

SAPROPHYTIC PARASITE AND MYCOSIS BY BLACK FUNGUS*¹Dr. Dhrubo Jyoti Sen, ¹Kushal Nandi, ¹Dr. Beduin Mahanti and ²Dr. Dhananjay Saha¹Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.²Deputy Director, Directorate of Technical Education, Bikash Bhavan, Salt Lake City, Kolkata-700091, West Bengal, India.***Corresponding Author: Dr. Dhrubo Jyoti Sen**

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ABSTRACT

Mucormycosis, previously called zygomycosis, refers to several different diseases caused by infection with fungi in the order Mucorales. Rhizopus species are the most common causative organisms. In descending order, the other genera with mucormycosis-causing species include Mucor, Cunninghamella, Apophysomyces, Lichtheimia (formerly Absidia), Saksenaia, Rhizomucor, and other species. Most mucormycosis infections are life-threatening, and risk factors such as diabetic ketoacidosis and neutropenia are present in most cases. Severe infection of the facial sinuses, which may extend into the brain, is the most common presentation. Mucormycosis is a life-threatening infection that occurs in patients who are immunocompromised because of diabetic ketoacidosis, neutropenia, organ transplantation, and/or increased serum levels of available iron. Because of the increasing prevalence of diabetes mellitus, cancer, and organ transplantation, the number of patients at risk for this deadly infection is increasing. Despite aggressive therapy, which includes disfiguring surgical debridement and frequently adjunctive toxic antifungal therapy, the overall mortality rate is high. New strategies to prevent and treat mucormycosis are urgently needed. Understanding the pathogenesis of mucormycosis and the host response to invading hyphae ultimately will provide targets for novel therapeutic interventions. In this supplement, we review the current knowledge about the virulence traits used by the most common etiologic agent of mucormycosis, Rhizopus oryzae. Because patients with elevated serum levels of available iron are uniquely susceptible to mucormycosis and these infections are highly Angio invasive, emphasis is placed on the ability of the organism to acquire iron from the host and on its interactions with endothelial cells lining blood vessels. Several promising therapeutic strategies in preclinical stages are identified.

KEYWORDS: Mucormycosis, Zygomycosis, Hyphae, Sporangium, Columnella, Fungus.**INTRODUCTION**

Fungus is any of a kingdom (Fungi) of saprophytic and parasitic spore-producing eukaryotic typically filamentous organisms formerly classified as plants that lack chlorophyll and include molds, rusts, mildews, smuts, mushrooms, and yeasts. Mucor is a microbial genus of approximately 40 species of moulds commonly found in soil, digestive systems, plant surfaces, some cheeses like tomme de savoie, rotten vegetable matter and iron oxide residue in the biosorption process.^[1,2]

Kingdom: Fungi

Division: Mucoromycota

Subdivision: Mucoromycotina

Order: Mucorales

Family: Mucoraceae

Genus: Mucor

Mucormycosis, also known as black fungus, can turn dangerous if left untreated, doctors said on Friday amid reports of re-emergence of the rare deadly fungal infection among Covid-19 patients across hospitals in Delhi, Pune and Ahmedabad. The fungal infection is caused by a group of molds called mucormycetes. The most common types that cause mucormycosis are Rhizopus species and Mucor species. Other examples include Rhizomucor species, Syncephalastrum species, Cunninghamella bertholletiae, Apophysomyces, Lichtheimia (formerly Absidia), Saksenaia, and Rhizomucor. If your skin is infected, the area can look blistered, red, or swollen. It might turn black or feel warm or painful. The infection can also spread to other parts of your body through your blood. This is called disseminated mucormycosis. Mucormycosis is any fungal infection caused by fungi in the order Mucorales.

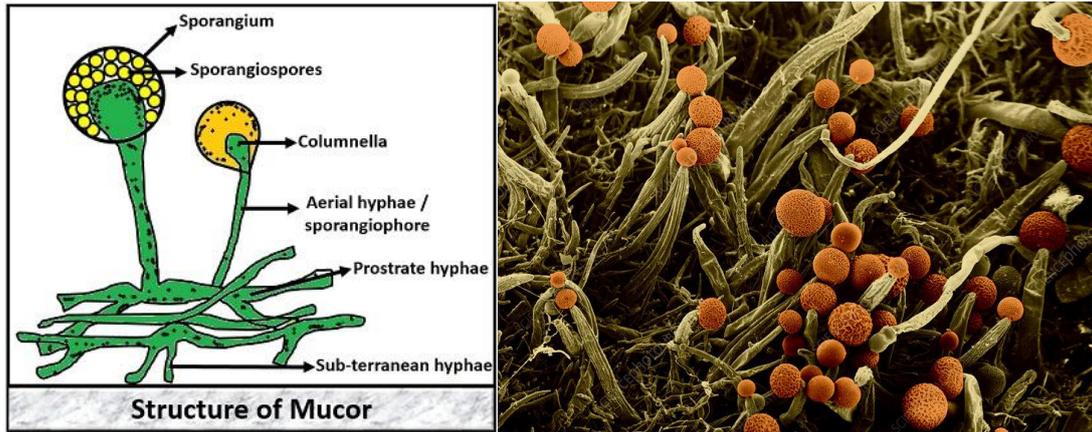


Figure-1: Mucor and Sporangium in SEM.



Figure-2: Mucormycosis.

Generally, species in the Mucor, Rhizopus, Absidia, and Cunninghamella genera are most often implicated. Common sources of infections are from soil, damp walls on old buildings etc.

The disease is often characterized by hyphae growing in and around blood vessels and can be potentially life-threatening in diabetic or severely immunocompromised individuals. "Mucormycosis" and "zygomycosis" are sometimes used interchangeably. However, zygomycota has been identified as polyphyletic, and is not included in modern fungal classification systems. Also, while zygomycosis includes Entomophthorales, mucormycosis excludes this group. The condition is informally referred to as black fungus.^[3-5]

Types

Rhinocerebral (sinus and brain) mucormycosis is an infection in the sinuses that can spread to the brain. This form of mucormycosis is most common in people with uncontrolled diabetes and in people who have had a kidney transplant. Pulmonary (lung) mucormycosis is the most common type of mucormycosis in people with cancer and in people who have had an organ transplant or a stem cell transplant.

Gastrointestinal mucormycosis is more common among young children than adults, especially premature and low birth weight infants less than 1 month of age, who have had antibiotics, surgery, or medications that lower the body's ability to fight germs and sickness.



Figure-3: SEM of hyphae of mucor/fungus.

Cutaneous (skin) mucormycosis occurs after the fungi enter the body through a break in the skin (for example, after surgery, a burn, or other type of skin trauma). This is the most common form of mucormycosis among people who do not have weakened immune systems.^[6-8]

Disseminated mucormycosis occurs when the infection spreads through the bloodstream to affect another part of the body. The infection most commonly affects the brain, but also can affect other organs such as the spleen, heart, and skin.

Signs & Symptoms: Mucormycosis frequently infects the sinuses, brain, or lungs. While infection of the oral cavity or brain are the most common forms of mucormycosis, the fungus can also infect other areas of the body such as the gastrointestinal tract, skin, and other organ systems. In rare cases, the maxilla may be affected by mucormycosis. The rich blood vessel supply of maxillofacial areas usually prevents fungal infections, although more virulent fungi, such as those responsible for mucormycosis, can often overcome this difficulty.

There are several key signs which point towards mucormycosis. One such sign is fungal invasion into the blood vessels which results in the formation of blood clots and surrounding tissue death due to a loss of blood supply. If the disease involves the brain, then symptoms may include a one-sided headache behind the eyes, facial pain, fevers, nasal congestion that progresses to black discharge, and acute sinusitis along with eye swelling. Affected skin may appear relatively normal during the earliest stages of infection. This skin quickly becomes reddened and may be swollen before eventually turning black due to tissue death. Other forms of mucormycosis may involve the lungs, skin, or be widespread throughout the body; symptoms may also include difficulty breathing, and persistent cough. In cases of tissue death, there may be nausea and vomiting, coughing up blood, and abdominal pain. The symptoms of mucormycosis also depend on where in the body the fungus is growing.^[9-11]

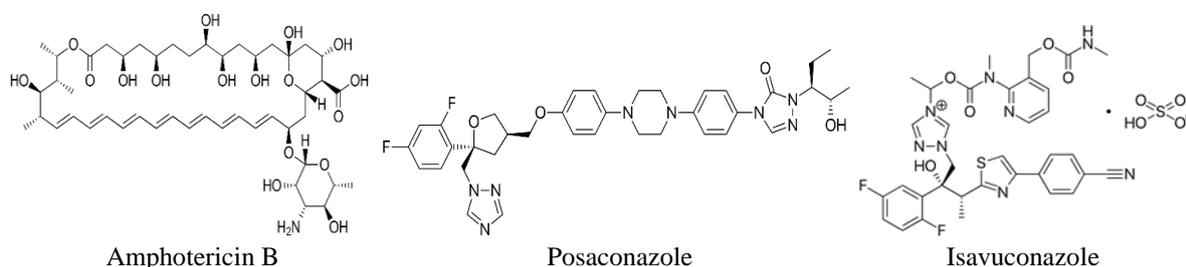


Figure-4: Medications of mucormycosis.

Surgical therapy can be very drastic, and in some cases of disease involving the nasal cavity and the brain, removal of infected brain tissue may be required. In some cases, surgery may be disfiguring because it may involve removal of the palate, nasal cavity, or eye structures. Surgery may be extended to more than one operation. It has been hypothesized that hyperbaric

Symptoms of rhinocerebral (sinus and brain) mucormycosis include: One-sided facial swelling, Headache, Nasal or sinus congestion, Black lesions on nasal bridge or upper inside of mouth that quickly become more severe, Fever **Symptoms of pulmonary (lung) mucormycosis include:** Fever, Cough, Chest pain, Shortness of breath, Cutaneous (skin) mucormycosis can look like blisters or ulcers, and the infected area may turn black. Other symptoms include pain, warmth, excessive redness, or swelling around a wound.

Symptoms of gastrointestinal mucormycosis include: Abdominal pain, Nausea and vomiting, Gastrointestinal bleeding Disseminated mucormycosis typically occurs in people who are already sick from other medical conditions, so it can be difficult to know which symptoms are related to mucormycosis. Patients with disseminated infection in the brain can develop mental status changes or coma.

Treatment: If mucormycosis is suspected, amphotericin B therapy should be immediately administered due to the rapid spread and high mortality rate of the disease. Amphotericin B is usually administered for an additional 4–6 weeks after initial therapy begins to ensure eradication of the infection. Isavuconazole was recently FDA approved to treat invasive aspergillosis and invasive mucormycosis.

Mucormycosis is a serious infection and needs to be treated with prescription antifungal medicine, usually amphotericin B, posaconazole, or isavuconazole. These medicines are given through a vein (amphotericin B [polyene], Posaconazole [triazole], isavuconazole [triazole]) or by mouth (posaconazole, isavuconazole). After administration of either amphotericin B or posaconazole, surgical removal of the "fungus ball" is indicated. The disease must be monitored carefully for any signs of re-emergence.

oxygen may be beneficial as an adjunctive therapy because higher oxygen pressure increases the ability of neutrophils to kill the fungus.^[12-16]

CONCLUSION

Mucormycosis, also known as black fungus, is a rare but dangerous infection. It's caused by a group of molds

called mucormycetes and often affects the sinuses, lungs, skin, and brain. You can inhale the mold spores or come into contact with them in things like soil, rotting produce or bread, or compost piles.

The infection can happen to anyone at any age. Most people will come into contact with the fungus at some point in their everyday lives. But you're more likely to get sick if you have a weakened immune system because of a medication you're taking or because you have a health condition like: Diabetes, especially when it isn't under control, HIV or AIDS, Cancer, Organ transplant, Stem cell transplant, Neutropenia (low white blood cell count), Long-term steroid use, Injected drug use, High levels of iron in your body (hemochromatosis), Bad health from poor nutrition, Uneven levels of acid in your body (metabolic acidosis), Premature birth or low birth weight. It's also more likely if you have a skin injury like a burn, cut, or wound. And cases have been reported in people with COVID-19. Mucormycosis isn't contagious. The symptoms of mucormycosis will depend on where in your body the fungus is growing. They may include: Fever, Cough, Chest pain, Shortness of breath, Swelling on one side of your face, Headache, Sinus congestion, Black lesions on the bridge of your nose or the inside of your mouth, Belly pain, Nausea and vomiting, Gastrointestinal bleeding, Blood in your stool, Diarrhea. If your skin is infected, the area can look blistered, red, or swollen. It might turn black or feel warm or painful. The infection can also spread to other parts of your body through your blood. This is called disseminated mucormycosis. When this happens, the fungus can affect organs like your spleen and heart. In severe cases, you may have changes to your mental state or go into a coma. It can even be deadly. If you suspect mucormycosis, your doctor will give you a physical exam and ask about your medical history. Let them know if you've been around spoiled foods or other places in which fungal spores are often found.

If it looks like you have a lung or sinus infection, your doctor may take a sample of the fluid from your nose or throat and send it to be tested in a lab. They might also do a tissue biopsy, taking out a small piece of infected tissue for testing. Your doctor may do imaging tests like CT or MRI scans to find out whether the infection has spread to your brain or other organs. If you're diagnosed with mucormycosis, you should start treatment as soon as possible with prescription antifungal medications. These medicines stop the growth of the fungus, destroy it, and bring the infection under control.

Preferred medicine for prophylaxis: Amphotericin B, Isavuconazole, Posaconazole.

You get these medications through a vein (intravenous or IV) or as pills that you swallow. Your doctor may start with high doses through an IV until the infection is under control, which can take several weeks. Then, you'll switch to pills.

Let your doctor know if a medication has troublesome side effects like stomach pain, heartburn, or trouble breathing. They may be able to change your treatment plan. In severe cases, your doctor may recommend surgery to remove infected or dead tissue to keep the fungus from spreading. This might include removing parts of your nose or eyes. It can be disfiguring. But it's crucial to treat this life-threatening infection. Complications of mucormycosis include: Blindness, Blood clots or blocked vessels, Nerve damage. Mucormycosis can be deadly without treatment. Because the infection is so rare, the exact mortality rate isn't clear. But researchers estimate that overall, 54% of people with mucormycosis die. The likelihood of death depends on which part of the body is affected. The outlook is better for people who have sinus infections than it is for lung or brain infections. There's no way to avoid breathing in spores. But you can do a few things to lower your chances of mucormycosis. It's especially important if you have a health condition that raises your risk. Stay away from areas with a lot of dust or soil, like construction or excavation sites. If you have to be in these areas, wear a face mask like an N95. Avoid infected water. This can include floodwater or water-damaged buildings, especially after natural disasters like hurricanes or floods. If you have a weakened immune system, avoid activities that involve dust and soil, like gardening or yard work. If you can't, protect your skin with shoes, gloves, long pants, and long sleeves. Wash cuts or scrapes with soap and water as soon as you can. If you get mucormycosis, be sure to take your medications as directed. If side effects cause problems or the infection doesn't get better, let your doctor know right away.

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