiodomycosis and Sporotrichosis.[3]

## TYPES OF FUNGI INFECTIONS:

Fungal infections, also called mycoses, are broadly classified according to the depth of tissue involvement and mode of entry of the pathogen. They can be grouped into the following categories:

Superficial mycoses: These infections involve only the outermost layers of the skin, hair, and nails. They do not invade living tissues and are generally non-inflammatory.

**Common examples include:**

- *Tinea versicolor* (caused by Malassezia furfur),
- *Tinea capitis* (scalp infection),
- *Tinea corporis* (body ringworm),
- *Tinea pedis* (athlete's foot),
- *Tinea unguium* (onychomycosis or nail infection).

Symptoms usually include itching, scaling, and discoloration of the affected area. The human body hosts a variety of environmental microbes and their infections, some of which are commensal, posing no harmful or no disease-causing potential, while others have the potential to cause infections in various parts of the human body.[4] However, the keratinized epithelia of the human body serve as a natural barrier for microbes and assist the body in defending itself against many fungal infections This layer prevents the invasion of microbes to deeper tissues, which can cause more severe diseases. As well, the skin secretes various substances (e.g., sweat, sebum, transferrin, antimicrobial peptides) which can prevent the growth of microbes. Nevertheless, some fungal species possess the capability of breaking through the defensive mechanisms of the human body, colonizing the surface skins, and causing infections. The infections of the skin, hair, and nails that are confined to the keratinized layers are considered superficial or cutaneous mycoses Dermatophytosis fungal illnesses, often known as tinea infections, are the most prevalent type of infection with high recurrence and can affect the entire body.

They can be classified into three distinct genera, specifically Trichophyton, Microsporum, and Epidermophyton. They can be spread from human to human (anthropophilic), animal to human (zoophilic), or soil to human (geophilic) . These fungi thrive in warm and moist environments, making them more prevalent in tropical and subtropical regions. In addition, black piedra and white piedra also have fungal infections of the hair shafts caused by Piedraia hortae and Trichosporon beigelii, respectively.[5]

Symptoms of these diseases can vary in appearance, including inflammation, swelling, and vesicles. The nails may be brittle, raised, discolored, and thicker if they have a fungus infection.

Cutaneous mycoses: These infections extend deeper into the epidermis and keratinized tissues such as hair and nails. They are primarily caused by dermatophytes belonging to genera Trichophyton, Microsporum, and Epidermophyton. Cutaneous mycoses provoke inflammatory responses and are contagious.[6] Typical infections are ringworm, athlete's foot, and jock itch. Subcutaneous mycoses: These infections occur when fungi are inoculated into the dermis or subcutaneous tissue through cuts or trauma. They are usually caused by soil saprophytes such as Sporothrix schenckii or Madurella mycetomatis. Lesions are characterized by nodules, ulcers, or abscesses that may spread locally but rarely become systemic. Examples: Sporotrichosis, Chromoblastomycosis, and Mycetoma. Subcutaneous mycoses typically occur when the fungus is being implanted through a cut or lesions on the skin. Most often, barefoot workers, including farmers, gardeners, and

children, are susceptible to these infections. The common subcutaneous infections are chromoblastomycosis, hyalohyphomycosis, phaeohyphomycosis, mycetoma and sporotrichosis . The symptoms of subcutaneous infections can vary with the disease, but they typically present as fistulae, localized nodules, granulomatous tissue, subcutaneous masses with abscesses, and ulcerations.The most common subcutaneous mycoses are chromoblastomycosis, entomophthoromycosis, mycetoma, phaeohyphomycosis and sporotrichosis.[7]

Systemic mycoses: These infections involve internal organs and deep tissues such as lungs, brain, or liver. The fungi enter the body via inhalation of spores or occasionally through bloodstream spread. They can be life-threatening, especially in immunocompromised individuals.

Examples include: Histoplasmosis (caused by Histoplasma capsulatum), Coccidioidomycosis, Blastomycosis, Aspergillosis, Cryptococcosis.

Symptoms vary depending on the organ affected. The fungal infections known as systemic mycoses can affect internal organs, including the lungs and brain, subsequently affecting the whole body Mainly, these infections occur by inhaling spores or hyphae and are disseminated via the bloodstream to multiple organs. The severity of the infection depends on the clinical status of the patient, and fever, cough, and loss of appetite are the common symptoms. There are two types of systemic mycosis, including endemic respiratory infections and opportunistic infections. Although endemic respiratory infections affect both immunocompetent and immunocompromised hosts, immunocompromised patients are more at risk of opportunistic infections. Some of the most common systemic mycoses are aspergillosis, blastomycosis, coccidiodomycosis, histoplasmosis, and paracoccidiodomycosis.[8-11]

Opportunistic mycoses: It is Caused by normally non-pathogenic fungi that become invasive in individuals with weakened immune systems. Common opportunistic fungi include Candida albicans, Aspergillus fumigatus, Mucor, and Cryptococcus neoformans. Seen in patients with HIV/AIDS, diabetes, cancer chemotherapy, or organ transplantation. Manifestations include oral thrush, systemic candidiasis, aspergillosis, and mucormycosis. Opportunistic mycoses are fungal infections that typically do not cause disease in healthy persons but can lead to illness in people with weakened immune systems. However, the virulence and pathogenicity of these fungi are explained by their ability to survive and reproduce in conditions that are not favorable for their growth. The human immune system recognizes and defends itself against various infections, but immunocompromised individuals are more vulnerable to severe diseases.[12] There are many risk factors for opportunistic fungal infections , such as HIV infections, anticancer chemotherapy, solid-organ transplantation, granulocytopenia, old age, premature birth, the use of broad-spectrum antibiotics, gastro-intestinal surgery, and central vascular catheters. In addition, some chronic diseases and other debilitating situations afford suitable environmental conditions for the metabolism of fungi, such as malignant tumors, tuberculosis, amebic abscess of the liver, and surgical procedures. Some of the main opportunistic mycoses are aspergillosis, candidiasis, cryptococcosis, fusariosis, hyalohyphomycosis, mucormycosis, penicilliosis, phaeohyphomycosis, pneumocystosis, scedosporiosis, and zygomycosis.[12]

Mycoses, as defined and explained above, affect humans, and present diverse clinical

manifestations essential for accurate diagnosis and effective treatment. Understanding these aspects is crucial in clinical practice. Manifestations vary based on the causative agent and infection site. Superficial mycoses show localized skin lesions (e.g., tinea pedis). Cutaneous mycoses present as inflammatory or non-inflammatory lesions (e.g., candidiasis). Subcutaneous mycoses cause chronic localized infections, while systemic mycoses lead to systemic symptoms . Diagnostic methods include clinical examination, microscopy, culture, and molecular techniques . Superficial and cutaneous mycoses' diagnosis often involves microscopy and the culture of skin samples. Systemic mycoses' diagnosis may employ blood cultures and serological tests. Treatment varies depending on the infection type and severity. Antifungal agents like azoles and polyenes are common. Topical antifungals suffice for superficial infections, while systemic infections require systemic therapy.[13]

## ROUTES OF ACQUISITION OF PATHOGEN:

There are two main routes of fungal infections, including exogenous and endogenous origins of disease. Exogenous mycoses are those that can transmit disease to individuals through an external route, such as airborne, cutaneous, or per-cutaneous contacts For instance, coccidioidomycosis (valley fever) caused by Coccidioides immitis and C. posadasii can be inhaled by humans when the spores rise in dust storms. Subsequently, it can infect the lungs and surrounding tissues, and various symptoms can occur (i.e., cough, fatigue, fever, headache, muscle aches or joint pains, rashes on the upper body or legs). In addition, paracoccidiomycosis caused by Paracoccidioides brasiliensis also occurs by the inhalation of spores and can affect the skin, lungs, lymph nodes, and internal organs. In contrast, endogenous mycoses originate from fungi that are part of the normal human microbiota. For instance, Candida species exist harmlessly in the body under normal conditions, but when the balance of the immune system or microbiota is disrupted, they can cause infections. In severe cases, Candida infections can spread to the veins, leading to potentially life-threatening systemic candidiasis. In particular, candidiasis is the most common endogenous mycosis, affecting mucous membranes, skin folds, and other areas of the body. In addition, Cryptococcus neoformans infects the lungs or the central nervous system and can cause a pneumonia-like illness with fever, cough, shortness of breath, and chest pains.[14,15]

Fungal infections occur when pathogenic or opportunistic fungi gain entry into the human body through different routes. The mode of acquisition depends upon the fungal species, its natural habitat, and the immune status of the host. One of the most common routes is the inhalation of fungal spores that are ubiquitously present in the environment, particularly in soil, decaying vegetation, or bird droppings. When inhaled, these spores may reach the respiratory tract and settle in the lungs, where they can germinate and proliferate. In healthy individuals, immune defense mechanisms usually eliminate the spores; however, in immunocompromised patients, they may lead to serious systemic infections such as aspergillosis, histoplasmosis, or cryptococcosis. Another important route is direct inoculation or contact through the skin, which generally occurs following minor cuts, abrasions, or traumatic injuries. Fungi present in soil or on plant material can penetrate the deeper layers of the skin, resulting in subcutaneous infections such as sporotrichosis or chromoblastomycosis.[16]

Individuals involved in agricultural or outdoor activities are at a higher risk of such infections. In

addition to this, surface colonization is a common mechanism in which fungi grow on the keratinized layers of skin, hair, and nails without invading living tissues. These infections are transmitted through direct contact with infected individuals, contaminated objects, or unhygienic practices, leading to conditions such as tinea capitis, tinea corporis, and pityriasis versicolor. Fungal pathogens may also originate from endogenous sources, especially in the case of opportunistic fungi like Candida albicans, which form part of the normal microbial flora of the oral cavity, gastrointestinal tract, and vagina. Under certain predisposing conditions, including prolonged antibiotic therapy, diabetes, immunosuppression, or hormonal imbalance, these normally harmless fungi can overgrow and cause infections such as oral thrush, vaginal candidiasis, or systemic candidiasis. Furthermore, infections can also be iatrogenic, acquired during medical interventions or hospital stays. The use of contaminated medical devices, catheters, or surgical instruments, and prolonged hospitalization can facilitate fungal invasion, particularly in patients with weakened immunity. Common hospital-acquired fungal infections are caused by Candida, Aspergillus, and Mucor species. fungal pathogens can invade the human body through inhalation, direct inoculation, surface colonization, endogenous overgrowth, or iatrogenic transmission. Understanding these routes of acquisition is crucial for developing effective preventive and therapeutic strategies, including topical antifungal formulations like medicated shampoos that act directly at the site of infection to control fungal proliferation.[17]

## PATHOGENESIS OF FUNGAL INFECTIONS:

The pathogenesis of fungal infections involves a complex interaction between the invading fungal pathogen and the host's defense mechanisms. Fungi are eukaryotic microorganisms that can exist as yeasts, molds, or dimorphic forms, and only a few among the large fungal population are pathogenic to humans. The development of infection begins when fungal spores or hyphae come in contact with a susceptible host through routes such as inhalation, direct inoculation, or surface colonization. Once the fungus gains entry, its ability to adhere, colonize, and invade host tissues determines its pathogenic potential. The initial step in infection is the adhesion of fungal cells to the host epithelial surface, mediated by adhesins and cell wall proteins. This is followed by colonization, during which the fungi multiply and establish themselves at the site of infection.[18]

After colonization, pathogenic fungi may produce various virulence factors that help them overcome host defenses. These include enzymes such as proteases, lipases, and keratinases, which degrade host tissues and allow deeper penetration into skin, nails, or mucosal layers. Certain fungi also produce toxins or metabolites that suppress local immune responses and facilitate persistence. In systemic mycoses, the fungal cells or spores disseminate through the bloodstream or lymphatic system to distant organs, where they can cause granulomatous or necrotic lesions. The severity of infection largely depends on the virulence of the fungal strain, the size of the inoculum, and the immune status of the host.[19]

The host immune system plays a crucial role in controlling fungal infections. Innate immunity, including intact skin barriers, mucosal defenses, and phagocytic cells such as macrophages and neutrophils, acts as the first line of defense. These cells recognize fungal cell wall components like β-glucans and mannans through pattern recognition receptors and initiate inflammatory responses. Adaptive immunity, particularly T-cell–mediated

responses, provides long-term protection by activating macrophages and promoting antibody production. However, in individuals with weakened immunity—such as those with HIV/AIDS, diabetes, or undergoing chemotherapy— these defense mechanisms are compromised, allowing opportunistic fungi like Candida, Aspergillus, and Mucor to cause invasive infections.

Environmental factors also play a significant role in fungal pathogenesis. Warm and humid conditions favor fungal growth and spore survival on the skin surface, enhancing the risk of superficial infections such as dermatophytosis and dandruff. On the scalp, excessive sebum production and accumulation of keratin provide a nutrient-rich environment for fungi like Malassezia furfur to proliferate. In such cases, topical antifungal agents help to reduce fungal load, relieve inflammation, and restore scalp health. Therefore, understanding the pathogenesis of fungal infections is essential for designing effective treatment strategies and developing novel topical formulations such as antifungal shampoos that can deliver the drug directly to the site of infection, ensuring better therapeutic outcomes with minimal systemic effects.

The development of fungal infection can be divided into four key stages—adhesion, colonization, invasion, and immune evasion. Each stage represents a potential target for antifungal therapy. Topical antifungal agents, such as itraconazole, act by disrupting the synthesis of ergosterol, an essential component of the fungal cell membrane. This results in increased membrane permeability, leakage of cellular contents, and ultimately fungal death. When combined with herbal extracts possessing antifungal, antioxidant, or soothing properties, such formulations not only inhibit fungal growth but also promote healing and scalp comfort. the pathogenesis of fungal infections involves the coordinated action of fungal virulence factors, host susceptibility, and environmental influences. Understanding these mechanisms is crucial for designing targeted therapeutic approaches. In the context of superficial and scalp infections, developing antifungal shampoos containing potent agents like itraconazole and natural plant extracts represents an effective strategy to control fungal colonization, reduce inflammation, and restore scalp health while minimizing systemic side effects.[20]

## COMMON FUNGI AFFECTING SCALP AND SKIN:

Tinea capitis is a fungal infection of the scalp hairs. Tinea capitis is also known as ringworm and herpes tonsurans infection. It is caused primarily by the dermatophyte species Microsporum and Trichophyton. The fungi can penetrate the hair follicle outer root sheath and ultimately may invade the hair shaft. Clinically, tinea capitis divides into inflammatory and non-inflammatory types. The non-inflammatory type usually will not be complicated by scarring alopecia. The inflammatory type may result in a kerion (painful nodules with pus) as well as scarring alopecia. Tinea capitis occurs primarily in children between 3 and 14 years of age, but it might affect any age group. It may also involve the eyelashes and eyebrows.

Tinea capitis is caused by the dermatophyte species which have the capabilities to infect keratin and keratinized tissue including the hair. Dermatophytes include several genera like Trichophyton, Microsporum, and Epidermophyton. Some common organisms include Trichophyton Sudanese, Trichophyton tonsurans, Trichophyton verrucous, Trichophyton

rubrum, and Microsporum canis. Transmission of the infection takes place through direct contact with organisms from: Humans (Anthrophillic organisms) Animals (Zoophilic organisms) Soil (Geophilic organisms) Indirectly through fomites: hats, hairbrushes, etc.

Tinea Capitis is a common dermatological disease. Tinea capitis is seen almost all over the world. It is most common in hot, humid climates such as Africa, Southeast Asia, and Central America. Sexual predilection varies depending on the causative dermatophytes, e.g., Trichophyton infections will affect both sexes equally during the childhood years. Microsporum canis affects boys more than girls. Tinea capitis affects children more than adults.[21]

Fungal infections of the hair and scalp, collectively referred to as dermatophytoses or tinea capitis, are caused primarily by keratinophilic fungi that utilize keratin as a nutrient source. The most common fungi that affect hair belong to the genera Trichophyton, Microsporum, and Epidermophyton, among which Trichophyton species are the predominant pathogens in humans. These fungi invade the hair shaft, follicle, and surrounding skin, leading to hair breakage, scaling, itching, and inflammation. Trichophyton tonsurans and Trichophyton violaceum are the leading causes of endothrix infections, where the fungal spores (arthroconidia) develop inside the hair shaft, resulting in brittleness and hair loss. Microsporum canis, Microsporum audouinii, and Microsporum gypseum cause ectothrix infections, in which the fungal elements coat the outside of the hair shaft and produce a characteristic fluorescence under ultraviolet light. These infections are highly contagious and commonly spread through direct contact with infected individuals, animals, or contaminated objects like combs, towels, or pillows.[22]

In addition to dermatophytes, lipophilic yeasts such as Malassezia furfur, Malassezia globosa, and Malassezia restricta are commonly associated with scalp disorders like seborrheic dermatitis, pityriasis versicolor, and dandruff. These fungi thrive in areas rich in sebaceous secretions, where they utilize sebum lipids as a carbon source and release irritating fatty acids that disrupt the scalp barrier and induce inflammation. Opportunistic yeasts like Candida albicans, Candida tropicalis, and Candida parapsilosis can also infect the scalp, particularly in immunocompromised individuals or those using broad-spectrum antibiotics, causing secondary fungal overgrowth and itching.

Non-dermatophyte molds such as Aspergillus niger, Aspergillus flavus, and Scopulariopsis brevicaulis have also been reported as causative agents of scalp infections, especially in individuals with damaged or weakened hair follicles. These molds produce keratin-degrading enzymes that erode the hair shaft, leading to hair thinning and localized alopecia. Environmental factors like high humidity, excessive sweating, and poor scalp hygiene provide favorable conditions for fungal proliferation. The combination of fungal virulence and compromised scalp health results in symptoms such as itching, scaling, inflammation, and hair fall. Because these infections are often chronic and recurrent, antifungal agents such as itraconazole are widely used in treatment. Incorporating itraconazole into topical formulations like medicated shampoos enhances its local availability, minimizes systemic side effects, and allows direct targeting of fungal colonies on the scalp. The addition of natural plant extracts with antifungal and anti inflammatory properties further improves efficacy, helping to

restore scalp balance and promote healthy hair growth.[23,24]

A wide range of fungi are known to infect the hair and scalp, leading to conditions such as tinea capitis, seborrheic dermatitis, and fungal folliculitis. Apart from the well-known dermatophytes like Trichophyton, Microsporum, and Epidermophyton, several other fungal species have been identified as pathogenic to hair. Trichophyton rubrum, Trichophyton mentagrophytes, and *Trichophyton soudanense* are significant causative agents of chronic scalp infections, often resulting in scaly patches, pustules, and hair fragility. *Trichophyton schoenleinii* is responsible for favus, a severe form of tinea capitis characterized by the formation of yellowish crusts known as scutula, accompanied by scarring alopecia and a distinctive musty odor. Microsporum ferrugineum is another species causing widespread scalp infections, particularly among school-aged children in humid regions.

In addition to these dermatophytes, various opportunistic fungi are also implicated in hair and scalp disorders. Yeasts of the genus *Malassezia,* including Malassezia furfur, Malassezia globosa, Malassezia restricta, and Malassezia sympodialis, are commonly found on the scalp surface and can overgrow under oily conditions, leading to dandruff, pityriasis versicolor, and seborrheic dermatitis. Candida albicans, Candida tropicalis, and Candida krusei are opportunistic yeasts that may colonize the scalp in individuals with compromised immunity, excessive moisture, or poor hygiene, causing itching, erythema, and localized hair loss.[25]

**EPIDEMIOLOGY OF FUNGAL INFECTIONS**:

*Candida* bloodstream infection, known as candidemia, is the most common invasive Candida infection; at the genus level, Candida ranks as one of the most prevalent causes of health care–associated infections in North America. Data from a nationally representative US-based surveillance system indicated a decline in incidence from 2009 to 2013, which stabilized at approximately 9 cases per 100,000 population from 2013 to 2017. This decrease occurred primarily among patients with health care exposure, specifically those with central venous catheters and, therefore, may be related to increased infection control practices in catheter care. Of particular note, a large proportion of cases historically occurred in children less than 1 year of age, yet candidemia incidence among this age group sharply decreased from 2009 to 2012, likely because of increased prophylaxis and improved catheter-related care among neonates. In the United States, neonatal incidence decreased from approximately 32 cases per 100,000 births in 2009 to less than 12 cases per 100,000 births by 2012, and has remained stable since then. Despite overall declines through 2013 in the United States across all age groups, incidence remains the highest among those 65 years and older. Large racial disparities persist across all age groups (the incidence among Blacks is 2.3 times higher than among non-Blacks). All-cause hospital mortality among all persons infected remains high at approximately 25% (yet varies by age group ranging from 10% among 1- to 18-year-olds to 32% among those ≥65 years old).[26]

In contrast with the United States, Canada's estimated incidence of candidemia is less than 3 cases per 100,000, with little change over the past 15 years. Similar to the United States, incidence is highest among those 65 years and older, followed by those less than 1 year old. Few studies have examined trends in Mexico; 1 study using

demographic data and population-based surveys estimated national incidence to be 5 cases per 100,000 population, with the intensive care unit (ICU) incidence 10-fold higher than the non-ICU incidence. In 14 medical centers in Mexico from 2010 to 2011, Candida species accounted for nearly all (98%) fungal bloodstream infections among pediatric patients. The major risk factors for invasive Candida infections have varied little over the past decade. These include the presence of indwelling catheters (mainly central venous catheters) and other medical devices, hematologic or solid organ malignancies, recent abdominal surgeries, hemodialysis, diabetes, receipt of systemic antibiotics or immunosuppressive medications including steroids, and receipt of total parenteral nutrition. Recently, injection drug use emerged as a risk factor; it is becoming more common in the context of the opioid epidemic.[27]

Five species account for most candidemia infections worldwide: C albicans, C glabrata, C tropicalis, C parapsilosis, and C krusei. Worldwide, these 5 species are estimated to account for more than 90% of all infections; however, the precise distribution and rank order of Candida species differ by geographic area, health care unit, underlying conditions, and patient demographic characteristics. Although C albicans remains the most common Candida species causing invasive infection in most clinical settings in North America, an increasing proportion of diagnoses in recent years have been attributed to non-albicans species, particularly C glabrata and C parapsilosis. In some settings, these species have even surpassed C albicans. The increased proportion of C parapsilosis infections is concerning because this species can colonize health care workers' hands, ultimately causing outbreaks.9 In one US surveillance site, the proportion of cases caused by C albicans decreased from 52% (1992–1993) to 41% (2008–2011), whereas C glabrata cases increased from 12% to 27% over the same time period. Similar trends have been documented in Canada, where in 1 multicenter study the proportion of C albicans cases declined from 61% to 42% and C glabrata cases increased from 17% to 22% from 2011 to 2016.[28]

Furthermore, non-albicans species often have decreased susceptibility to first-line antifungal therapies used to treat candidemia, including azoles and echinocandins. Approximately 10% of C glabrata isolates in the United States are resistant to fluconazole. Yet similar to species distributions, resistance patterns vary geographically and by medical institution (eg, a Canadian study found fluconazole resistance in only 1% among C glabrata isolates, whereas susceptibility testing from 2 Mexican tertiary care hospitals revealed fluconazole resistance to be 11% among C glabrata isolates). However, multidrug resistance remains uncommon among these top 5 species.

## REFERENCES


1. Berman J., Krysan D.J. Drug resistance and tolerance in fungi. Nat. Rev. Microbiol. 2020;18(6):319–331.
2. Campuzano A., Wormley F.L. Innate immunity against Cryptococcus, from recognition to elimination. J. Fungi (Basel). 2018;4:33.
3. Da Rosa D.W., Gezuele E., Calegari L., Goñi F. Asteroid body in sporotrichosis. Yeast viability and biological significance within the host immune response. Med. Mycol. 2008;46(5):443–448.
4. Das R., Kotra K., Singh P., Loh B., Leptihn S., Bajpai U. Alternative treatment strategies for secondary bacterial and fungal infections

associated with COVID-19. Infect. Dis. Ther. 2021;22:1–25.
5. Diep A.L., Hoyer K.K. Host response to Coccidioides infection: fungal immunity. Front. Cell. Infect. Microbiol. 2020;10
6. Elsegeiny W., Marr K.A., Williamson P.R. Immunology of cryptococcal infections: developing a rational approach to patient therapy. Front. Immunol. 2018;9:651.
7. Garfoot A.L., Shen Q., Wüthrich M., Klein B.S., Rappleye C.A. The Eng1 β-glucanase enhances histoplasma virulence by reducing β-glucan exposure. MBio. 2016;7(2):e01388–e0138815.
8. Hernández-Chávez M.J., Pérez-García L.A., Niño-Vega G.A., Mora-Montes H.M. Fungal strategies to evade the host immune recognition. J. Fungi (Basel). 2017;3:51.
9. Hokken M.W.J., Zwaan B.J., Melchers W.J.G., Verweij P.E. Facilitators of adaptation and antifungal resistance mechanisms in clinically relevant fungi. Fungal Genet. Biol. 2019;132
10. Kim, J.H., Cheng, L.W., Chan, K.L., Tam, C.C., Mahoney, N., Friedman. M., Shilman, M.M., Land, K.M., 2020. Antifungal drug repurposing. Antibiotics (Basel). 9(11), 812. [
11. Lee P.P., Lau Y.-.L. Cellular and molecular defects underlying invasive fungal infections—revelations from endemic mycoses. Front. Immunol. 2017;8:735. doi: 10.3389/fimmu.2017.00735.
12. Li Z., Lu G., Meng G. Pathogenic fungal infection in the lung. Front. Immunol. 2019;10:1524. doi: 10.3389/fimmu.2019.01524.
13. Ma L., Chen Z., Huang D.W., Kutty G., Ishihara M., Wang H., Abouelleil A., Bishop L., Davey E., Deng R., et al. Genome analysis of three pneumocystis species reveals adaptation mechanisms to life exclusively in mammalian hosts. Nat. Commun. 2016;7:10740.
14. Marcos, C.M., de Oliveira, H.C., de Melo, W.C., da Silva, J.F., Assato, P.A., Scorzoni, L., Rossi, S.A., de Paula, E. Silva.A.C., Mendes-Giannini, M.J., Fusco-Almeida, A.M., 2016. Anti-immune strategies of pathogenic fungi. Front. Cell. Infect. Microbiol. 6, 142.
15. Nett J.E., Andes D.R. Antifungal agents: spectrum of activity, pharmacology, and clinical indications. Infect. Dis. Clin. North Am. 2016;30(1):51–83.
16. Newland J.G., Abdel-Rahman S.M. Update on terbinafine with a focus on dermatophytoses. Clin. Cosmet. Investig. Dermatol. 2009;2:49–63.
17. Padmavathi A.R., Murthy S.M., Das A., Priya A., Sushmitha T.J., Pandian S.K. Impediment to growth and yeast-to-hyphae transition in Candida albicans by copper oxide nanoparticles. Biofouling. 2020;36:56–72.
18. Perlroth J., Choi B., Spellberg B. Nosocomial fungal infections: epidemiology, diagnosis, and treatment. Med. Mycol. 2007;45(4):321–346.
19. Reddy G.K.K., Nancharaiah Y.V. Alkylimidazolium ionic liquids as antifungal alternatives: antibiofilm activity against Candida albicans and underlying mechanism of action. Front. Microbiol. 2020;11:730.
20. Sam Q.H., Yew W.S., Seneviratne C.J., Chang M.W., Chai L.Y.A. Immunomodulation as therapy for fungal infection: are we closer? Front. Microbiol. 2018;9:1612.
21. Schwebke J.R., Sobel R., Gersten J.K., Sussman S.A., Lederman S.N., Jacobs M.A., Chappell B.T., Weinstein D.L., Moffett A.H., Azie N.E., Angulo D.A., Harriott I.A., Borroto-Esoda K., Ghannoum M.A., Nyirjesy P., Sobel J.D. Ibrexafungerp versus placebo

for vulvovaginal candidiasis treatment: a phase 3, randomized, controlled superiority trial (VANISH 303) Clin. Infect. Dis. 2021:ciab750.
22. Scorzoni L., de Paula e Silva A.C., Marcos C.M., Assato P.A., de Melo W.C., de Oliveira H.C., Costa-Orlandi C.B., Mendes-Giannini M.J.S., Fusco-Almeida A.M. Antifungal therapy: new advances in the understanding and treatment of mycosis. Front. Microbiol. 2017;8:36.
23. Scriven J.E., Tenforde M.W., Levitz S.M., Jarvis J.N. Modulating host immune responses to fight invasive fungal infections. Curr. Opin. Microbiol. 2017;40:95–103.
24. Silva S., Rodrigues C.F., Araújo D., Rodrigues M.E., Henriques M. Candida species biofilms' antifungal resistance. J. Fungi (Basel). 2017;3(1):8.
25. Spitzer M., Robbins N., Wright G.D. Combinatorial strategies for combating invasive fungal infections. Virulence. 2017;8(2):169–185.
26. Van Matre E.T., Evans S.L., Mueller S.W., MacLaren R., Fish D.N., Kiser T.H. Comparative evaluation of isavuconazonium sulfate, voriconazole, and posaconazole for the management of invasive fungal infections in an academic medical center. Ann. Clin. Microbiol. Antimicrob. 2019;18(1):13. doi: 10.1186/s12941-019-0311-3.
27. Vitale R.G. Role of antifungal combinations in difficult to treat Candida infections. J. Fungi (Basel). 2021;7(9):731.
28. Wiederhold N.P. The antifungal arsenal: alternative drugs and future targets. Int. J. Antimicrob. Agents. 2018;51(3):333–339.

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