IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Fungal Infection of the Skin –In The Current Scenario

Rohan Ganesh Tayade[1] and Miss. Shruti Wankhede[2]
Student, Vardhaman College of Pharmacy, Karanja (Lad), Maharashtra, India[1]
Assistant Professor and Guide, Vardhaman College of Pharmacy, Karanja (Lad), Maharashtra, India[2]

Abstract: *The incidence of fungal infections is increasing at an alarming rate, presenting an enormous challenge to healthcare professionals. COVID-19 associated Mucormycosis (CAM) was mostly isolated during the second wave with mortality rate of almost 31-50%. Superficial and subcutaneous fungal infections affect the skin, keratinous tissues and mucous membranes. Included in this class are some of the most frequently occurring skin diseases, affecting millions of people worldwide. Although rarely life threatening, they can have debilitating effects on a person's quality of life and may in some circumstances spread to other individuals or become invasive. Most superficial and subcutaneous fungal infections are easily diagnosed and readily amenable to treatment. The indications for the use of currently available diagnosis and test, antifungal agents, their adverse effects, drug interactions, drugs resistance and COVID-19–associated mucormycosis in India.*

Keywords: Antifungal Agents, Covid19, Mucormycosis (CAM), Drug Resistance

I. INTRODUCTION

Fungal skin infection(1-2)
Fungal infections of the skin are also known as _mycoses'. They are common and generally mild. However, in very sick or otherwise immune suppressed people, fungi can sometimes cause severe disease.
Symptoms –
Requires a medical diagnosis
Symptoms depend on the area affected, but can include skin rash or vaginal infection resulting in abnormal discharge.
People may experience: Skin: Darkening of the skin, loss of colour, peeling, rashes, or small bump
Also common: Deformed toenail, itching, or vaginal discharge
Treatments – Treatments include antifungal medication.
History (3-4)
In 500BC, an apparent account of ulcers in the mouth by Hippocrates may have been thrush. The Hungarian microscopist based in Paris David Gruby first reported that human disease could be caused by fungi in the early 1840s.
Severe acute respiratory syndrome (SARS) 2003
During the 2003 SARS outbreak, fungal infections were reported in 14.8–33% of people affected by SARS, and it was the cause of death in 25–73.7% of people with SARS.
Fungal infections in Covid19
The novel coronavirus has recently been linked to two serious fungal infections: COVID-19 associated pulmonary aspergillosis (CAPA) and COVID-19 associated mucormycosis (CAM). The resurgence of these rare fungal infections has medical personnel concerned.
A 2021 study found that more than 47,000 cases of CAM were reported in just three months in India. And with the Delta variant spreading worldwide, reports suggest that the number of cases is likely much higher.

TYPE OF FUNGAL INFECTIONS (5-17)

Fungi are a large group of heterotrophic organisms existing as saprophytes, parasites or commensals. Fungi may be contaminants, opportunistic invaders or true pathogens. Cutaneous fungal infections are extremely common in the hot

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

and humid environments that prevail in the Indian subcontinent. They may be classified as superficial and deep infections (Table No. 01).

Table No. 01: Clinicopathological Classification of Cutaneous Fungal Infection

Type	Diseases	Causative organism
Superficial	-Pityriasis versicolor -Dermatophytosis -Candidiasis	*Pityrosporus orbiculare Dermatophytes Candida albicans and other candida sp.*
Subcutaneous	-Chromomycosis -Mycotic mycetoma -Rhinosporidiosis	*Fonsecaea pedrosoi and related sp. Madurella mycetomic and other Rhinosporidium seeberi*
Systemic Pathogenic	-Histoplasmosis -Blastomycosis -Paracoccidioidomycosis	*Histoplasma capsulatum Blastomyces dermatitidis Paracoccidioides brasiliensis*
Systemic Opportunistic	-Cryptococcosis -Aapergillosis -Candidiasis	*Cryptococcus neoformans Aspergillus fumigatus,etc* *Candida albicans*

Superficial Fungal Infections -

They are seen frequently in day-to-day practice and include pityriasis versicolor, dermatophytosis and candidiasis. Knowledge about their diagnosis and management is must.

Pityriasis Versicolor (Tinea Versicolor)

A common infection caused by overgrowth of the lipophilic fungus Malassezia furfur,which is a normal inhabitant of sebaceous duct in hair follicles and cause lesions in 'seborrhoeic regions' of young adults whose sebaceous glands are most active.

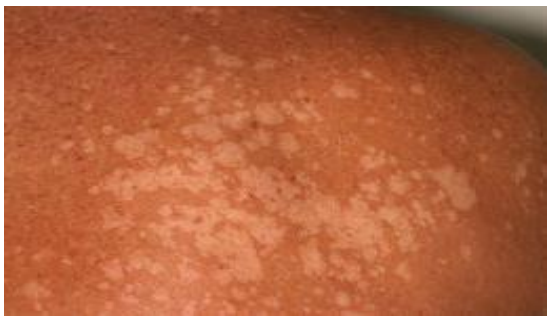

Fig. No. 01:Pityriasis Versicolar

Clinical Features :

Young adults and adolescents are typical patients. It is more common in males. Oily skin and sweating predispose to this infection. Asymptomatic, variably sized, well-defined hypopigmented macules and patches, covered with barely visible, powdery thin scales (Fig. 1) characterise this condition. Scales can be made more prominent by stroking the lesions (scratch sign). Occasionally, lesions may be pigmented brown or black. Chest, upper central back, neck, axillae, other parts of trunk, groins, proximal extremities and inframammary folds in females are affected.

Dermatophytosis

Dermatophytosis is caused by a group of keratinophilic fungi, dermatophytes. They may spread from human to human (anthropophilic by sharing of clothes and personal articles), animal to human (zoophilic, by close contact with pets) or soil to human (geophilic, contact with soil). Microbiologically these fungi have been classified into three genera Trichophyton, Microsporum and Epidermophyton.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Clinical Features :

Dermatophytosis is extremely common in India due to its tropical climate Adults, young and middle-aged, are typically affected Predisposing factors include obesity, diabetes mellitus, sweating wearing damp or non-absorbent or thick clothing or footwear in a humid atmosphere and sharing personal articles like towels. Sharing caps, combs and shaving blades may lead to tinea capitis and tines barbae respectively. According to the site of affection dematophytosis is categorised as tinea capitis, tinea corporis, tinea cruris, tinea unguium, tinea barbae, tinea manuum, tinea pedis and tinea cruris Pruritus is common to all types of dermatophytosis.

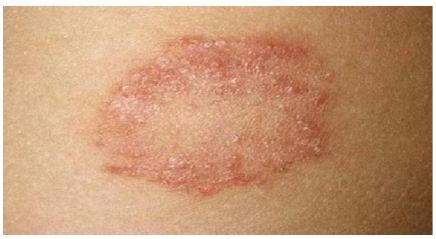

Fig. No. 02:Tinia Corporis.

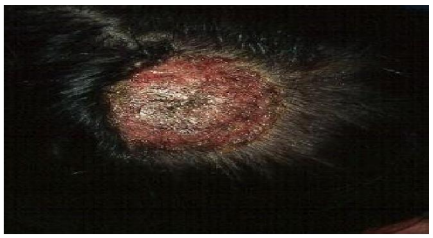

Fig. No. 03:Tinia Capitis

Tinea Corporis and Tinea Cruris (Ringworm)

A typical case shows a ring of active margin made up of erythematous papules, tiny vesicles and pustules around a scaly variably pigmented patch (Fig. 2). Lesions resolve centrally and progress peripherally to produce the ring-like configuration, hence the name ringworm.Tinca corporis indicates affection of waistline, axillae, buttocks, other parts of the trunk and extremities excluding palms and soles.Dermatophytic infection of the groin is called tinea cruris. Also known as "Dhobik itch', it is predominantly seen in males, on the genitocrural areas and the medial aspects of upper thighs.

Tinea Barbae and Tinea Capitis

Tinea barbae refers to involvement of the beard region. Grouped erythematous papules and pustules, some of which are follicular, are suggestive.Tinea capitis may be of inflammatory type as an indurated oedematous plaque covered with pustules (Fig. 3) or as a non inflammatory type, with scaling patches of hair loss. Hairs within the patch are fragile and lustreless.

Tinea Manunum and Tinea Pedis

Affection of hands (manuum) and feet (pedis) has many similarities.The lesions may be either non-inflammatory type comprising poorly defined scaly erythematous patches (Fig. 4) or inflammatory type characterised by grouped vesicles based on erythema and oedema.These can progress to tender bullae, erosions with foul smelling discharge especially in the toe web spaces (athlete's foot).Tinea manuum may also present as hyperkeratosis of the palms and fingers, with accentuation of the scaling in palmar flexural creases. Many a times the lesions are unilateral.

Tinea Unguium

This commonly accompanies tinea manuum and pedis. All the nails are rarely affected. Involved nails become thick, fragile, yellowish or greyish-brown in colour and develop subungual hyperkeratosis (Fig. 5).

Candidiasis

This common opportunistic yeast infection is caused by Candida albicans or other Candida species.

Predisposing Factors : The yeast proliferates whenever hot and humid conditions prevail Trauma, maceration and occlusion predispose. Iron deficiency, malnutrition, pregnancy, systemic diseases like diabetes mellitus and endocrinopathies like Cushing's syndrome, immunodeficiency states like AIDS, and drugs like corticosteroids, immunosuppressives, antibiotics and oral contraceptives are the principal predisposing factors.

Clinical Manifestations :

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

According to the site of affection, the different clinical manifestations of candidiasis include the following:-

Candidal Intertrigo

Overweight adults and chubby infants are common victims. Affection of finger webs is common in housemaids whereas toe webs are involved in those using occlusive footwear (Fig. 6). Moist, erythematous or white sodden patches restricted to apposing surfaces of body folds characterise this disease. Groins, (Fig. 7) axillae, submammary folds (in females), toe webs and finger webs are common sites of affection. Neck folds and natal cleft are involved in chubby infants and obese adults. Smear of scrapings from the surface (especially the periphery) of the lesions reveals budding yeasts and pseudohyphae. Candida can be cultured on Sabouraud's agar.

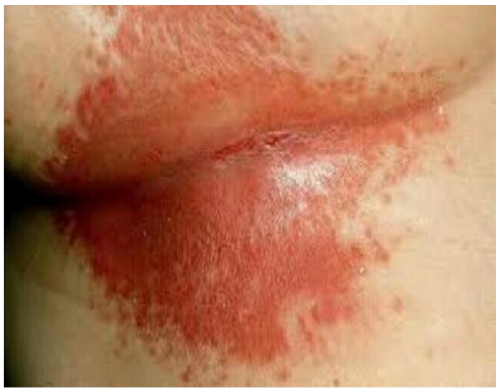

Fig. No. 06: Candidal Intertrigo

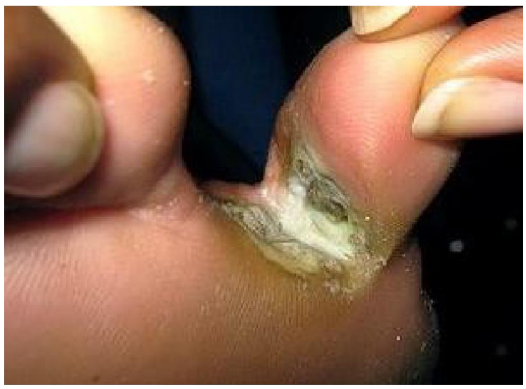

Fig. No. 07: Candidal Intertrigo

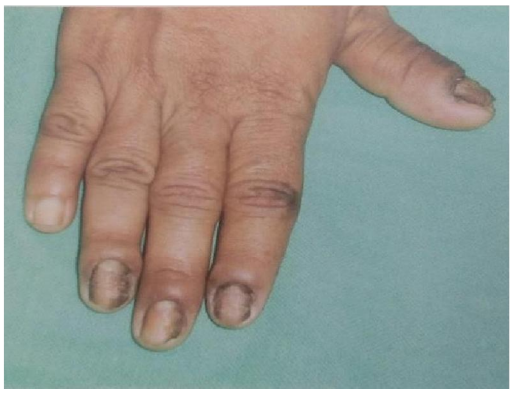

Fig. No. 08: Candidal Paronychia

Candidal Paronychia (Chronic Paronychia)

The potential space between proximal nail-fold and nail-plate is ordinarily sealed by the cuticle.When the cuticle is damaged due to persistent action of water and detergents the opened up space provides ideal environment for growth of Candida. Superadded staphylococcal infection leads to periodic exacerbation. Persons involved in wet work e.g. housemaids, dishwashers, cooks are at risk.Erythema, oedema and hyperpigmentation of proximal nail-folds (Fig. 8) of involved finger and toe nails suggest the diagnosis.Pressure upon the proximal nail-fold is painful and may elicit a bead of pus. Candida can be demonstrated, in addition to staphylococci, from a smear of the discharge from the nail-fold.

Candidal Stomatitis (Oral Thrush, Candidal Glossitis)

Neonates, infants, malnourished, debilitated, immunocompromised individuals (including HIV infected), patients on systemic steroids of antibiotics, diabetics, elderly persons with ill-fitting dentures or those using antiseptic lozenges develop this form of candidosis.In this HIV era, advancing HIV infection may be announced by the occurrence of oral candidiasis. When associated with dysphagia in the HIV infected, it is a good marker of oesophageal candidiasis.Presence of a curdy-white discharge over the inflamed mucosa of cheeks, lips, tongue, gingiva or palate is

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

characteristic. Thick discharge may form a pseudomembrane, dislodging which with a spatula reveals underlying erythema or erosions. Smear of the discharge proves the diagnosis. Identifying and correcting the predisposing factors is essential for preventing recurrences.

Perlèche (angular stomatitis) is seen as erythema and whitish discolouration of the lips at the angles of the mouth. Excess moisture resulting from overlapping lips in the elderly or from ill-fitting dentures is a common cause.

Candidal Balanoposthitis

A stereotypical case is an un-circumcised male with either an affected sex partner or underlying uncontrolled diabetes mellitus. Pruritic erythema, white discharge over the glans and prepuce and radial fissures along the inner aspect of the prepuce characterise this disease. Persistent infection leads to oedema of the prepuce and phimosis.

Candidal Vaginitis

Normal acidic pH of the vagina prevents the growth of Candida. During pregnancy and menstruation altered pH predisposes to vaginal candidosis. Complaints are pruritus, burning and whitish discharge per vaginum. Speculum examination reveals curdy white discharge, erythema and erosions of vaginal walls and introitus.

Deep Fungal Infections -

These are uncommon and may be classified according to their pathogenicity into subcutaneous and systemic fungal infections.

Subcutaneous fungal infections include mycotic mycetoma, sporotrichosis and chromomycosis. They are caused by organisms in the environment that usually need penetrating injuries to initiate an infection.

Systemic fungal infections are caused by either pathogens or opportunists. Pathogens causing diseases like (Table No.01) blastomycosis, coccidioidomycosis and paracoccidioidomycosis are rare in India except for histoplasmosis. However, they do occasionally affect the skin of immunocompromised individuals following reactivation and dissemination of old infection.

Opportunistic infections like cryptococcosis, candidiasis, mucomycosis or aspergillosis are more commonly seen in the HIV era. Other causes of immunosuppression like uncontrolled diabetes may also be responsible. Skin lesions of cryptococcosis vary from asymptomatic papules, nodules, lesion resembling molluscum contagiosum to ulcers with mucoid discharge.Skin lesions in aspergillosis and candidaemia include nodules and ulcers with purpura suggestive of septic vasculitis. Mucomycosis is seen as a noduloulcerative lesion over the root of the nose with thinitis, epistaxis, ocular oedema and gaze palsies

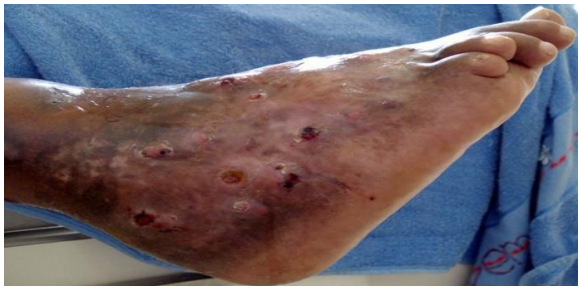

Fig. No. 09: Mycetoma

Mycetoma (Madura Foot)

This is a recalcitrant infection with either filamentous bacteria (actinomycotic mycetoma) or fungi (cumycotic mycetoma). Organisms are discharged as 'grains' through sinuses. Actinomycotic mycetoma is caused by the Actinomycetes whereas cumycotic mycetoma, producing black grains is caused by Madurella spp. The organisms abound in the environment and are introduced into the skin by a penetrating injury.Triad of subcutaneous nodules, discharging sinuses and grains is characteristically observed in mycetoma. Foot being prone to trauma, is most frequently affected (Fig. 9). Actiologic diagnosis requires examination of grains under the microscope and culture of the organisms. Biopsy is frequently helpful.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

DIAGNOSIS AND TEST (18-20)

Fungal culture test -

Your health care provider may order a fungal culture test if you have symptoms of a fungal infection. The symptoms vary depending on the type of infection.

Symptoms of a superficial fungal infection include:

Red rash, itchy skin, itching or discharge in the vagina (symptoms of a vaginal yeast infection), White patches inside the mouth (symptoms of a mouth yeast infection, called thrush), Hard or brittle nails

Symptoms of a more serious, systemic fungal infection include:

Fever, Muscle aches, Headaches, Chills, Nausea, Fast heartbeat

Fungi can occur in different places in the body. Fungal culture tests are performed where fungi is likely to be present. The most common types of fungal tests and their uses are listed below.

Skin or nail scraping

Used to diagnose superficial skin or nail infections

Swab test

Used to diagnose yeast infections in your mouth or vagina. It may also be used to diagnose certain skin infections.

Blood Test

Used to detect the presence of fungi in the blood. Blood tests are often used to diagnose more serious fungal infections.

Urine Test

Used to diagnose more serious infections and sometimes to help diagnose a vaginal yeast infection

Sputum Culture

Sputum is a thick mucus that is coughed up from the lungs. It is different from spit or saliva.

Used to help diagnose fungal infections in the lungs These tests are called "sensitivity" or "susceptibility" tests.

Rash evaluation test -

Symptoms of a contact dermatitis rash include:

Redness, Itching, Pain (more common with an irritant rash), Dry, cracked skin

Other types of rashes may have similar symptoms. Additional symptoms vary depending on the cause of the rash.

While most rashes are not serious, in some cases a rash can be a sign of a serious health condition.

The following symptoms are:

Severe pain

Blisters, especially if they affect the skin around the eyes, mouth, or genitals

Yellow or green fluid, warmth, and/or red streaks in the rash area. These are signs of infection.

Fever. This could be a sign of a viral or bacterial infection. These include scarlet fever, shingles, and measles.

Sometimes a rash can be the first sign of a severe and dangerous allergic reaction called anaphylaxis.

Patch test:

A provider will place small patches on the skin. The patches look like adhesive bandages. They contain small amounts of specific allergens (substances that cause an allergic reaction).

Patient wear the patches for 48 to 96 hours and then return to your provider's office.

Remove the patches and check for rashes or other reactions. There is no test for irritant contact dermatitis.

A rash evaluation may also include a blood test and/or a skin biopsy.

Blood test:

A blood sample taken from a vein arm, using a small needle. After the needle is inserted, a small amount of blood will be collected into a test tube or vial.

Biopsy:

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

A special tool use or a blade to remove a small piece of skin for testing. Other names: patch test, skin biopsy

Sputum culture –
A sputum culture is a test that checks for bacteria or another type of organism that may be causing an infection in your lungs or the airways leading to the lungs. Sputum, also known as phlegm, is a thick type of mucus made in your lungs. If you have an infection or chronic illness affecting the lungs or airways, it can make you cough up sputum.
Sputum is not the same as spit or saliva. Sputum contains cells from the immune system that help fight the bacteria, fungi, or other foreign substances in your lungs or airways. The thickness of sputum helps trap the foreign material. This allows cilia (tiny hairs) in the airways to push it through the mouth and be coughed out.
Sputum can be one of several different colors. The colors can help identify the type of infection you may have or if a chronic illness has become worse:
Clear. This usually means no disease is present, but large amounts of clear sputum may be a sign of lung disease.
White or gray. This may also be normal, but increased amounts may mean lung disease.
Dark yellow or green. This often means a bacterial infection, such as pneumonia. Yellowish-green sputum is also common in people with cystic fibrosis. Cystic fibrosis is an inherited disease that causes mucus to build up in the lungs and other organs.
Brown. This often shows up in people who smoke. It is also a common sign of black lung disease. Black lung disease is a serious condition that can happen if you have long-term exposure to coal dust.
Pink. This may be a sign of pulmonary edema, a condition in which excess fluid builds up in the lungs. Pulmonary edema is common in people with congestive heart failure.
Red. This may be an early sign of lung cancer. It may also be a sign of a pulmonary embolism, a life-threatening condition in which a blood clot from a leg or other part of the body breaks loose and travels to the lungs.

TREATMENT (ANTIFUNGAL AGENTS) (21-60)
These are drugs used for superficial and deep (systemic) fungal infections.
A disquietening trend after 1950s is the rising prevalence of more sinister type of fungal infections which are, to a large extent, iatrogenic. Fungal infections are mostly associated with the use of broad-spectrum antibiotics, cortico steroids, anticancer/immunosuppressant drugs, dentures, indwelling catheters and implants, and emergence of AIDS. As a result of breakdown of host defence mechanisms by the above agents, saprophytic fungi easily invade living tissue.
Many topical antifungals have been available since the antiseptic era. Two important antibio tics viz. amphotericin B-to deal with systemic mycosis, and griseofulvin-to supplement attack on dermatophytes were introduced around 1960. Antifungal property of flucytosine was noted in 1970, but it could serve only as a companion drug to amphotericin. The development of imidazoles in the mid 1970s and triazoles in 1980s provided safer and more convenient alternatives to amphotericin B and griseofulvin. Terbinafine is a novel antifungal. A group of potent semisynthetic antifungal antibiotics, the Echinocandins are the latest addition.
Amphotericin B
Antifungal Class:Antibiotic (specifically Polyene)
Antimicrobial Spectrum: Fungi: Candida albicans, C. tropicalis, C. parapsilosis, C. krusei, C. guilliermondii, Cryptococcus neoformans, Aspergillus fumigatus, A. flavus, A.niger, Absidia corymbifera, Rhizopus oryzae, R. rhizopodiformis, Blastomyces dermatitidis, Coccidioides immitis, Histoplasma capsulatum, Paracoccidioides brasiliensis, Sporothrix schencki, Malasezzia furfur
Mechanism of Action: Induces membrane permeability by forming complexes with ergosterol located in fungal membranes, leading to intracellular leakage and cell death.
Adverse Effects: 1)CNS – headache, chills, fever, 2)Renal – nephrotoxicity, 3)Gastrointestinal – dyspepsia, epigastric pain, anorexia, cramping, weight loss, 4)Cardiovascular – hypotension, 5)Respiratory – tachypnea, 6)Hematologic – normochromic normocytic anemia, 7)Other – muscle and joint pain, anaphylaxis (rare), hypomagnesemia, hypokalemia

Dosage :

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Amphotericin B can be administered orally (50-100 mg QID) for intestinal moni liasis; also topically for vaginitis, otomycosis.
Systemic mycosis: IV - Available as 50mg vial -suspended in 10 ml water and then diluted with 500 ml glucose
-0.5mg/kg to 1 mg/kg
Total dose- 3-4 gm over 2-3 months
Intestinal Monoliasis: 50-100 mg QID Orally
Vaginitis: topical
Otomycosis: 3% drops Intrathecal: 0.5 mg BD in fungal meningitis
Drug Interactions: Aminoglycosides, cyclosporine, antineoplastic agents (cisplatin, nitrogen mustard compounds) – nephrotoxic effects
Skeletal muscle relaxants and digitalis glycosides – hypokalemia may be exaggerated Flucytosine – amphotericin B may increase the toxicity of flucytosine
Nystatin
Antifungal Class: Antibiotic (specifically Polyene)
Antimicrobial Spectrum: Candida albicans Cryptococcus neoformans, Histoplasma capsulatum, Coccidioides immitis,
Mechanism of Action: Induces membrane permeability by forming complexes with ergosterol located in fungal membranes, leading to intracellular leakage and cell death.
Adverse Effects: 1)Gastrointestinal - Nausea, vomiting, diarrhea, 2)Dermatologic - Rare case reports of contact dermatitis, and skin eruptions have been reported
Dosage:
Topical: Powder 50 Million Units/10g, Cream 100,000 Units/g, Ointment, Oral pastilles 200,000 Units,
Suspension: 100,000 Units/ml, Vaginal
Tablets: 100,000 Units
Adults: Oral candidiasis: Swish and swallow 4-6mL (400,000 to 600,000 Units) PO four times daily
Topical: Apply cream or ointment two to three times daily to affected areas, OR apply topical powder to affected area two to three times daily
Vaginal infections: Insert 1 vaginal tablet into vagina at bedtime nightly x 14 days.
Infants:
Oral candidiasis: Using dropper, apply 1 mililiter to each buccal membrane (total of 2 milliliters OR 200,000 units) four times daily.
Children:
Oral candidiasis: Swish and swallow 4-6mL (400,000 to 600,000 Units) PO four times daily
Drug Interactions: Conjugated estrogen, digoxin, ambrisentan, atorvastatin, benzylpenicilli – Nystatin decreases excretion

Caspofungin
Antifungal Class : Antibiotic (specifically Echinocandins)
Antifungal Activity: Candida sp. Including azole-resistant strains. Activity against molds difficult to quantify but includes Aspergillus sp
Mechanism of Action: Non-competitive inhibition of the enzyme b-(1,3)-glucan synthase. flushing, wheals, rash.
Dosage:
Intravenous only – available as 50mg and 70mg powder for reconstitution vials.
70mg loading dose IV x 1, followed by 50mg IV q24h
Drug Interactions:
Cyclopsorin: Increases the AUC of Caspofungin by 35%, with associated elevations in ALT and AST elevations
Tacrolimus: Concomitant administration decreases AUC of tacrolimus by 20%. Montoring of tacrolimus blood concentrations recommended

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Other: Reductions in caspofungin concentrations may occur when coadministered with inducers of drug clearance such as efavirenz, nevirapine, phenytoin, dexamethasone, or carbamazepine. Caspofungin dose escalation may be considered in this setting

Griseofulvin

Antifungal Class: Antibiotic (specifically Heterocyclic Benzofuran)

Antimicrobial Spectrum: Dermatophytes: Epidermophyton, Trichophyton, Microsporum, etc.

Mechanism of Action: Griseofulvin interacts with polymerized microtubules and disrupts the mitotic spindles thus arresting fungal mitosis.

Adverse Effects: Toxicity of griseofulvin is low and usually not serious. Headache is the commonest.com plaint, followed by g.i.t. disturbances. CNS symptoms and peripheral neuritis are occasional. Rashes, photoallergy, hepatitis warrant discontinuation.

Dosage: 125-250 mg QID with meals.

Duration of therapy depends on the site of infection (turnover rate of Keratin).

Scalp - 4 weeks

Palm, soles - 6 to 8 week , Finger nails-6to8month

Toe nails – 10 to 12 months

Drug Interactions: Griseofulvin induces CYP450 enzymes and hastens warfarin metabolism. Efficacy of oral contraceptives may be lost.

5. Flucytosine

Antifungal Class: Antimetabolite

Antimicrobial Spectrum: Fungi: Candida albicans, C. glabrata, C. lusitaniae, C. krusei (less susceptible), Cryptococcus neoformans, Cladosporium spp., Phialophora spp., Fonsecaea pedrosoi, Saccharomyces cerevisiae, sporotrichosis, Rhodotorula, Penicillium, Paecilomyces, Aspergillus spp. (less susceptible)

Mechanism of Action: Penetrates the fungal cell wall and is converted to 5-fluorouracil which competes with uracil, thus interfering with fungal RNA and protein synthesis.

Adverse Effects: 1) Hematologic -leucopenia, thrombocytopenia, bone marrow aplasiaaplasia, 2) Gastric- intestinal perforation, ulcerating enterocolitis, 3) Hepatic - elevated liver enzymes, hepatitis, jaundice, azotemia, 4) Dermatologic - photosensitivity reaction, 5) CNS (rare) - headache, drowsiness, confusion, hallucinations

Dosage:

Oral dose: recommended dose 100 mg/kg/day in divided doses

Oral dose for severe infections: up to 250 mg/kg/day

Cryptococcal meningitis: 100 mg/kg/day

Drug Interactions:

Non-CYP mediated: Aluminum hydroxide/Magnesium hydroxide – delay absorption of flucytosine

Zidovudine, ganciclovir, trimethoprim-sulfamethoxazole – may potentiate hematological toxicity

Amphotericin B and foscarnet – may potentiate toxicities related to excessive flucytosine levels

Clotrimazole

Antifungal Class: Azoles (specifically Imidazole)

b.Antifungal Spectrum: Fungi: Blastomyces dermatitidis, Candida spp, Coccidioides immitis, Cryptococcus neoformans, Dermatophytes (Trichophyton, Microsporum, Epidermophyton), Histoplasma capsulatum, Malassezia furfur, Naegleria fowleri, Nocardia spp, Paracoccidioides brasiliensis, Sporotrichum schenckii

c . Mechanism of Action: Bind to the heme moiety of the fungal cytochrome P-450 dependent enzyme lanosterol 14-a-demethlyase. Inhibits 14-a-demethlyase, blocks formation of ergosterol and leads to the buildup of toxic methylated 14-a-sterols. Both effects serve to inhibit cell growth.

d . Adverse Effects: Oral tablets - Gastrointestinal: nausea, vomiting

Vaginal - 1)Genitourinary: vaginal/vulvar bleeding, 2)Burning or itching of penis of sexual partner; polyuria; vulvar itching, soreness, edema, discharge.

e. Dosage:

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

1) Cream, topical: 1% (15g, 30g, 45g, 90g);
2) Cream, vaginal: 1% (45g, 90g), 2% (25g);
3) Lotion: 1% (30 mL);
4) Solution, topical: 1% (10 mL, 30 mL);
5) Tablet, vaginal: 100mg, 200mg, 500mg;
6) Troche: 10mg
Adults and children > 3 years:- Troche: 10 mg troche dissolved 5 times/day for 14 days. Adults and children > 12 years: Vaginal cream 1%: Insert 1 applicatorful daily (preferably at bedtime) for 7 – 14 days.
2%: Insert 1 applicatorful daily (preferably at bedtime) for 3 consecutive days. Vaginal tablets: Insert 100 mg/day for 7 days or 500 mg single dose.
Topical: Apply to affected area twice daily (morning and evening).
Drug Interactions: Clotrimazole is an inhibitor of the cytochrome P450 3A4, 2A6, 2C8/9, and 2E1 isoenzymes. Caution should be exercised and monitoring is suggested when concomitantly administering clotrimazole with drugs that have narrow therapeutic windows and are substrates of aforementioned CYP substrates.

Oxiconazole
Antifungal Class: Azoles (specifically Imidazoles)
Antimicrobial Spectrum: pathogenic dermatophytes, yeasts, dematiaceous fungi, asper gilli, mucoraceae as well as aerobic ac tinomycetes. gram-positive bacteria, including Corynebacterium minutissimum.
Mechanism of Action: Oxiconazole inhibits ergosterol biosynthesis, which is required for cytoplasmic membrane integrity of fungi. It acts to destabilize the fungal cyctochrome P450 51 enzyme (also known as Lanosterol 14-alpha demethylase). This is vital in the cell membrance structure of the fungus.
Adverse Effects:Erythema, pruritus, and burning/stinging sensation are common. Folliculitis, papules, fissure, maceration, rash, and nodules have been reported.

Dosage:
Cream: 1% (30, 60, 90 g), Lotion: 1% (30, 60 mL)
Both preparations contain propylene glycol, cetyl alcohol, stearyl alcohol, and 0.2% benzoic acid.
≥12 yr to adult: Pityriasis versicolor: Apply cream to affected and surrounding areas once daily × 2 wk.
Tinea corporis, tinea cruris, and tinea pedis: Apply cream or lotion to affected and surrounding areas once daily to twice a day; treat tinea corporis and tinea cruris for 2 weeks and tinea pedis for 1 month.
7.6 Drug Interactions: metabolism of Clindamycin, Ranolazine can be increased when combined with oxiconazole, The serum concentration of Capmatinib can be decreased when it is combined with oxiconazole.
Ketoconazole
Antifungal Class: Azoles (specifically Imidazole)
Antifungal Spectrum:
Opportunisitic yeasts: Candida albicans,Candida tropcialis, Candida glabrata, Cryptococcus neoformans, Candida krusei (variable activity)
Opportunistic hyaline moulds: Scedosporium spp. (variable activity)
Dimorphic moulds: Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Parracoccidioides brasiliensis, Sporothrix schenkii, Penicillium marneffei Dematiaceous moulds: variable activity
Mechanism of Action: Inhibition of 14-a-demethlyase blocks formation of ergosterol and leads to the buildup of toxic methylated 14-a-sterols and depletes ergosterol in the cell membrane.
Adverse Effects: 1)Gastrointestinal: nausea, vomiting, abdominal pain, anorexia, 2)Skin and appendages pruritus, rash, potentially exfoliative, 3)Liver and biliary system: Elevation of hepatic transaminases (<10%), hepatitis, 4)Immunologic: anaphylaxis, 5)Endocrine: adrenal insufficiency, decreased testosterone synthesis, menstrual irregularities, 6)Special senses: photophobia, 7)Nervous System: headache
Dosage:
1)Cream, topical: 2% (15g, 30g, 60g)

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

2)Shampoo, topical: 1% (6mL, 120 mL, 210mL)
3)Tablet: 200 mg;
4)Mucosal infections/cutaneous infection: 200 mg/day for 2 weeks
5)Extensive mucosal infection/recalcitrant dermatophyte infections: 400 mg/day for 4 weeks;
6)Systemic mycoses: 400 mg/day for 6-12 months
7)Shampoo: Apply twice weekly for 4 weeks with at least 3 days between each shampoo; 8)Topical: Rub gently into the affected area once daily to twice daily.
Drug Interactions: Ketoconazole is a potent inhibitor of the cytochrome P450 3A4 isoenzyme system. Caution should be exercised and monitoring is suggested when concomitantly administering ketoconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates.
Fluconazole
Antifungal Class: Azoles (specifically Triazoles)
Antifungal Spectrum:
Opportunisitic yeasts: Candida albicans, Candida tropcialis, Cryptococcus neoformans, Candida glabrata (variable activity)
Dermatophytes: variable activity
Dimorphic moulds: Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Parracoccidioides brasiliensis, Sporothrix schenkii, Penicillium marneffei (variable activity)
Mechanism of Action: Inhibits fungal cytochrome P450 3A dependent enzyme, decreases ergosterol synthesis and inhibits cell membrane formation.
: Adverse Effects: 1)Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain; 2)Cardiovascular System: pallor, angioedema; 3)Central Nervous System: headache, dizziness; 4)Endocrine: hypertriglyceridemia, hypokalemia; 5)Hepatic: hepatic failure, hepatitis, abnormal LFTs; 6)Respiratory: dyspnea; 7)Hematologic: thrombocytopenia, leukopenia; 8)Dermatologic: skin rashes, alopecia
Dosage: 1)Infusion: 2 mg/mL (100 mL, 200 mL), 2)Powder for oral suspension: 10 mg/mL (35 mL), 40 mg/mL (35 mL), 3)Tablet: 50 mg, 100 mg, 150 mg, 200 mg
Invasive infections: - 1)Adults: prophylaxis - 100 to 400 mg once daily; Treatment - 400 to 800 mg once daily, 2)Pediatric patients: prophylaxis: 3 to 6 mg/kg once daily; Treatment: 6 to 12 mg/kg once daily, 3)Premature neonates: prophylaxis - 72 hour dosing interval at the same dosage as older children for first two weeks of life, followed by a dosing interval of 48 hours during week 3 and 4
Drug Interactions: Fluconazole is a potent inhibitor of the cytochrome P450 3A4 isoenzyme system. Caution should be exercised and monitoring is suggested when concomitantly administering fluconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates.

Itraconazole
Antifungal Class: Azoles (specifically Triazoles)
Antifungal Spectrum: Opportunisitic yeasts: Candida albicans, Candida tropcialis, Cryptococcus neoformans, Candida glabrata (variable activity), Candida krusei (variable activity)
Opportunistic hyaline moulds: Aspergillus spp., Scedosporium spp. (variable activity) imorphic moulds:
Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Parracoccidioides brasiliensis, Sporothrix schenkii, Penicillium marneffei Zygomycetes: Entomophthorales (variable activity)
Dematiaceous moulds: variable activity
Mechanism of Action: Inhibits fungal cytochrome P450 3A dependent enzyme, decreases ergosterol synthesis and inhibits cell membrane formation.
Adverse Effects: 1) Gastrointestinal: nausea, vomiting, abdominal pain, 2) Cardiovascular System: edema, hypertension, 3) Dermatologic: skin rashes, pruritus, 4)Central Nervous System: headache, dizziness, fatigue, 5) Endocrine & metabolic: hypertrigliceridemia, decreased libido, hypokalemia, 6) Hepatic: abnormal LFTs, hepatitis, 7) Renal: albuminuria
Dosage:

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Capsule: 100 mg; Injection,
solution: 10 mg/mL (25 mL)
Solution,oral: 100mg/10mL (150 mL)
Adults:- Oral: 100-400 mg/day (capsules); 2.5 mg/kg (HP-beta-CD solution)
Children < 18 years:- Oral: 5 to 8 mg/kg/d with a loading dose of 4 mg/kg three times a day for the first three days (capsules); 2.5 mg/kg twice a day (HP-beta-CD solution)
Drug Interactions: Itraconazole is a potent inhibitor of the cytochrome P450 3A4 isoenzyme system. Caution should be exercised and monitoring is suggested when concomitantly administering itraconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates.
Voriconazole
Antifungal Class: Azoles (Specifically Triazoles)
Antifungal Spectrum:
Opportunisitic yeasts: Candida albicans, Candida tropcialis, Candida glabrata, Candida krusei, Cryptococcus neoformans,
Opportunistic hyaline moulds: Aspergillus spp., Fusarium spp. (variable activity), Scedosporium spp.
Dimorphic moulds: Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Parracoccidioides brasiliensis, Sporothrix schenkii, Penicillium marneffei Dematiaceous moulds: variable activity
Mechanism of Action: Inhibits fungal cytochrome P450 3A dependent enzyme, decreases ergosterol synthesis (prinicipal sterol in fungal cell wall membrane) and inhibits cell membrane formation.
Adverse Effects: 1) Ocular: visual changes (photophobia, color changes, increased or decreased visual acuity, or blurred vision), 2) Cardiovascular System: tachycardia, hypertension, hypotension, vasodilation, peripheral edema, 3) Central Nervous System: fever, chills, headache, hallucinations, dizziness, 4) Endocrine: hypokalemia, hypomagnesemia, 5)Gastrointestinal: nausea, vomiting, abdominal pain, diarrhea, xerostomia, 6)Hematologic: thrombocytopenia, 7)Hepatic: alkaline phosphatase increased, serum transaminases increased, 8)Renal: acute renal failure
Dosage:
Injection, powder for reconstitution: 200 mg
Tablet: 50 mg, 200 mg Adults and pediatric patients > 2 years
IV: 6 mg/kg BID on day 1, followed by 4 mg/kg BID
PO: 400 mg BID on day 1 (<40 kg: 200 mg BID), followed by 200 mg BID (<40 mg: 100 mg q12h)
Drug Interactions: Voriconazole is a potent inhibitor of the cytochrome P450 3A4 isoenzyme system. Caution should be exercised and monitoring is suggested when concomitantly administering voriconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates.
Terbinafine
Antifungal Class: Allyl amine
Antimicrobial Spectrum: Dermatophytes, Candida albicans, Trichophyton species, Microsporum canis, Epidermophyton floccosum, Tinea species,Candida species and Malassezia furfur.
Mechanism of Action: Terbinafine has a fungicidal effect by inhibiting the enzyme squalene monooxygenase which is involved in the synthesis of sterol in fungi. This inhibits fungal sterol biosynthesis by decreasing ergosterol levels.
Adverse Effects: Taste and visual disturbances, hepatic dysfunction, hematological Disorder, no inhibition of cyto P450.
Dosage: Adult and Pediatric Dosage Forms and Strengths –
Tablet: 250 mg, Packet, oral granules: 125 mg, 187.5 mg Dosage Considerations – Should be Given as Follows:
Onychomycosis: 250 mg (1 tablet) orally daily for 6 weeks (fingernail) or 12 weeks (toenail) Tinea Pedis (Off-label): 250 mg/day orally in a single dose or divided every 12 hours for 2-6 weeks
Tinea Corporis, Tinea Cruris: 250 mg/day orally in a single dose or divided every 12 hours for 2-4 week
Sporotrichosis, Lymphocutaneous and cutaneous: 500 mg/day orally every 12 hours for 2-6 weeks; treat for additional 2-4 weeks after resolution of all lesions (resolution may take 3-6 months)
Tinea Capitis, Pediatric: Children over 4 years (less than 25 kg): 125 mg/day orally for 6 weeks;

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Children over 4 years (25-35 kg): 187.5 mg/day orally for 6 weeks, Children over 4 years (greater than 35 kg): 250 mg/day orally for 6 weeks.
Drug Interactions: Terbinafine is a CYP450 2D6 inhibitor and can therefore lead to increased levels of other drugs metabolized by this enzyme. Therefore, caution is advised when taken with antidepressants, beta-blockers, and class IC antiarrhythmics.

ANIDULAFUNGIN
Antifungal Class: Antibiotic (specifically Echinocandins)
Antifungal Spectrum: Candida species, including C. albicans, C. glabrata, C. tropicalis, C. parapsilosis, C. famata, C. rugosa, and C. stellatoidea. C. kruse, C. lusitaniae.
Mechanism of Action: Anidulafungin inhibits
glucan synthase, an enzyme present in fungal, but not mammalian cells. This results in inhibition of the formation of 1,3-β-D-glucan, an essential component of the fungal cell wall.
Adverse Effects: Flushing or hot flashes, dizziness, diarrhea, constipation, headache, nausea, vomiting, or injection site reactions (pain, swelling, or irritation).
Dosage: Usual Adult Dose for Candidemia -
Initial dose: 200 mg IV as a single loading dose on Day 1,Maintenance dose: 100 mg IV once a day thereafter
Usual Adult Dose for Esophageal Candidiasis –
Initial dose: 100 mg IV as a single loading dose on Day 1,Maintenance dose: 50 mg IV once a day there after
Duration of therapy: At least 14 days and at least 7 days after resolution of symptoms

EFINACONAZOLE
Antifungal Class: Triazole
Antibacterial spectrum: C. albicans, Cryptococcus neoformans. Aspergillus fumigatus, Trichophyton rubrum and Trichophyton mentagrophytes
Mechanism of Action: Efinaconazole inhibits fungal lanosterol 14α-demethylase involved in the biosynthesis of ergosterol, a constituent of fungal cell membranes.
Adverse Effects: Pain, redness, swelling, burning, stinging, itching, or blisters where the medicine was applied; or ingrown toenail.
Dosage: Topical solution 10%
Onychomycosis -Apply to affected toenail(s) once I Day for 48 weeks using the integrated flow-through brush applicator
Drug Interactions: In vitro studies have shown that JUBLIA, at therapeutic concentrations, neither inhibits nor induces cytochrome P450 (CYP450) enzymes.

TABABOROLE
a.Antifungal Class: Benzoxaborol
b.Antifungal Spectrum: Trichophyton rubrum or Trichophyton mentagrophytes
c.Mechanism of Action: Tavaborole exerts its antifungal activity by blocking cellular protein synthesis through the formation of an adduct with cytoplasmic leucyl-aminoacyl transfer RNA (tRNA) synthetase.
d.Adverse Effects: skin peeling or redness where the medicine was applied; itchinng or ingrown toenail.
e. Dosage:
LSolution - 43.5 (5%), Onychomycosis of the Toenail - Apply to affected toenails qDay for 48 weeks
f.Drug Interactions: In vitro studies have shown that tavaborole, at therapeutic concentrations, neither inhibits nor induces cytochrome P450 (CYP450) enzymes.
16. LULICONAZOLE
a. Antifungal Class: Azole (specifically imidazole)
b.Antifungal Spectrum: Trichophyton rubrum and Epidermophyton floccosum
c. echanism of Action: Luliconazole appears to inhibit

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

ergosterol synthesis by inhibiting the enzyme lanosterol demethylase. Inhibition of this enzyme‘s activity by azoles results in decreased amounts of ergosterol, a
constituent of fungal cell membranes, and a corresponding accumulation of lanosterol.
d.Adverse Effects:Skin irritation
e. Dosage: For topical use only.
Cream, 1% is not for ophthalmic, oral, or intravaginal use. When treating interdigital tinea pedis, a thin layer of LUZU Cream, 1% should be applied to the affected area and approximately 1 inch of the immediate surrounding area(s) once daily for two (2) weeks.
When treating tinea cruris or tinea corpori LUZU Cream, 1% should be applied to the affected area and approximately 1 inch of the immediate surrounding
area(s) once daily for one (1) week
f. Drug Interactions: The serum concentration of Albendazole, Benzocaine, Acenocoumorol, Amitriptyline, Benzocaine, Cenobamate can be increased when it is combined with Luliconazole

OTHER TOPICAL ANTIFUNGALS
All these drugs are used for dermatophytosis.
Tolnaftate: It is an effective drug for tinea cruris and tinea corporis, and most cases respond in 1-3 weeks. Because of poor penetrability,it is less effective in tinea pedis and other hyperkeratinized lesions. For the same reason, it is ineffective in tinea capitis (involving scalp) and tinea unguium (involving nails). Symptomatic relief occurs early, but if applications are discontinued before the fungus bearing tissue is shed-relapses are common. Tolnaftate causes little irritation, but is inferior in efficacy to imidazoles. It is not effective in candidiasis or other types of superficial mycosis.
Ciclopirox olamine: It is a newer drug effective in tinea infections, pityriasis versicolor and dermal candidiasis. High cure rates are reported. It penetrates superficial layers and reaches hair roots but systemic absorption is negligible. Local tolerance without irritation is good. Sensitization occurs occasionally. Formu lated as nail lacquer (painted like nail polish), it has been used in onychomycosis, but cure rate is low. Vaginal candidiasis can be treated by 1% ciclopirox vaginal cream.
Butenafine: It is a benzylamine congener of terbinafine with the same mechanis of action. However, it is used only topically in dermatophytosis. Efficacy in tinea cruris/ f corporis/pedis is similar to that of topical terbinafine.

ANTIFUNGAL DRUG RESISTANCE (61-64)
Some species of fungi are naturally resistant to treatment with certain types of antifungal drugs. For example, the drug fluconazole does not work against infections caused by the fungus Aspergillus, a type of mold. Resistance can also develop over time when fungi are exposed to antifungal drugs. This resistance can occur when antifungal drugs are used improperly to treat sick people (e.g., when dosages are too low, or when treatment courses are not long enough), or even when antifungal drugs are used pproperly. Use of fungicides in agriculture to prevent and treat fungal diseases in crops can also contribute to resistance in people exposed to those fungicides.
Some studies have indicated that antibiotics —which include antifungal drugs—may also contribute to antifungal resistance in Candida. This resistance could occur in a variety of ways. For example, antibiotics can reduce good and bad germs in the gut, which creates favorable conditions for Candida growth. It is not known if decreasing the use of all or certain antibiotics can reduce Candida infections, but appropriate use of antibiotics and antifungal drugs is one of the most important factors in fighting drug resistance. Certain strains of fungi have become more resistant to antifungal medicines. They‘re known as superbugs. These fungi continue to multiply and cause infections even when you take medication.
There are only three classes of antifungal medicines: azoles, echinocandin and polyenes. A fungus that develops resistance to one drug may not respond to any available treatments.
Fungal infections with superbug status include:
Aspergillus fumigatus: This mold causes a lung infection called aspergillosis. Approximately 200,000 people worldwide develop aspergillosis every year. They typically get it from breathing in the mold spores. The infection is becoming more resistant to azole antifungals.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Candida: This yeast naturally occurs on the skin and inside the body. Candida can enter the bloodstream, causing a potentially life-threatening infection called candidemia. This infection no longer responds well to azole medicines.
Candida glabrata: C. glabrata affects the urinary system.

MUCORMYCOSIS (65-84)

Mucormycosis (previously called zygomycosis) is a rare but serious angio-invasive infection caused by a group of fungi called mucormycetes.
Many different species of fungi can cause mucormycosis. They belong to a large group of molds called Mucorales. These molds include Rhizopus, Rhizomucor, and Mucor.
Spores of these ubiquitous fungi (commonly found in soil, fallen leaves, compost, animal dung and air) can be inhaled and then infect the lungs, sinuses, and extend into the brain and eyes. Less often, infection may develop when the spores enter the body through a cut or an open wound.
Mucormycosis is not a contagious disease, it cannot be spread from one person to another.
Mucormycosis mainly affects people who are immunocompromised, or patients already infected with other diseases. High risk groups include people with diabetes (especially diabetic ketoacidosis), solid organ transplantation, neutropenia (low neutrophils, a type of white blood cells), long-term systemic corticosteroid use, and iron overload (hemochromatosis). The risk is high for people living with HIV, and those using immunomodulating drugs, including the anti-fungal voriconazole in some high-risk groups.
Clinical presentation is classified according to the organ involvement. It can be rhino- orbital cerebral, pulmonary, cutaneous, gastrointestinal, or disseminated.
Mucormycosis is an aggressive, life-threatening infection requiring prompt diagnosis and early treatment. Treatment usually consists of antifungal medications and surgery.

History

In 1855, Kurchenmeister described case of mucormycosis in a patient with neoplastic lung on the basis of its histopathology. Furbringer in 1876, described pulmonary mucormycosis for the first time, which was caused by Absidia (now, Lichtheimia).
Platauf coined term 'Mycosis Mucorina' and described a well-documented case of systemic infection in 1885, which was popularly called as mucormycosis during those days. In 1943, Gregory and colleagues, in a series of three fatal cases associated with diabetic ketoacidosis,
reported more typical findings of advanced rhinocerebral mucormycosis. Many newer species of mucorales have been reported in recent times.

Clinical Presentation

Mucormycosis is a very rapidly progressive disease thereby may prove fatal if timely diagnosis is not made entailing delay in institution of specific treatment. These clinical types are given below:

Rhinocerebral (sinus and brain) mucormycosis -
Rhino ocular cerebral Mucormycosis (ROCM) is the most common form, and it is often seen in patients with diabetic ketoacidosis or with uncontrolled diabetes mellitus. A study from India reported that 88% of the patients with ROCM had diabetes mellitus. A similar finding was reported from the United States, where 83% of the patient had diabetes mellitus. Most commonly, it spreads from nasal mucosa to turbinate bones, paranasal sinuses, orbit and palate with

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

eventual extension into brain where massive invasion of blood vessels causes major infarct (Fig.No.10). Several species of mucormycetes have been reported as etiological agents but majority of cases are caused by Rhizopus arrhizus.

The presenting symptoms (Table No.02)include facial pain, headache, lethargy and in advanced cases, loss of vision. The physical examination reveals brownish, bloodstained nasal discharge on the affected side, black eschar on palate due to haemorrhage and tissue necrosis, fixed and dilated pupil and global proptosis and ptosis with dysfunction of cranial nerves, especially fifth and seventh nerves.

There is an extensive and rapid destruction of surrounding tissues. Sometimes, spread may also occur to lungs, gastrointestinal tract, skin and occasionally to other organs. The rhinocerebral mucormycosis is usually fatal as patient dies within a week's time and invariably diagnosed on autopsy if clinician could not reach tentative diagnosis during life. The signs and symptoms of orbital mucormycosis include chemosis, periorbital cellulitis, ophthalmoplegia,proptosis, ptosis, abrupt visual loss, orbital pain and facial Hypoesthesia.

Clinical Progression

Stage 1: Infection of nasal mucosa and sinuses

Stage 2: Orbital Involvement - Superior orbital fissure syndrome; and Orbital Apex Syndrome

Stage 3: Cerebral Involvement - spread through Opthalmic artery; Superior Orbital Fissure

Cribriform plate.

Pulmonary Mucormycosis -

The mucormycetes may present as pulmonary disease through inhalation of sporangiospores. The patients are severely immunocompromised by virtue of an absolute lack of circulating neutrophils, secondary to hematologic malignancy like leukemia, lymphoma, profound immunosuppression or bone marrow transplantation. The lesions may be focal or diffuse and usually uncommon in patients having underlying diabetes mellitus in comparison to rhinocerebral type. The clinical manifestations are nonspecific and may include chest pain, dyspnea and hemoptysis. This entity is suspected when patients have a reverse halo sign on CT of the chest, along with the right clinical findings. Hypersensitivity pneumonitis due to Rhizopus has been reported in Scandinavian Sawmill workers (so-called Wood trimmer's disease) and in farm workers.

Cutaneous Mucormycosis –

The clinical manifestations of cutaneous mucormycosis are varied and range from pustules or vesicles to wounds with wider areas of necrotic zones. In their early stages, lesions resemble ecthyma gangrenosum; cotton-like growth may be seen over surface of tissues, a clinical sign known as 'hairy pus'. The cutaneous type of mucormycosis can be either primary infection or secondary to the disseminated form.

Gastrointestinal Mucormycosis –

The gastrointestinal mucormycosis occurs rarely accounting for ~7% of all cases of mucormycosis, most often involving stomach. It is primarily found among patients suffering from extreme malnutrition and is believed to be acquired by ingesting food contaminated with fungal spores. The agents of gastrointestinal mucormycosis are Lichtheimia corymbifera of Mucorales and Basidiobolus ranarum of Entomophthorales.

Isolated Renal Mucormycosis –

The isolated renal mucormycosis is one of the emerging clinical entity, which is an unusual cause of renal infarction and may be fatal if not timely detected. Any of the species of Mucorales may infect the kidneys. The patients usually present with flank pain, fever, and pyuria.

Disseminated Mucormycosis –

The mucormycetes may become widely disseminated affecting lungs, kidney, gastrointestinal tract, heart and brain however lungs being the most commonly involved site. The clinical syndromes most frequently reported include pneumonia, stroke, subarachnoid hemorrhage, brain abscess, cellulitis or gangrene of a skin structure.

Complications - Cavernous sinus thrombosis, Multiple cranial nerve palsies, visual loss, Frontal lobe abscess, carotid artery or jugular vein thrombosis.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

Types of fungi that most commonly cause mucormycosis

Examples are : Rhizopus species, Mucor species, Rhizomucor species, Syncephalastrum species, bertholletiae, Apophysomyces species, and Lichtheimia (formerly Absidia) species.8

Symptoms

The symptoms of mucormycosis depend on where in the body the fungus is growing.

The most common presentation is a sinus infection (sinusitis) that is accompanied by nasal congestion, nasal discharge, and sinus pain.

A fever and headache may also occur

II. CONCLUSION

With the evolving changes in antifungal therapy, treatment of fungal infections has become more manageable. Although resistance is on the rise, special precautions to reduce the overuse of antifungals, broad-spectrum antibiotics, and other predisposing factors should be followed in order to slow the progression of resistance and enhance patient outcomes. Recognizing those patients at increased risk for developing fungal infections, especially invasive fungal infections, will aid in improving morbidity and mortality associated with these infectious diseases. With a number of antifungal agents available, it is important for pharmacists to be aware of each drug' s characteristics so that they are better equipped to make sound therapeutic decisions in the treatment of various fungal infections.

The epidemiology of mucormycosis is evolving. In light of COVID-19 disease, diabetes mellitus still remains the main underlying risk factor for developing this disease. In developed countries most common underlying diseases are haematological malignancies. An unholy trinity of diabetes, rampant use of corticosteroid in a background of COVID-19 appears to increase mucormycosis. All efforts should be made to maintain optimal glucose and only judicious use of corticosteroids in patients with COVID-19

REFERENCES

[1]. Author: Hon A/Prof Amanda Oakley, Dermatologist, Hamilton, New Zealand, 2003. https://dermnetnz.org/topics/introduction-to-fungal-infections
[2]. https://g.co/kgs/fKkweF ; symptoms and treatment
[3]. https://en.m.wikipedia.org/wiki/Fungal_infection
[4]. https://www.pfizer.com/news/hot- topics/the_truth_about_covid_19_and_black_fungus
[5]. Editor in Chief Dr. Siddhartha N. Shah, API textbook of Medicine, 8th Edition Volume 2, Page no. 1368
[6]. Editor in Chief Dr. Siddhartha N. Shah, API textbook of Medicine, 8th Edition Volume 2, Page no. 1368
[7]. Editor in Chief Dr. Siddhartha N. Shah, API textbook of Medicine, 8th Edition Volume 2, Page no. 1368-1372
[8]. https://dermnetnz.org/imagedetail/6850?copyright=&label=+&caption=+
[9]. https://discover.hubpages.com/health/Tinea-Corporis
[10]. https://www.pcds.org.uk/imager/gallery/clinical/tinea-capitis-scalp/13145/Fig_25_kerion_DW_fee391183f15cb4d62773032fe0be92d.jpg
[11]. https://www.ncbi.nlm.nih.gov/books/NBK470421/figure/article-30210.image.f1/
[12]. Editor in Chief Dr. Siddhartha N. Shah, API textbook of Medicine, 8th Edition Volume 2, Page no. 1369
[13]. https://en.m.wikipedia.org/wiki/File:Intertrigo_interdigital_%C3%A0_CA.jpg
[14]. .https://images.app.goo.gl/iNDfKv4gBEN4koHu5
[15]. https://www.altmeyers.org/en/dermatology/candida-paronychia-120619.amp
[16]. Editor in Chief Dr. Siddhartha N. Shah, API textbook of Medicine, 8th Edition Volume 2, Page no. 1372
[17]. https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.112.000846
[18]. https://medlineplus.gov/lab-tests/fungal-culture-test/
[19]. https://medlineplus.gov/lab-tests/rash-evaluation/
[20]. https://medlineplus.gov/lab-tests/sputum-culture/
[21]. KD Tripati MD, Ex-Director-Professor and Head of Pharmacology Maulana Azad Medical College and associated LN and GB Pant Hospitals, Essential of Medical Pharmacology, Eight Edition 2019, page no. 838

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

[22]. New Delhi, Indiahttp://www.antimicrobe.org/drugpopup/amphotericin%20B.htm
[23]. https://www.slideshare.net/nasertadvi/antifungal-drugs-14709424
[24]. http://www.antimicrobe.org/drugpopup/nystatin.htm
[25]. https://go.drugbank.com/drugs/DB00646
[26]. http://www.antimicrobe.org/drugpopup/caspofungin.htm
[27]. Medically reviewed by Drugs.com. Last updated on Aug 5, 2021,Caspofungin Pregnancy and Breastfeeding Warnings
[28]. https://www.slideshare.net/nasertadvi/antifungal-drugs-14709424
[29]. http://www.antimicrobe.org/drugpopup/Flucytosine.htm
[30]. Medically reviewed by Drugs.com. Last updated on Mar 1, 2021. Pregnancy W
[31]. http://www.antimicrobe.org/drugpopup/clotrimazole.htm
[32]. KD Tripati MD, Ex-Director-Professor and Head of Pharmacology Maulana Azad Medical College and associated LN and GB Pant Hospitals, Essential of Medical Pharmacology, Eight Edition 2019, page no.844
[33]. One Daily Application of Oxiconazole Cream Is Sufficient for Treating Dermatomycoses, A-A. Ramelet, E. Walker-Nasir, Lausanne and Laboratoires Sauter SA, Vernier-Genève, Switzerland
[34]. https://pubchem.ncbi.nlm.nih.gov/compound/Oxiconazole
[35]. https://reference.medscape.com/drug/oxistat-oxiconazole-topical-343492#6
[36]. https://go.drugbank.com/drugs/DB00239
[37]. http://www.antimicrobe.org/drugpopup/ketoconazole.htm
[38]. http://www.antimicrobe.org/drugpopup/fluconazole.htm
[39]. http://www.antimicrobe.org/drugpopup/itraconazole.htm
[40]. http://www.antimicrobe.org/drugpopup/voriconazole.htm
[41]. https://www.aocd.org/page/Terbinafine
[42]. https://www.rxlist.com/consumer_terbinafine_lamisil/drugs-condition.htm#what_are_dosages_of_terbinafine
[43]. https://www.scynexis.com/pipeline
[44]. Medically reviewed by Drugs.com on Aug 3, 2021. Written by Cerner Multum. https://www.drugs.com/mtm/ibrexafungerp.html
[45]. https://reference.medscape.com/drug/brexafemme-ibrexafungerp-4000174
[46]. Last reviewed on RxList: 6/10/2021
[47]. This monograph has been modified to include the generic and brand name in many instances.
[48]. https://www.rxlist.com/brexafemme-drug.htm
[49]. Astellas Receives FDA Approval for CRESEMBA® (isavuconazonium sulfate) for the Treatment of Invasive Aspergillosis and Invasive
[50]. https://newsroom.astellas.us/2015-03-06-Astellas-Receives-FDA-Approval-for-CRESEMBA-isavuconazonium-sulfate-for-the-Treatment-of-Invasive-
[51]. Aspergillosis-and-Invasive-Mucormycosis (press release)
[52]. PDF ON Isavuconazonium sulfate (Cresemba) Spectrum of Activity
[53]. Last reviewed on RxList: 9/30/2020
[54]. This monograph has been modified to include the generic and brand name in many instances. https://www.rxlist.com/eraxis-drug.htm#dosage
[55]. Jose A. Vazquez, Jack D. Sobel Anidulafungin: A Novel Echinocandin ,Clinical Infectious Diseases, Volume 43, Issue 2, 15 July 2006, Pages 215– 222,https://doi.org/10.1086/505204. Published: 15 July 2006 https://academic.oup.com/cid/article/43/2/215/334446
[56]. Medically reviewed by Drugs.com. Last updated on Nov 10, 2020. https://www.drugs.com/dosage/anidulafungin.html
[57]. https://go.drugbank.com/drugs/DB00362
[58]. Authors: Shari Lipner, Richard Scher Efinaconazole in the treatment of onychomycosis, June 2015, Infection and Drug Resistance 8:163, DOI:10.2147/IDR.S69596 Last reviewed on RxList: 5/12/2020

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

[59]. This monograph has been modified to include the generic and brand name in many instanceshttps://www.rxlist.com/jublia-drug.htm
[60]. 204427s000lbl.pdf - Accessdata.fda.gov
[61]. https://go.drugbank.com/drugs/DB09041
[62]. https://reference.medscape.com/drug/kerydin-tavaborole-999935
[63]. https://go.drugbank.com/drugs/DB08933
[64]. 204153s000lbl.pdf -Accessdata.fda.gov
[65]. KD Tripati MD, Ex-Director-Professor and Head of Pharmacology Maulana Azad Medical College and associated LN and GB Pant Hospitals, Essential of Medical Pharmacology, Eight Edition 2019, page no.847
[66]. Lortholary O, Desnos-Ollivier M, Sitbon K, Fontanet A, Bretagne S, Dromer F, et al. Recent exposure to-caspofungin or fluconazole influences the epidemiology of candidemia: a prospective multicenter study involving 2,441 patientsexternal icon. Antimicrob Agents Chemother 2011;55:532– 8. https://www.cdc.gov/fungal/antifungal-resistance.html
[67]. Shah DN, Yau R, Lasco TM, Weston J, Salazar M, Palmer HR, et al. Impact of prior inappropriate fluconazole dosing on isolation of fluconazole-nonsusceptible Candida species in hospitalized patients with candidemiaexternal icon. Antimicrob Agents Chemother 2012;56:3239–43.https://www.cdc.gov/fungal/antifungal-resistance.html
[68]. Ben-Ami R, Olshtain-Pops K, Krieger M, Oren I, Bishara J, Dan, M, et al. Antibiotic exposure as a risk factor for fluconazole-resistant Candida bloodstream infectionexternal icon. Antimicrob Agents Chemother 2012;56:2518–23.https://www.cdc.gov/fungal/antifungal-resistance.html
[69]. https://my.clevelandclinic.org/health/articles/21557-antifungal-resistance
[70]. Oliver A Cornely, Ana Alastruey-Izquierdo 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: e405–
[71]. Accessed online from https://www.thelancet.com/action/showPdf?pii=S1473- 3099%2819%2930312-3 on 26 May
[72]. 2021.https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis
[73]. Evidence based advisory in the times of COVID-19. https://www.icmr.gov.in/pdf/covid/techdoc/ Mucormycosis_ADVISORY_FROM_ ICMR_In_COVID19_time.pdf accessed 26 May 2021.https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis
[74]. Pongas et al. Voriconazole-associated zygomycosis: a significant consequence of evolving antifungal prophylaxis and immunosuppression practices?. Clin Microbiol Infect 2009; 15 (Suppl. 5): 93–97.https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis
[75]. Russell E. Lewis, Guangling Liao, Weiqun Wang, Randall A. Prince & Dimitrios
[76]. P. Kontoyiannis (2011) Voriconazole pre-exposure selects for breakthrough mucormycosis in a mixed model of Aspergillus fumigatus-Rhizopus oryzae pulmonary infection, Virulence, 2:4, 348-355, DOI: 10.4161 /viru.2.4.17074.https://www.who.int/india/emergencies/coronavirus- disease-(covid-19)/mucormycosis
[77]. Trifilio, S., Bennett, C., Yarnold, P. et al. Breakthrough zygomycosis after voriconazole administration among patients with hematologic malignancies who receive hematopoietic stem-cell transplants or intensive chemotherapy. Bone Marrow Transplant 39, 425–429 (2007).https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis
[78]. Mucormycosis in COVID 19. AIIMS Guidance https://covid.aiims.edu/mucormycosis-in-covid-19 accessed 26 May 2021.https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis
[79]. Aastha Maini, Gaurav Tomar, Deepak Khanna, Yogesh Kini, Hardik Mehta, V. Bhagyasree. Sino-orbital mucormycosis in a COVID-19 patient: A case report, International Journal of Surgery Case Reports, Volume 82, 2021. https://www.sciencedirect.com/science/article/pii/S2210261221004594#!.https://www.who.int/india/emergencies/coronavirus-disease-(covid-19)/mucormycosis
[80]. Singh AK, Singh R, Joshi SR, Misra A, Mucormycosis in COVID-19: Asystematic review of cases reported worldwide and in India, Diabetes & Metabolic Syndrome: Clinical Research & Reviews (2021), doi:

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, December 2024

https://doi.org/10.1016/j.dsx.2021.05.019.https://www.who.int/india/emergencies/ coronavirus-disease-(covid-19)/mucormycosis

[81]. Chakrabarti, A.; Dhaliwal, M. Epidemiology of mucormycosis in India. Curr. Fungal Infect. Rep. 2013, 7, 287–

[82]. 292.https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis

[83]. H. Prakash, A. Chakrabarti; Global epidemiology of mucormycosis; J Fungi, 5 (2019).https://www.who.int/india/emergencies/coronavirus-disease-(covid- 19)/mucormycosis

[84]. Revannavar SM, P S S, Samaga L, et al .COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? BMJ Case Reports CP 2021;14:e241663.https://www.who.int/india/emergencies/coronavirus-disease- (covid-19)/mucormycosis

[85]. Sarkar, Sandip; Gokhale, Tanmay; Choudhury, Sushmita Sana1; Deb, Amit Kumar COVID-19 and orbital mucormycosis, Indian Journal of Ophthalmology: April 2021 - Volume 69 - Issue 4 - p 1002-1004 doi: 10.4103/ijo.IJO_3763_20.https://www.who.int/india/emergencies/coronavirus- disease-(covid-19)/mucormycosis

[86]. https://www.cdc.gov/fungal/diseases/mucormycosis/.https://www.who.int/india/e mergencies/coronavirus-disease-(covid-19)/mucormycosis

[87]. Guideline for management of Mucormycosis in Covid – 19 patients. DGHS. Accessed on 26 May 2021 from https://dghs.gov.in/WriteReadData/News/202105171119301555988Mucormycosis managementinCovid-19.pdf.https://www.who.int/india/emergencies/coronavirus- disease-(covid-19)/mucormycosis)

[88]. Mucormycosis in COVID-19: A Clinico-Microbiological Dilemma, Ragya Bharadwaj, S. Thilagavathy L, Infection Control Officer, Kauvery Hospital, Trichy, Tamilnadu, India, Consultant Microbiologist and Head of Diagnostic Laboratory, Neuberg Ehrlich Laboratory & Kauvery Hospital, Trichy, Tamilnadu, India, Correspondence: Tel.: +91 97624 75919;

[89]. email: dr.ragya@kauveryhospital.com https://www.kauveryhospital.com/kauverian-scientific-journal/mucormycosis-in- covid-19-a-clinico-microbiological-dilemma

[90]. https://www.cdc.gov/fungal/diseases/mucormycosis/definition.html

[91]. Mucormycosis(Zygomycosis), By Sanjay G. Revankar, MD, Wayne State University School of Medicine, Last full review/revision Apr 2021 https://www.msdmanuals.com/en-in/home/infections/fungal-infections/mucormycosis

[92]. https://days.gov.in Guideline for management of Mucormycosis in Covid - 19 patients

[93]. https://www.cdc.gov/fungal/diseases/mucormycosis/treatment.html

[94]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6162664/