



## ABSTRACT

Mucormycosis diseases – Revised Treatment protocol for patients with Mucormycosis infection - Approved - Orders – Issued.

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### HEALTH AND FAMILY WELFARE (P1) DEPARTMENT

G.O.(Ms).No.298

Dated: 22.06.2021

Pilava, Aani – 08

Thiruvalluvar Aandu – 2052

Read :

1. G.O.(Ms).No.249, Health and Family Welfare (P1) Department, dated 20.05.2021.
2. G.O.(Ms).No.262, Health and Family Welfare (P1) Department, dated 02.06.2021.
3. From the Director of Medical Education, letter Ref.No.38348/H&D/2/3/2021, dated 15.06.2021.

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### ORDER:

In Government order first read above, the MUCORMYCOSIS has been declared as a notified disease in the State of Tamil Nadu.

2. In Government order second read above, the Government have approved for Treatment protocol for patients with Mucormycosis infection.

3. In the letter third read above, the Director of Medical Education has stated that the Expert Committee have recommended the revised draft treatment protocol according to the latest Guidelines and requested the Government to issue a Order on the same.

4. The Government have examined the request of the Director of Medical Education and approve revised treatment protocol according to the latest Guidelines for Mucormycosis.

5. The revised Treatment protocol for Mucormycosis disease patients with the latest Guidelines is annexed with this order in supersession of the treatment protocol issued in the Government Order second read above.

(BY ORDER OF THE GOVERNOR)

J.RADHAKRISHNAN  
PRINCIPAL SECRETARY TO GOVERNMENT

To

The Director of Medical Education, Chennai – 600 010.

The Director of Medical and Rural Health Services, Chennai- 600 006.

The Director of Medical and Rural Health Services (ESI), Chennai- 600 006.  
The Director of Public Health and Preventive Medicine, Chennai- 600 006.  
The Mission Director, National Health Mission, Chennai – 600 006.  
The Commissioner, Greater Chennai Corporation, Chennai – 600 003.  
The Project Director, Tamil Nadu Health System Project, Chennai – 600 006.  
All District Collectors.

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✓ The Health and Family Welfare (Data cell) Department, Chennai - 600 009.  
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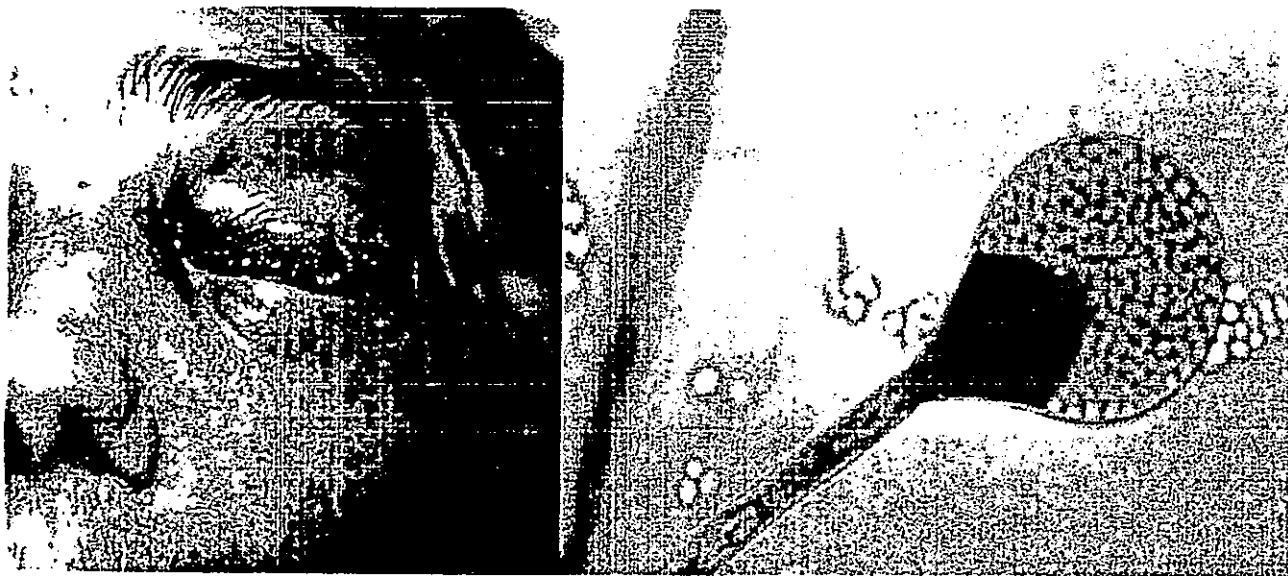
**//FORWARDED BY ORDER//**

*R. S. Srinivasan*  
22/6/21  
**SECTION OFFICER**  
22/6/21

Annexure to the G.O.(Ms) No.298, Health and Family Welfare (P1) Department  
Dated: 22.06.2021.

# MUCORMYCOSIS

22.06.2021



An Epidemic in the



COVID-19 Pandemic

MANAGEMENT GUIDELINES 2.0

HEALTH AND FAMILY WELFARE DEPARTMENT  
DIRECTORATE OF MEDICAL EDUCATION

CHENNAI, INDIA

S.NO	CONTENTS	PAGE NO
1	Introduction	1
2	High Risk group	1
3	Clinical Presentation	1
4	Diagnosis	3
5	Management Algorithm for Mucormycosis	5
6	Administration Guidelines for Amphotericin B	6
7	Salvage Therapy	9
8	Surgical Management	10
9	Follow up	11
10	Preventive Measures	11
11	Reference & Acknowledgement	12
	Annexure I - List of Regional Centers	
	Annexure II - Diabetes Management Protocol	

## INTRODUCTION

Mucormycosis is an acute or sub-acute, infection caused by member of the Phylum Mucoromycota. This is an opportunistic aggressive, devastating fungal infection commonly involving Nasal, Orbital and Cerebral regions. It is acquired primarily via inhalation of spores through nasal route. It is a rapidly progressive fungal disease and any delay in identification and management leads to high morbidity and mortality.

The fungus is angio-invasive, causing occlusion of blood vessels, leading to tissue necrosis. Other forms of clinical presentation are Pulmonary, Cutaneous, Gastrointestinal, bone and joint infection and disseminated Mucormycosis.

## PREDISPOSING FACTORS

- Concurrent / Recently treated COVID -19
- Uncontrolled Diabetes Mellitus
- Use of Steroids
  - High doses of steroids
  - Steroids use for prolonged periods as per indications
- Immunocompromised / Suppressed individuals
  - Organ Transplant recipients
  - Malignancy
  - AIDS
- Prolonged use of broad-spectrum antibiotics
- People under long standing Oxygen therapy
- Prolonged ICU stays
- People under mechanical ventilation
- Nosocomial - Contaminated linen, ICU gadgets - if not properly sterilized.

## CLINICAL PRESENTATION

### I. General Symptoms:

- i. Headache
- ii. Low Grade Fever
- iii. Malaise and Lethargy

### II Nasal Symptoms.

- i. Nasal Obstruction
- ii. Nasal Discharge - bloody, brownish, or blackish.



III. Ocular Manifestations:

- i. Pain and redness around eyes, watering
- ii. Swelling of eyes / Blackish Discoloration
- iii. Double vision / Diminution of vision
- iv. Protrusion of eyeball
- v. Restricted eye movements
- vi. Facial Swelling and pain, abnormal sensation, Numbness in the infra orbital region



IV. Oral Manifestations:

- i. Tooth ache /Loosening of teeth
- ii. Blackish discoloration of oral mucosa
- iii. Loss of sensation/ numbness, ulceration/ perforation over palatal region



V. Pulmonary Manifestations:

- i. Refractory fever on broad-spectrum antibiotics
- ii. Non-productive cough
- iii. Progressive dyspnea
- iv. Chest pain

VI. Cutaneous and soft tissue Manifestations

- i. Redness/ Thickening
- ii. Black eschar at trauma/puncture site
- iii. Muscle pain (with deeper involvement)

VII. Gastrointestinal Manifestations:

- i. Fever
- ii. Bleeding per anus
- iii. Mass like lesions
- iv. Perforation of gut



VIII. Bones and Joints Manifestations:

Local pain, Redness, Swelling

IX. Cerebral involvement:

Altered sensorium

- **START INJ. AMPHOTERICIN – B IMMEDIATELY WITHOUT WAITING FOR INVESTIGATION REPORTS IN CASE OF VERY HIGH CLINICAL SUSPICION.**
- **IF FACILITIES FOR APPROPRIATE SURGICAL MANAGEMENT / MEDICAL MANAGEMENT (ADMINISTRATION AND MONITORING OF AMPHOTERICIN–B) ARE NOT AVAILABLE, IMMEDIATELY REFER THE PATIENT TO DESIGNATED REGIONAL CENTERS. (As per Annexure I)**

## DIAGNOSIS

**Nasal endoscopy:** Ulceration / Blackish necrotic eschar

**Oral Examination:** Black eschar on the Palate

**Ocular Examination :**

- Congestion, Erythema
- Proptosis, Periorbital edema, ecchymosis
- Ophthalmoplegia
- Decreased Corneal Sensation
- Fundus examination: cherry red spot or disc edema or both.

**Microbiology:**

I. KOH smear

Specimen:

- Nasal mucosal scraping in NORMAL SALINE
- Tissue biopsy from suspected mucosa in NORMAL SALINE

II. Fungal culture

**Pathology:**

Specimen:

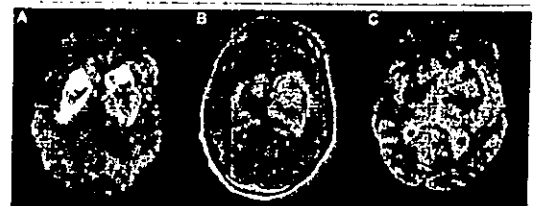
- Debrided tissue IN 10% FORMALIN.

**Radiology:**

- HRCT Scan of Orbit, Paranasal sinuses & Brain, with contrast if renal status permits.
- MRI Paranasal sinuses and orbits (optional)

**Baseline Investigations:**

- CBC
- Fasting and Post Prandial Blood Sugar and Acetone
- HbA1C
- Liver Function Test
- Renal Function Test
- Serum electrolytes



# TREATMENT ALGORITHM

**POSSIBLE OR PROVEN ROCM**



**EMERGENCY  
SURGICAL  
DEBRIDEMENT**

**ADEQUATE GLYCEMIC  
CONTROL**

**+**

**Inj Amphotericin B Deoxycholate  
(0.75-1mg/kg/day)**

**OR**

**Inj Liposomal amphotericin B  
(5-10mg/kg/day)**

**(intra cranial involvement-10 mg/kg/day)**

**FOR 1 WEEK as loading dose**



**FOLLOWED BY**



**Posaconazole 300mg once a day orally**

**FOR 4 TO 6 WEEKS depending on severity**



## ADMINISTRATION OF DRUG:

Inj. Amphotericin B Deoxycholate (C-AmB)

### Testdose

- 1 mg in 100 mL D5 over 20 minutes

### Pre hydration

- 500 mL NS over 30 minutes

### DAY-1

- 0.5mg/kg in 100ml D5 over 1 HOUR

### DAY-2

- 0.75mg/kg in 100ml D5 over 2-3 hours

### Post Hydration

- 500 mL NS over 30 minutes

### Watch for

- Urine output , Renal function Test
- Fill Amphotericin monitoring chart

45 mg/day is given daily until a cumulative dose of 2 g is reached.

If the patient becomes normal before the stipulated dose of 2g the treatment schedule can be tailored as per tissue response.

### CREATININE MONITORING AND DOSAGE

<b>SERUM CREATININE (mg/dl)</b>	<b>DOSE OF DRUG</b>
<1.1	0.75mg/kg/body weight/day (full dose)
<i>Mild renal failure- 1.2-2.5</i>	0.35mg/kg/body weight/day (half dose)
<i>Moderate renal failure-2.5-3.5</i>	0.25mg/kg/body weight/day on alternate days
>5	0.25mg/kg/body/weight/day (Once in 3 days)

Inj.Liposomal amphotericin B (LAmB):

**Test  
dose**

- Inj. Liposomal Amphotericin- B 1 vial (50 mg) to be diluted in 12 ml of the diluent and 0.25ml (1 mg) of solution made, to be mixed in 100ml Dextrose and to be infused in 30 minutes.
- Observe for fever and reactions

**Prehydration**

- 500 mL NS over 30 minutes
- To reduce the risk of renal toxicity and hypokalaemia :- 500ml Normal Saline + 1 Amp (20mmol) KCL

**Therapeutic  
Dose**

- 5-10 mg /kg/day Amphotericin B in 500 mL D5 with 10 Units HIR (Human Insulin Regular) over 3 hrs
- To be covered in black sheet

**Post Hydration**

- 500 mL NS over 30 minutes

**Watch for**

- Urine output , Renal function Test after every dose
- Fill Amphotericin monitoring chart

**STEP DOWN OR SALVAGE THERAPY:**

In patients who cannot tolerate Amphotericin B due to severe renal impairment / allergy / selected cases for cerebral mucormycosis,



300mg IV BD / oral /Day 1 - followed by  
300mg OD for 4 – 6 weeks

**OR**

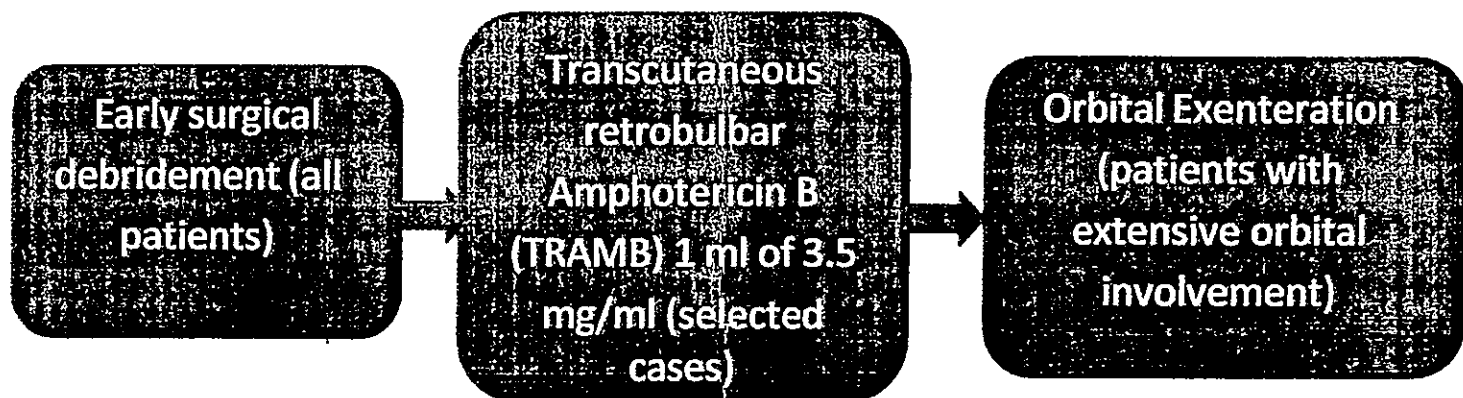


•200mg IV TID /oral X 2 days - followed by  
•200mg IV OD /oral X 4 – 6 weeks

**AMPHOTERICIN B DRUG CHART**

Date	Starting Time	Ending Time	Dose	Cumulative Dose	Route	Duration (days)	No.	KG	SGOT SGPT	Any Concomitans

## SURGICAL MANAGEMENT



**Nasal and sinus involvement**  
is present without bony erosion of maxilla/ zygoma and orbital floor

- Endoscopic sinus debridement

**Maxilla involvement**

- Maxillectomy (partial/ total)

**Maxilla + Minimal zygoma involvement**

Maxillectomy (partial/ total) with zygoma debridement

**Maxilla + Zygoma + orbit**

- Maxillectomy (partial/total), Zygoma debridement
- Debridement of Orbital floor/walls, Localised debridement of necrosed tissue in early localised orbital disease

**Exenteration of eye in case of**

- 1) Vision loss 2) Total ophthalmoplegia 3) Chemosis 4) Necrosis of orbital tissues
- NOTE: Loss of vision is not always the indication of exenteration

**Frontal bone and skull base**

- Anterior table: Debridement
- Posterior table: Cranialization
- Debridement of Osteomyelitic Skull bone and involved cerebral parenchyma (Safe maximum resection)

## FOLLOW UP AFTER SURGERY:

Relook nasal endoscopy of weekly intervals for 6 weeks to assess epithelization of nasal cavity and to remove any residual necrotic bone

Daily nasal douching with diluted Amphotericin B solution (50mg vial in 500ml of normal saline)

## PREVENTIVE MEASURES:

### 1. Personal Hygiene

Good Oral Hygiene

### 2. Medical Management

Judicious use of steroids.

Meticulous diabetes control and monitoring Acidosis

### 3. Hospital / Institutional level

A. Use of clean, sterile distilled water/ Normal saline for humidifiers during oxygen therapy and replaced daily

B. Disinfecting all gadgets in ICU regularly.

C. Not to Reuse disposable oxygen delivery devices like Nasal prongs, Facemasks etc.

### 4. Advice to the Patient and care-giver at the time of discharge:

a. Monitor blood glucose level in diabetics.

b. Use Clean drinking water to wash face.

c. Inform the patients about early symptoms and signs of Mucormycosis.

- Nasal blockage/Blood-tinged nasal discharge.
- Pain in the eye/swelling of the eye /double vision.
- Headache / numbness over the face.
- Tooth ache/loosening of teeth/discomfort during chewing
- Follow up on Day-7 and 3 weeks after discharge.

## REFERENCE

- Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases - 9th Edition. 2020. E-Book
- Management Protocol for Mucormycosis- AIIMS, Rishikesh
- Honavar SG. Code Mucor: Guidelines for the Diagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis in the Setting of COVID-19. Indian J Ophthalmol 2021;69:1361-5.

## ACKNOWLEDGEMENT

All the respected members of State Mucormycosis Task Force Committee, who shared their valuable input in formulating and revising this guideline.

## ANNEXURE I

### LIST OF RESIDENTIAL CENTERS WHERE MULTISPECIALARY TREATMENT IS AVAILABLE

1. RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI
2. COIMBATORE MEDICAL COLLEGE HOSPITAL, COIMBATORE
3. GOVERNMENT RAJAJI HOSPITAL, MADURAI
4. THANJAVUR MEDICAL COLLEGE HOSPITAL, THANJAVUR
5. TIRUNELVELI MEDICAL COLLEGE HOSPITAL, TIRUNELVELI
6. GOVERNMENT MOHAN KUMARA MANGALAM MEDICAL COLLEGE HOSPITAL,  
SALEM



## ANNEXURE II

### COVID-19 DIABETES MANAGEMENT GUIDELINES FOR PREVENTION AND TREATMENT OF MUCORMYCOSIS

1. Regular blood sugar monitoring should be done for all diabetic patients under Home Quarantine, COVID Care Centre, COVID Health Centre, Primary Health Centre and COVID Hospitals, particularly diabetic ketoacidosis.
2. Non-Diabetic patients may show increase in blood sugar after 3<sup>rd</sup> day of steroids. Hence blood sugar should be monitored for them too, including predinner blood sugar levels.
3. OHA's can be continued for patients who do not have hypoxia or organ dysfunction. Insulin should be added if adequate control is not achieved with OHA's.
4. Insulin should be initiated in all patients on steroids with oxygen support.
5. The regimen should include 3 doses of short acting insulin before breakfast, lunch and dinner & morning and night basal insulin.
6. Patients on steroids may require higher dose of Insulin at 1 to 2 units/kg body weight per day.
7. As and when steroid therapy is modified, insulin dose should be modified accordingly.
8. Patient with poor oral intake require RT feeding/ IV dextrose containing fluids if they are on subcutaneous insulin.
9. If fasting blood sugar is >400 mgs/dl (or) RBS > 500 mgs/dl, insulin infusion should be started at a rate of 5 units/hr. [Kindly add 25 units of regular insulin in 500 ml of NS and flow at 100 ml/hr. Hourly CBG monitoring should be done till blood sugar drops to 200 mgs/dl]. Thereafter subcutaneous insulin should be given depending on patient's oral intake. All patients started on insulin infusion should be monitored for serum potassium levels.
10. Patients should be monitored for both hypoglycemia and hypokalemia.

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SECTION OFFICER

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