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Emerging Trend in the Use of Antifungal Topical Cream

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Abstract

The most prevalent skin health problem worldwide is fungus-induced skin infections. Antifungal medications either topically or systemically are frequently used to treat fungal infections. Due to its tailored treatment and reduced adverse effects, topical fungal therapy is typically recommended. Advanced topical carriers' unique structural and functional characteristics enable them to overcome biopharmaceutical issues with traditional drug delivery vehicles, such as inadequate bioavailability and poor retention. Human fungal infections are a historically neglected area of disease research, yet they cause more than 1.5 million deaths every year. Our understanding of the pathophysiology of these infections has increased

considerably over the past decade, through major insights into both the host and pathogen factors that contribute to the phenotype and severity of these diseases. Growing knowledge of treatment processes and host susceptibility variables is starting to provide new conventional alternatives for the future, even as the rise of fungal strains that are less vulnerable to antifungal medications or that quickly acquire drug resistance is creating new risks. The pathobiology of human fungal infections is covered in detail in this review, particularly emphasising organisms that can cause invasive, potentially fatal infections. We also highlight the treatment, causes, and symptoms of the fungal infection.

Keywords: Fungal Infection, Delivery System, Topical, Systemically

Introduction

Fungal infection

Fungal infections are among the least researched and understood of all the microorganisms that may infect humans. However, their combined effect on human health is astounding, since fungal diseases kill over 2 million people annually and harm billions of people ^[1].

A fungal infection is a disease caused by fungi invading and multiplying in the body, affecting areas like the skin, nails, hair, or internal organs. It can range from mild, such as athlete's foot, to severe, especially in people with weakened immune systems ^[2].

Our understanding of the pathophysiology of fungal infections has significantly expanded during the last ten years. Startling and surprising new information on the fundamental processes of fungal virulence and host immunity and their effects on human health has been made public ^[3]. In this review, we include these fascinating new developments in a thorough analysis of fungal pathobiology from the viewpoints of the pathogen, host, and clinician. This study primarily focuses on fungi that can cause invasive, life-threatening infections, even though superficial fungal infections of the skin, hair, and nails as well as allergy fungal disorders can significantly increase human morbidity ^[4].

Fungal Virulency

Unfolding of virulency

Of the approximately 600 fungal species, only a tiny percentage have been known to infect humans. Over millions of years of evolution, the potential of fungus to infect humans has demonstrated itself several times, independently, throughout the kingdom ^[5]. Indeed, human-infecting species are found in about half of the fungal phyla. More human exposure to pathogens

and bigger populations with compromised host immune systems are causing an increasing variety of fungi to emerge as aetiological agents of human illness. For instance, the recent appearance of *Candida auris* is raising concerns in medical facilities around the globe^[6].

Despite their evolutionary variety, human fungal infections have phenotypic characteristics that are indicative of the biotic and abiotic stresses placed on mammalian host tissues^[7]. A crucial requirement for the ability to infect people is thermotolerance, which is one of these prevalent traits^[8].

Fungi that can infect humans must be able to withstand the ambient temperature of the site or sites they infect, regardless of whether they are primarily saprobic (like *Aspergillus*, *Histoplasma*, or *Talaromyces* species), belong to the commensal microbiota (like *Candida* species and other related yeast genera), or are inherently linked to their human host (like *Pneumocystis jirovecii*)^[9]. This is crucial because the global climate crisis may favour adaptive thermotolerance, which might result in the introduction of novel fungal infections and the expansion of the geographic range of already-existing ones^[10].

Human pathogenic fungi designated as acute, high and moderate risk inaction of levels are: -

1. Acute risk human pathogenic fungi classification: -^[11]

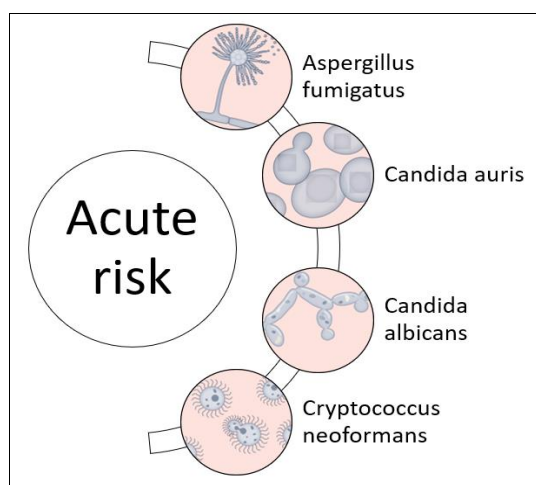


Fig 1

2. High-risk human pathogenic fungi classification: -^[12]

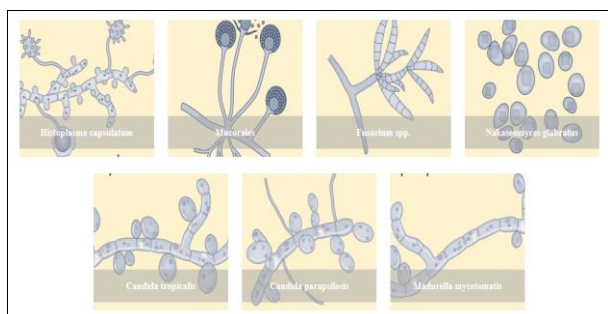


Fig 2

3. Moderate risk human pathogenic fungi classification: -^[13]

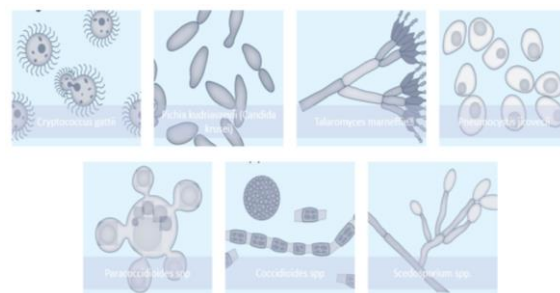


Fig 3

The Human Skin:

Human skin is a dynamic and multifunctional organ that provides a physical barrier against the hostile external environment through its highly organised and intricate landscape^[14]. Diverse environments found on the human skin can have a significant effect on the number or type of microorganisms that are found^[15]. For example, moist or humid body sites (e.g., the axilla, groin, toe web) usually create favourable conditions for fungal and microbial growth, and are therefore, often colonised by numerous microorganisms, while dry body sites (e.g., the forearms, legs) are not so microbiologically diverse^[16].

Skin is distributed in layers of partition where the fungal diseases act according to the layers of the skin. In which anti-fungal drugs act on the principle of absorption into the triple layer of skin^[17]. A fungal infection for topical skin disease is a condition where fungi infect the outer layers of the skin, causing symptoms like redness, itching, scaling, or rash. Common examples include athlete's foot, ringworm, and jock itch, which thrive in warm, moist areas of the body^[18].

Layers of skin are as follows

- Epidermis
- Dermis
- Hypodermis^[19]

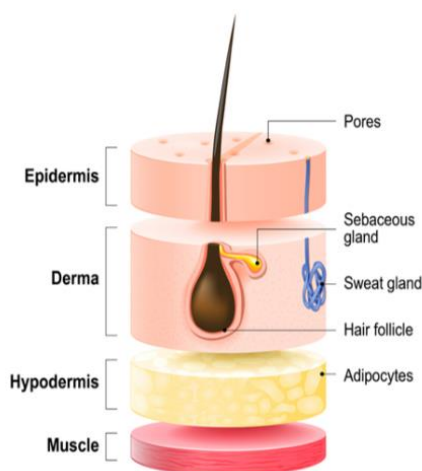


Fig 4: Layers of skin

Classification of Fungal Infection: -

Fungal infections, or mycoses, are caused by fungi and can affect various parts of the body. They are classified into 5 types.

1. Superficial Mycoses

- a) Tinea (Dermatophytosis): Infections like athlete's foot (tinea pedis), jock itch (tinea cruris), and ringworm (tinea corporis).
- b) Candidiasis: Affects the skin, mouth (oral thrush), or genitals (vaginal yeast infection).^[20]

2. Cutaneous Mycoses

- a) Onychomycosis: Fungal infection of the nails, causing thickening, discolouration, and brittleness.^[21]

3. Subcutaneous Mycoses

- a) Sporotrichosis: Also known as "rose gardener's disease," affecting the skin and lymph nodes.
- b) Chromoblastomycosis: Characterized by warty nodules, often on the legs and feet.^[22]

4. Systemic Mycoses

- a) Histoplasmosis: Caused by inhaling spores from soil contaminated with bird or bat droppings.^[23]
- b) Coccidioidomycosis (Valley Fever): Affects the lungs and can spread to other parts of the body.
- c) Blastomycosis: Typically affects the lungs, but can disseminate to the skin and bones.
- d) Cryptococcosis: Caused by *Cryptococcus neoformans*, leading to lung infections or meningitis, especially in immunocompromised individuals.^[24]

5. Opportunistic Mycoses

- a) Aspergillosis: Usually affects the lungs but can spread to other organs, especially in those with weakened immune systems.
- b) Pneumocystis Pneumonia (PCP): A serious infection common in people with weakened immune systems, like those with HIV/AIDS.
- c) Candidemia: Bloodstream infection caused by *Candida*, leading to severe systemic infections.^[25]

Causes of Fungal Infection: -**1. Pathogenic Fungi:**

- a. Dermatophytes: These fungi cause infections of the skin, hair, and nails (e.g., athlete's foot, ringworm).
- b. Yeasts: *Candida* species can cause infections in the mouth, throat, and genitals (e.g., oral thrush, vaginal yeast infections).
- c. Molds: *Aspergillus* species can cause lung infections (aspergillosis), especially in immunocompromised individuals.^[26]

2. Environmental Exposure:

- a. Soil: Fungi like *Histoplasma* and *Coccidioides* thrive in soil and can be inhaled, leading to lung infections.
- b. Water: Some fungi, such as those causing swimmer's ear, are found in water.
- c. Decaying Organic Matter: Fungi like *Sporothrix*, causing sporotrichosis, are found in decaying vegetation.^[27]

3. Human Factors:

- a. Hygiene: Poor hygiene can lead to overgrowth of fungi on the skin.
- b. Skin Injuries: Cuts or abrasions can provide entry points for fungi.
- c. Clothing and Footwear: Tight, non-breathable clothing and footwear can create a moist environment for fungal growth.^[28]

4. Weakened Immune System:

- a. Chronic Conditions: Diseases like diabetes or HIV/AIDS can compromise the immune system.
- b. Medications: Immunosuppressants or antibiotics can disrupt the body's natural defences.
- c. Cancer Treatments: Chemotherapy can weaken the immune system, increasing susceptibility to fungal infections.^[29]

5. Climate:

- a. Warm, Humid Environments: Fungi thrive in warm, moist conditions, making fungal infections more common in tropical and subtropical regions.^[30]

Symptoms of Fungal Infection: -

The symptoms of fungal infections can vary depending on the type and location of the infection.

1. Superficial Mycoses
2. Cutaneous Mycoses
3. Subcutaneous Mycoses
4. Systemic Mycoses
5. Opportunistic Mycoses^[31]

Here are some common symptoms of topical or superficial mycoses or infection

- a. Itching: Persistent itching in the affected area.
- b. Redness: Skin may appear red and inflamed.
- c. Scaling: Skin may become scaly or flaky.
- d. Blisters: Small blisters may form, especially in moist areas.
- e. Cracking: Skin may crack and peel, especially on the feet.^[32]

Treatment of Fungal Infection: -

The treatment of fungal infections depends on the type and severity of the infection.

Treating fungal infections in the topical (surface) regions of the body involves the use of antifungal medications applied directly to the affected area. Here are some common treatments.^[33]

1. Topical Antifungals:

- a. Creams and Ointments: Clotrimazole, miconazole, and terbinafine are commonly used to treat fungal infections like athlete's foot, ringworm, and jock itch. These are applied to the affected area, usually twice daily until the infection clears.
- b. Gels: Antifungal gels are absorbed quickly and are often used for moist areas, such as between the toes.
- c. Lotions: Antifungal lotions spread easily over large areas of skin, making them suitable for widespread infections.^[34]

2. Antifungal Nail Lacquers:

- a. Nail Lacquers: Products like amorolfine and ciclopirox are used to treat fungal nail infections. These lacquers are applied to the affected nails and help to penetrate the nail to reach the fungus.^[35]

3. Shampoos:

- a. Antifungal Shampoos: Ketoconazole and selenium sulphide shampoos are used to treat scalp infections such as tinea capitis. These are applied to the scalp and left on for a specified time before rinsing.^[36]

4. Powders and Sprays:

- a. Antifungal Powders: Powders containing miconazole or tolnaftate are used to keep the skin dry and treat infections in moist areas, such as athlete's foot.

- b. Sprays: Antifungal sprays are convenient for covering large areas or hard-to-reach places.^[37]

5. General Measures:

- Hygiene: Keeping the affected area clean and dry is crucial. Washing with antifungal soap can help.
- Protective Measures: Wearing breathable clothing and shoes, and using shower shoes in communal showers can help prevent reinfection.
- Avoiding Sharing Personal Items: Not sharing towels, shoes, or other personal items can prevent the spread of infection.^[38]

6. Advanced Topical Delivery Systems:

- Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs): These advanced systems improve drug delivery and skin penetration, offering controlled release and better treatment outcomes.^[39]

Topical Fungal Disease: -

Topical fungal diseases are infections that affect the outer layers of the body, including the skin, hair, and nails. These infections are usually caused by dermatophytes (a type of fungi), yeasts, and moulds.^[40]

Table 1: Topical fungal infection diseases are given with the classified fungi type^[41]

S. No	Topical fungal disease	Classified fungi type	Example
1	Athlete's Foot	Dermatophytes	Trichophyton rubrum
2	Ringworm	Dermatophytes	Trichophyton mentagrophytes, Microsporum floccosum
3	Jock Itch	Dermatophytes	Epidermophyton floccosum
4	Onychomycosis	Dermatophytes, Yeast, Molds	Trichophyton rubrum, candida spp., Aspergillus spp.
5	Oral Thrush	Yeast	Candida albicans
6	Vaginal Yeast Infection	Yeast	Candida albicans, candida glabrata
7	Scalp Ringworm	Dermatophytes	Trichophyton

Treatment of Topical Fungal Disease

Treating topical fungal infections involves the use of antifungal medications applied directly to the affected area.^[42]

Table 2

S. No	Fungal disease	Common Treatment	Application method
1	Athlete's Foot	Clotrimazole, Miconazole, Terbinafine	Topical cream, ointment, spray
2	Ringworm	Clotrimazole, Miconazole, Terbinafine	Topical cream, ointment
3	Jack Itch	Clotrimazole, Miconazole, Terbinafine	Topical cream, powder
4	Onychomycosis	Amorolfine, ciclopirox	Antifungal nail lacquers
5	Oral thrush	Nystatin, clotrimazole	Oral suspension, lozenges
6	Vaginal yeast infection	Clotrimazole, miconazole, fluconazole	Topical creams, suppositories

Conclusion

Fungal infections remain a continuous and growing threat to

human health. The number of humans succumbing to fungal infections is projected to increase, owing to a rapid rise in resistance to antifungal drugs, developments in modern medicine that alter protective immunity and the emergence of new pathogens, including zoonoses.^[43] Until recently, fungal infection has received much less attention than the threat of drug resistance in other pathogens. Clinically, the consequences of fungal infection are made worse by inadequate and late diagnosis and by the lack of availability and accessibility of antifungal options in impoverished regions of the world that have high burdens of IFDs^[44]. These infections are typically treated with topical antifungal medications, such as creams, ointments, and gels, applied directly to the affected area. Maintaining good hygiene and keeping the skin dry and clean can help prevent these infections. As we highlighted over a decade ago, we must continue to gain a better understanding of fungal pathobiology to aid the development of safer and more effective antifungal management strategies in the future for the treatment of fungal infections^[45].

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