

Review Article

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## Newer Aspects of Diagnosis and Treatment of Human Fungal Infection

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### ABSTRACT

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Human fungal infections are on the rise. Fungi causing skin infections are common but invasive fungi which are less known appear pathogenic and deadly. Environment, immunity and individual risk factors contribute for its susceptibility. Some of them can be fatal, if not diagnosed early and treated. Advances in molecular techniques help in early diagnosis. New modality of treatment such as antifungal peptides, fungal vaccines are in the pipeline. Improper and “Over the counter” medication must be avoided for the complete cure.

### Types of human fungal infections

In everyday life, human fungal infections (Mycoses) are not uncommon. Right from dandruff to deep invasive infections are caused by fungi present in the environment around us. Damp and moist environment, excessive sweating in skin folding, armpits, groin favors the fungal growth on human body. Based on the site of infection, mycoses are classified as superficial, subcutaneous and deep mycoses. Opportunistic infections and deep mycoses usually occur in immune compromised host. Despite prevalent mold infections, invasive *Candida* infections are

most common. *Candida* spp. are human commensal flora but many a times cause opportunistic infection once the host immune system goes down. There are more than hundred *Candida* species known till date. Among the human mycoses, fungi like *Aspergillus*, *Candida*, *Mucor*, *Rhizopus*, *Fusarium*, *Histoplasma*, *Pneumocystis*, *Cryptococcus*, *Malassezia*, *Sporothrix*, *Pythium*, *Curvularia*, *Trichophyton*, *Talaromyces* are common whereas *Blastomyces*, *Scedosporium*, *Paecilomyces*, *Acremonium*, *Trichoderma* and *Coccidioides* are rare. Out of the 250 species of *Aspergillus*, 40 species are known to cause

diseases in humans. For some of the fungal infection poor hygiene, low socioeconomic status, malnutrition, agricultural works, professions related to soil, fields, water logged area, humid and sultry environment are the risk factors apart from the host's own predisposing factors.

Majority of them cause lung infections such as chronic pulmonary aspergillosis. Many fungi also cause nosocomial (hospital borne) infections that hold a potential threat of secondary infection in post-surgical, organ transplantations, accidents and traumatic patients. Among them *Aspergillus* and *Candida* are the commonest one. Epidemiology of invasive fungal infection is based on the risk factors which are diverse and multifactorial in every host. Majority of the factors are neutropenia, intake of immunosuppressive drugs, diabetes mellitus, prolonged and broad spectrum antibiotic use, central venous and other indwelling lines – catheters etc., break in the mucosal barrier may be due to chemotherapy. Most of the organ systems that are involved by fungal and similar infections are conditions like Meningitis, sinusitis, osteomyelitis and enteritis.

Among the rare human fungal pathogens are *Fonsecaea*, *Monophora*, *Cladophialophora*, *Phialophora*, *Rhinocladiella* and *Exophiala* species which cause Chromoblastomycosis characterized by slowly progressive, coloured skin lesions.

Such infections are also seen in immune compromised people. It is difficult to treat and cure the fungal diseases in the full blown stage which makes many laborers and agricultural workers to retire forcefully depriving their livelihood. Knowing their importance, these diseases are declared as “Neglected Tropical Diseases “by World Health Organization (WHO).

There are varieties of new fungal species causing human infections. Some are difficult to diagnose and treat. Many recurring and chronic infections are also caused due to the biofilm forming ability of certain yeasts like and filamentous fungi especially in *Aspergillus* and *Candida* species. Most of such biofilm formers are found to be with high cell surface hydrophobicity. In case of *Candida* spp., certain adhesion and biofilm related genes are responsible this adhesion and colonization leading to biofilm formation. Trichosporonosis shows antifungal resistance in blood stream infection caused by indwelling medical devices. The biofilm former shows higher antifungal resistance due to their protective environment in ‘biofilm matrix’. Such fungi are of great challenge for treatment.

Filamentous fungi when found in Co-infection with bacteria, they exhibit a kind of antagonism and in some cases synergism during mutual growth in a host. It is found esp. between *Aspergillus fumigatus* and *Pasuedomonas aeruginosa*. Fungal infections due to *Mucor* are severe especially in diabetics and immune compromised people leading to frequent death. *Mucor* and *Rhizopus* rapidly invades blood stream through nose, lungs, skin and gastrointestinal tract causing tissue necrosis. It also infects muscle, central nervous system, kidney, bones and joints, hair, skin, nails and eyes. In such cases cell mediated immunity is lowered due to immune compromised condition.

The incidences of fungal infections of eyes are higher in India. Fungal eye infections are devastating as very few antifungal agents are available to treat these infections. Fungal ulcers of the cornea are the major causes of blindness caused by *Aspergillus* and *Fusarium*. Ear infection due to *Aspergillus* species is common among those with hearing aids. Constant usage of hearing aids,

accumulation of moisture in the ear and lack of hygiene causes Aspergillosis with painful episodes. Fungi also causes allergy leading to lung disorder.

### **Diagnosis of fungal infections**

Rise in the fungal infections especially invasive ones has made the diagnosis a challenging task. Skin infections can be easily diagnosed due to itching, discoloration and visible lesions compared to systemic infections. Scrapping the infected tissue, KOH mounting, lactophenol cotton blue, H and E staining and Calcoflour staining helps in the detection of fungi whereas culture and histopathological examinations are the standard diagnostic tools. Some fungi in culture need special additives like lipids, fatty acids and growth factors for better growth on Sabourud's dextrose agar. Antifungal sensitivity testing need to be made as routine measure in treating fungal infection.

Apart from the conventional methods, molecular methods like fungal nucleic acid amplification and Panfungal Polymerase chain reaction (PCR) are used for early diagnosis of invasive fungal infections. The conventional fungal PCR is affordable and highly sensitive with quick result but sometimes lacks specificity. In certain critical scenario, radiological diagnosis of invasive fungal infections can be done by computed tomography, Magnetic resonance imaging and ultrasonography.

### **Treatment of fungal infections**

Many fungal infections are turning out to be life threatening. To treat these infections, more often classical antifungals are used but its effect is associated with various factors like immune compromised condition, high toxicity and affordability. Resistance to antifungal agents especially for azole drugs is

on the rise. Similarity between human and fungal cell is also the concern to find the effective antifungal agent.

To treat many skin fungal infections various topical gels and ointments are available. The systemic antifungals used by clinicians are the drugs like aryamide, Inhibitors of fungal compounds, fluconazole, griseofulvin, terbinafine, echinocandins, Amphotericin B, Itraconazole, Triazole as per the clinician's sources. Inhaled antifungals are also in the offing. Among the nonclassical antifungals, potassium iodide is easily affordable and is used against subcutaneous infections by sporotrichosis and entomophthoromycosis. Whereas sulpha drugs are used commonly to treat pneumocystosis and paracoccidiomycosis effectively. In few mucor infections, hyperbaric oxygen is a modality of treatment. Alternatively cationic antifungal peptides of plant and animal origin that act against fungal virulence factors are also used as a part of treatment. Like the bacteriophages, use of viruses against fungi can be the prospective treatment measure.

In addition to HEPA filters, during surgery and organ transplant utmost care and asepsis is necessary to avoid fungal infections. Fungal ocular infections can be treated by immune mediators along with antifungal therapy but early diagnosis is necessary. Treatment of Chromoblastomycosis involves physical methods, chemotherapy of Itraconazole and Terbinafine and combination of both as recommended.

Even antifungal medications must be taken by consulting physician as infections like superficial dermatophytosis is difficult to treat due to the use of topical steroid antifungal creams procured 'over the counter', which need to be avoided. *Candida* and *Aspergillus* are the common diseases causing agents but resistant to azole treatment.

After the natural calamities like earthquakes, hurricane, floods etc. outbreak of invasive fungal infections can occur. These infections result from inhalation or cutaneous inoculation of fungal spores due to excessive exposure to the natural environment. Fungal outbreaks can also be caused due to construction activities with Aspergillosis and mucormycosis. One cannot avoid the contact of fungi as fungal spores are omnipresent. Hence in case of any kind of fungal diseases, care should be taken to get it diagnosed at the earliest and to get it treated.

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