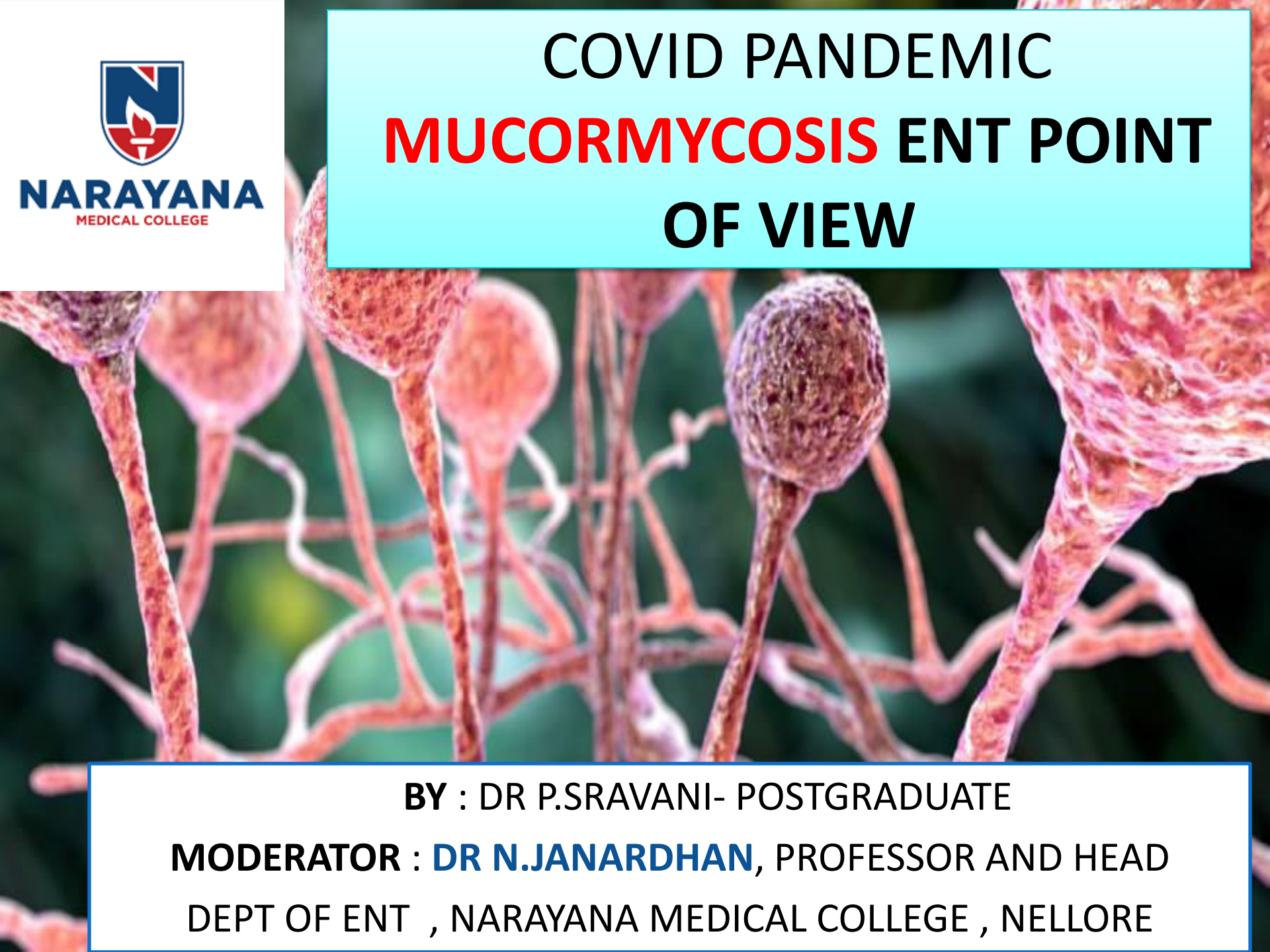
NARAYANA
MEDICAL COLLEGE

COVID PANDEMIC
MUCORMYCOSIS ENT POINT OF VIEW



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INTRODUCTION

- Mucormycosis is a potentially lethal, angioinvasive, opportunistic fungal infection seen in immunocompromised people.
- Recently , there is rapid surge of mucormycosis cases ,as COVID -19 infection leads to a weakened immune system - preventing the body from effectively protecting against infection.

CLASSIFICATION OF FUNGAL SINUSITIS

FUNGAL SINUSITIS

NON INVASIVE

- Allergic Fungal Rhino Sinusitis
- Fungus ball
- Saprophytic disease

INVASIVE

- Acute invasive
- Chronic invasive
- Granulomatous

- Mucormycosis is rare, non-contagious fungal infection caused by filamentous fungi of Mucoraceae family
- It has high morbidity, mortality rate of 50 % in immunocompromised
- Fungal spores are inhaled from air, invade sinus, goes into intraorbital, intracranial in immunocompromised people.
- CLINICAL CLASSIFICATION OF MUCORMYCOSIS IN COVID

1) Concomitant – mucormycosis occurs with active covid-19 infection

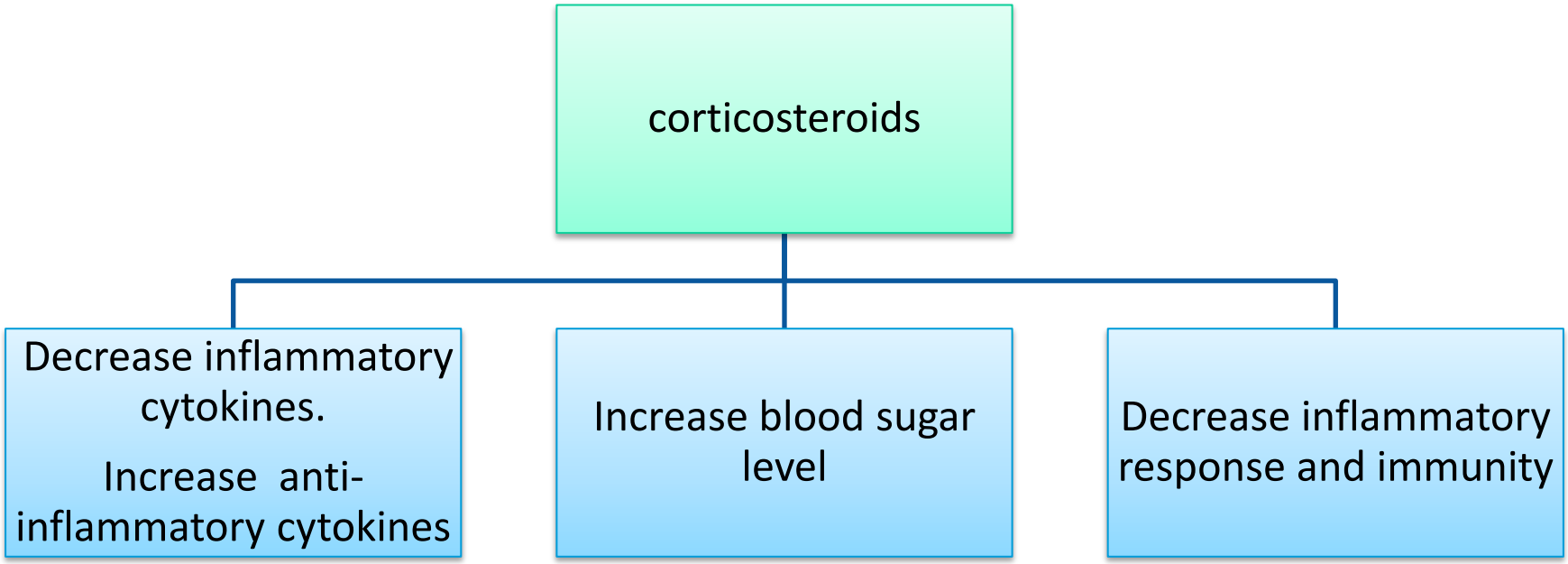
2) Sequential – weeks or months following recovery from covid (10 – 50 days)

PATHOPHYSIOLOGY

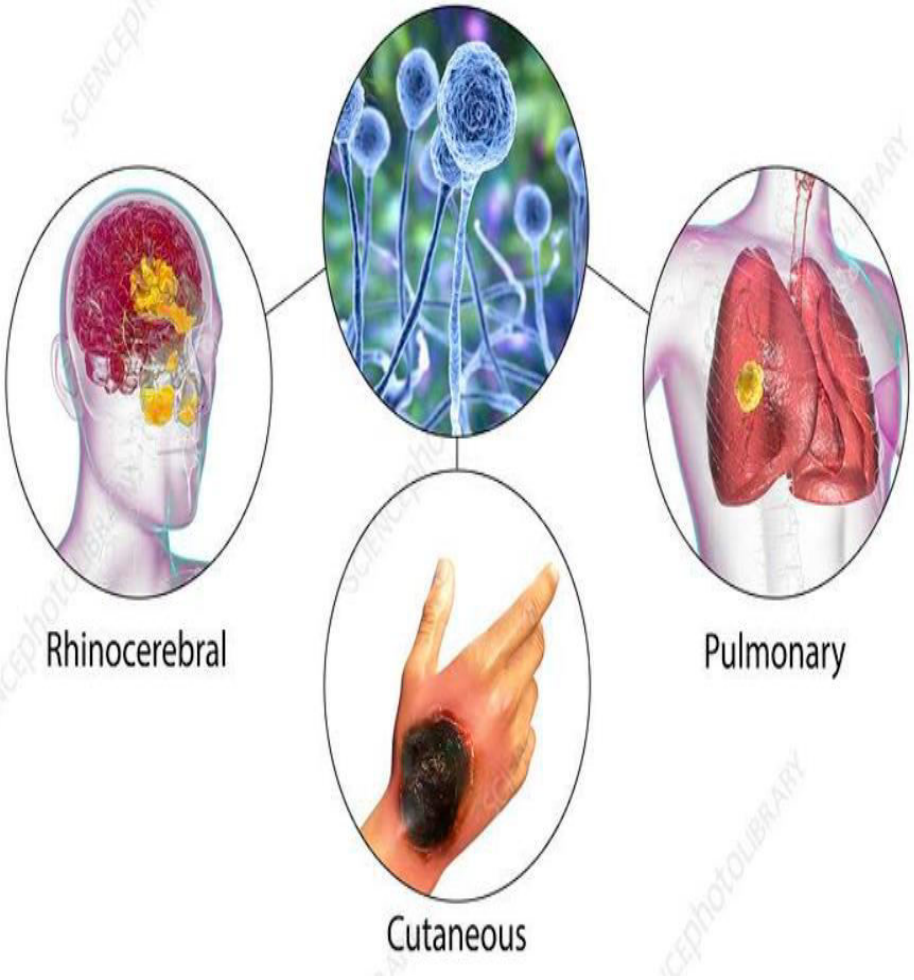
- In Diabetic patients –
- 1) Macrophages and Monocytes fail to suppress germination of spores
- 2) Impairment of Neutrophil function in Diabetic Ketoacidosis

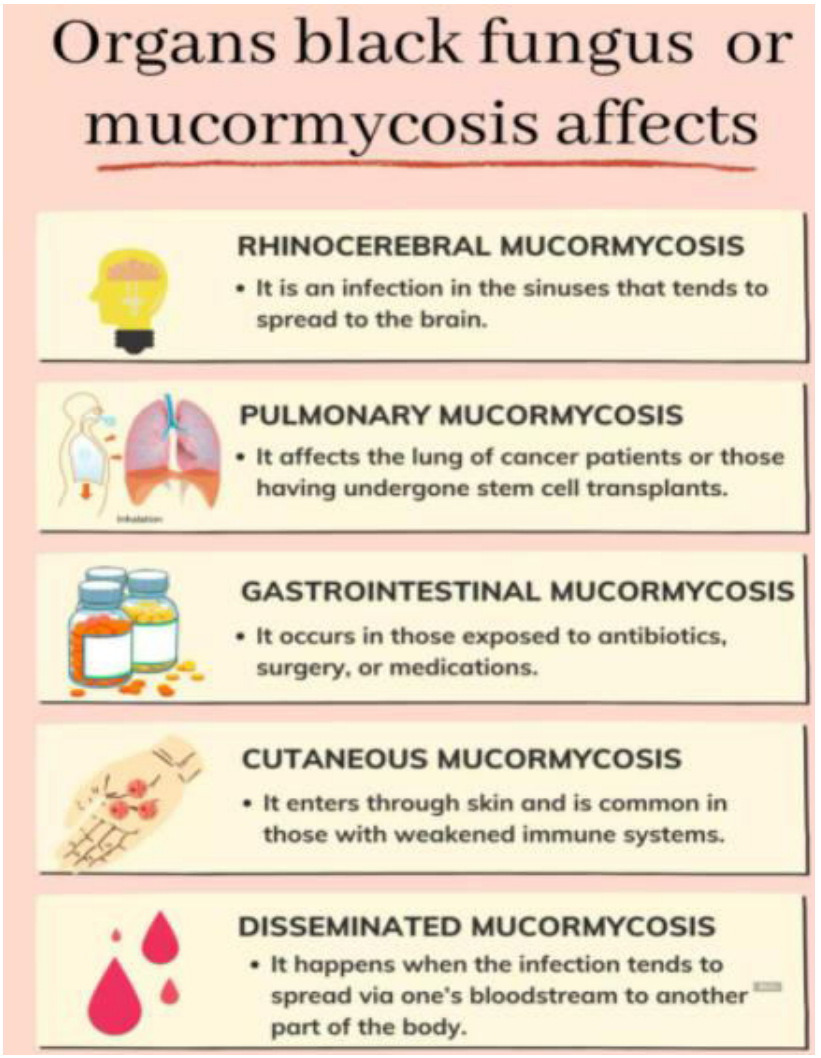
  3)Acidosis and hyperglycaemia provide an excellent environment for the fungus to grow
- At low pH ,the ability of serum apotransferrin to bind iron is reduced
- The fungal hyphae produce a substance called rhizoferrin, which binds iron avidly.
- This iron-rhizoferrin complex is then taken up by the fungus and it becomes available for the vital intracellular processes.

- Systemic corticosteroids which are used in severe and critically ill patients shown to be life saving and improves survival in covid patients
- Unfortunately, irrational use of steroids leads to secondary bacterial and fungal infections


corticosteroids
Decrease inflammatory cytokines.
Increase anti-inflammatory cytokines
Increase blood sugar level
Decrease inflammatory response and immunity

FORMS OF MUCORMYCOSIS





PRE DISPOSING FACTORS

- Uncontrolled D.M
- Immuno suppression by steroids or immunosuppressive drugs
- Prolonged ICU stay
- Comorbidities – post transplant, malignancy, sickle cell anemia
- Prolonged use of broad spectrum antibiotics
- Neutropenia
- Lymphopenia
- High levels of IL-6 and serum ferritin

- Hematological malignancies
- Solid organ transplant
- Prolonged corticosteroid use
- Graft vs host disease
- Prolonged voricanozole prophylaxis

WHEN TO SUSPECT ROCM

Sinusitis	Fever,nasal stuffiness,facial pain,numbness,retro-orbital headache,hyposmia,blood tinged /brownish black nasal discharge
Maxillary	Toothache,loosening of maxillary teeth,jaw involvement
Eye	Redness and swelling of eye,diplopia,visual loss
cerebral	*Altered sensorium or consciousness

CLINICAL EXAMINATION

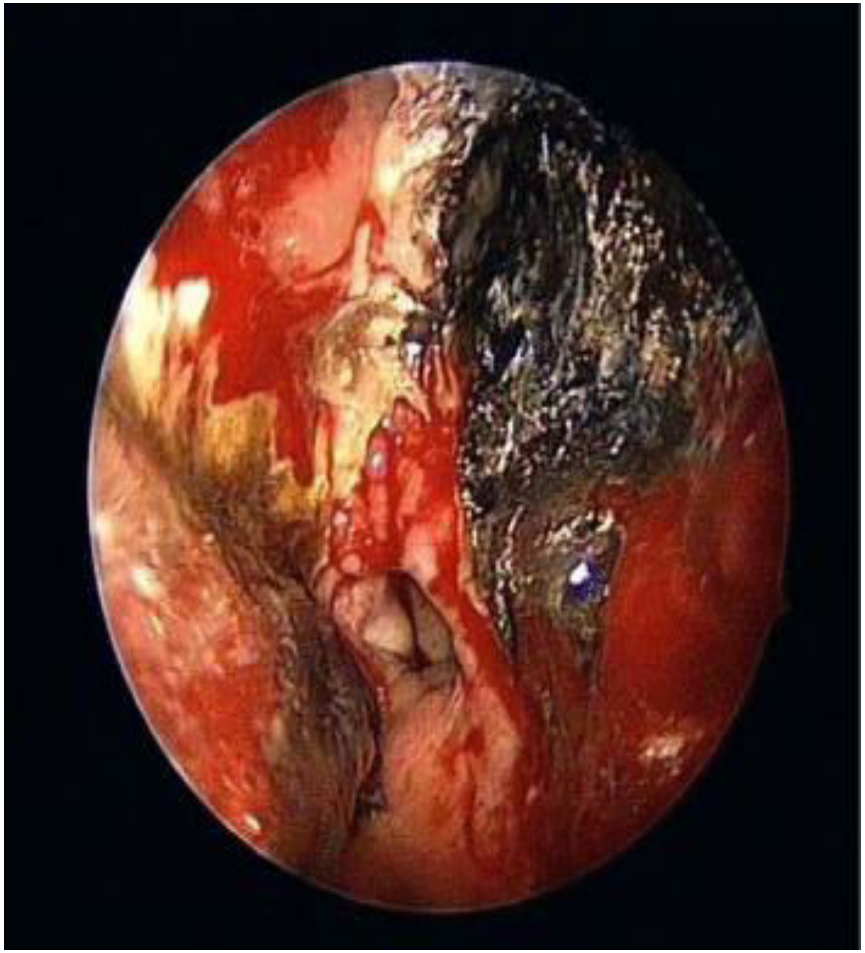
Complete ENT examination

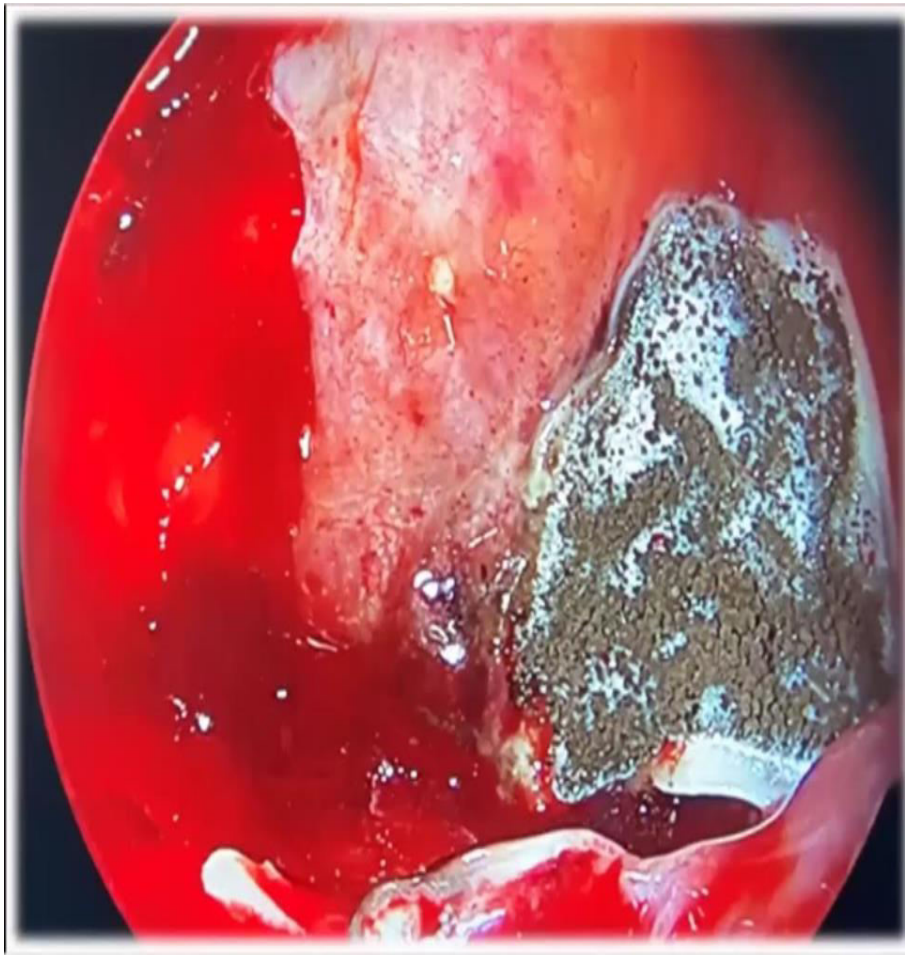
* Maxilla (cheeks – swelling,tenderness)
* Palate – ulceration,necrosis
* Teeth – caries / loose
* Eye – proptosis,vision,movement,corneal reflex
* Crusting of nose
* Paraesthesia around nose
* Loss of senation

Diagnostic nasal endoscopy :

* Look for discoloration,secretions

DIAGNOSIS : - DIAGNOSTIC NASAL ENDOSCOPY IMAGES





Diagnostic evaluation

Saline

Direct microscopy(KOH/ Calcoflour/PAS stain)

Aseptate/pauci-septate,irregular hyphae with obtuse angled branching.
Ribbon like hyphae with sporangium at terminal ends.
vessel occlusion

Formalin

Biopsy(HPE,PAS ,GMS)

To differentiate mucor from other moulds
To look for angiovasion

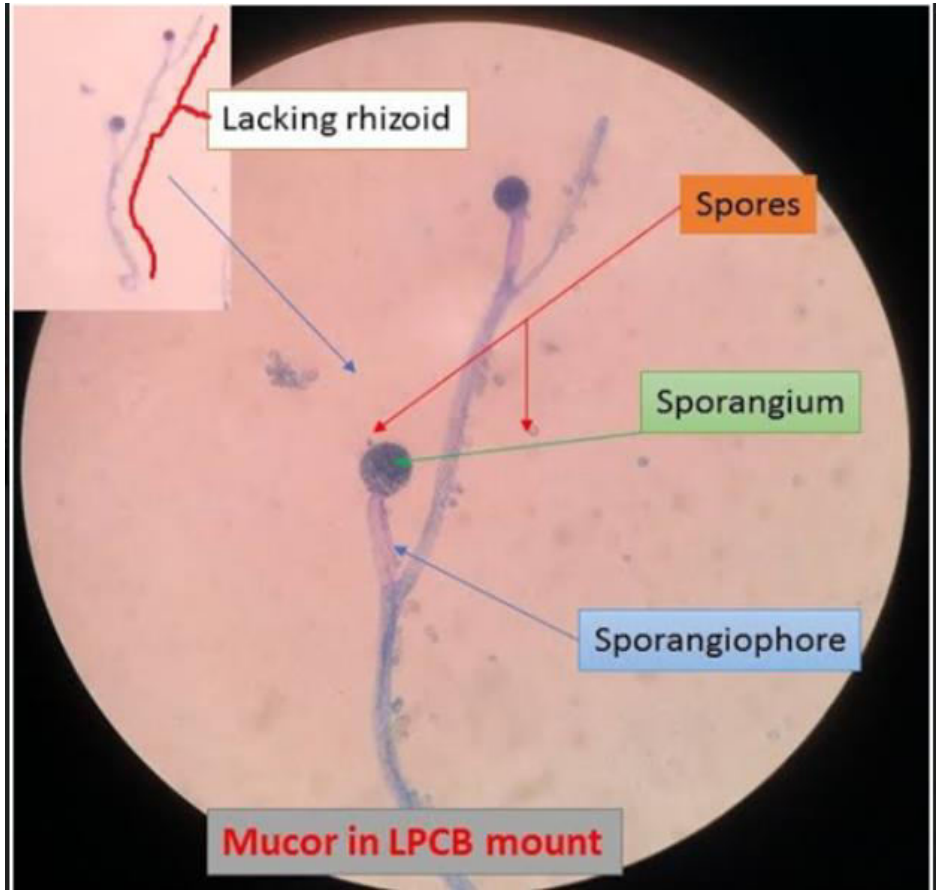
Saline

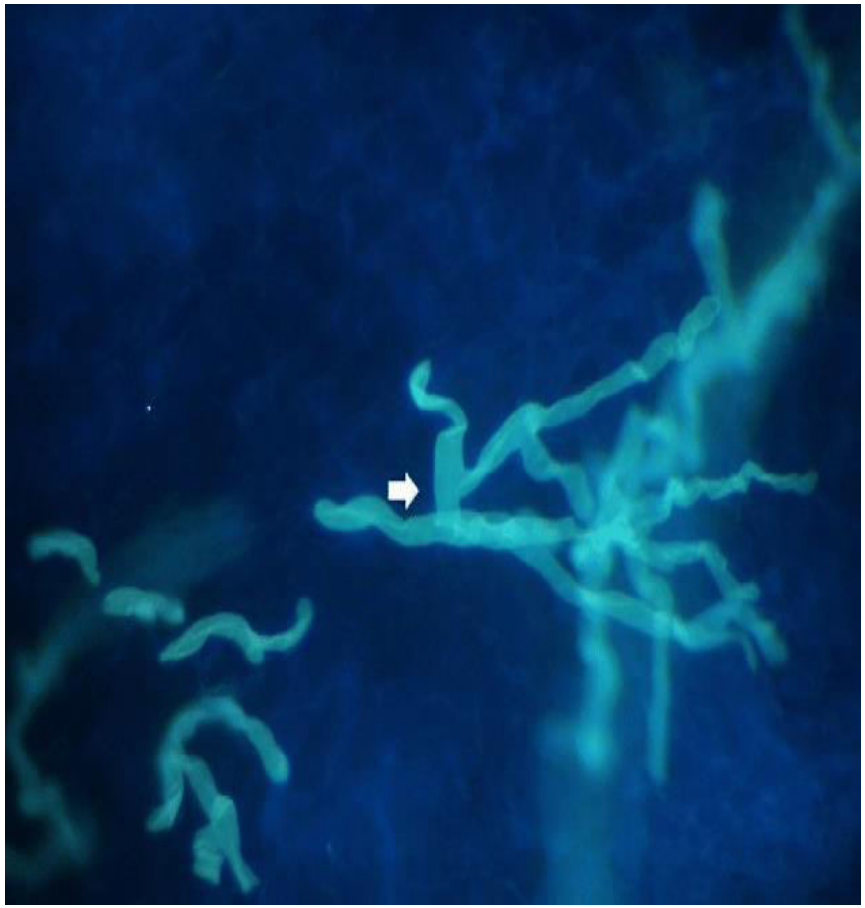
Culture from active parts of lesion improve diagnostic yield

Specimens should not be grounded to preserve viability. On SDA at 30,37 degrees
Growth in 2-7 days greyish black colony
Test for susceptibility

Blood tests: Galactomannan and beta-D-glucan are positive in Aspergillosis

Reference : IAOHNS


Lacking rhizoid
Spores
Sporangium
Sporangiophore
Mucor in LPCB mount



DIAGNOSTIC CRITERIA

POSSIBLE ROCM

- Typical signs and symptoms in the clinical setting of concurrent or recently(less than 6 wks)treated COVID 19,D.M,systemic steroids, mech.ventilation or supplemental oxygen
- No supportive evidence on DNE,CECT/ contrast enhanced MRI

PROBABLE ROCM

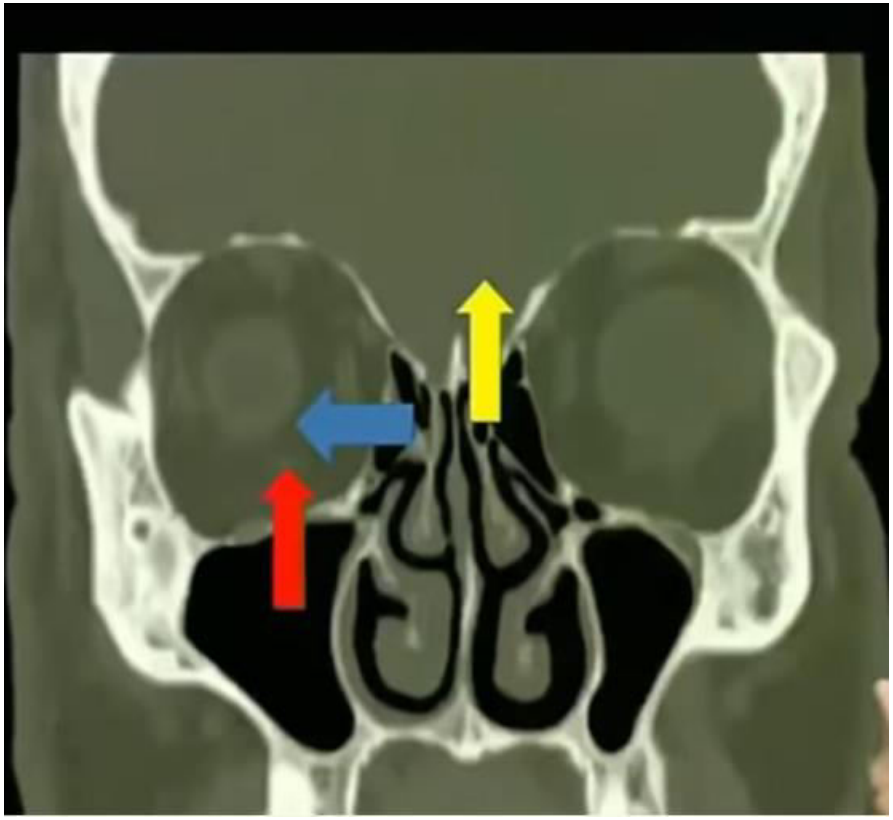
- Supportive evidence clinically and on DNE and / contrast enhanced MRI/CT
- No evidence on direct microscopy/culture/HPE/molecular diagnostics

PROVEN ROCM

- Supportive evidence clinically and on DNE and / contrast enhanced MRI/CT
- Confirmation on direct microscopy or culture or HPE or molecular diagnostics

Reference : IAOHNS

RADIOLOGY – CT SCAN



In imaging we have to look for :

1) Sinus opacification

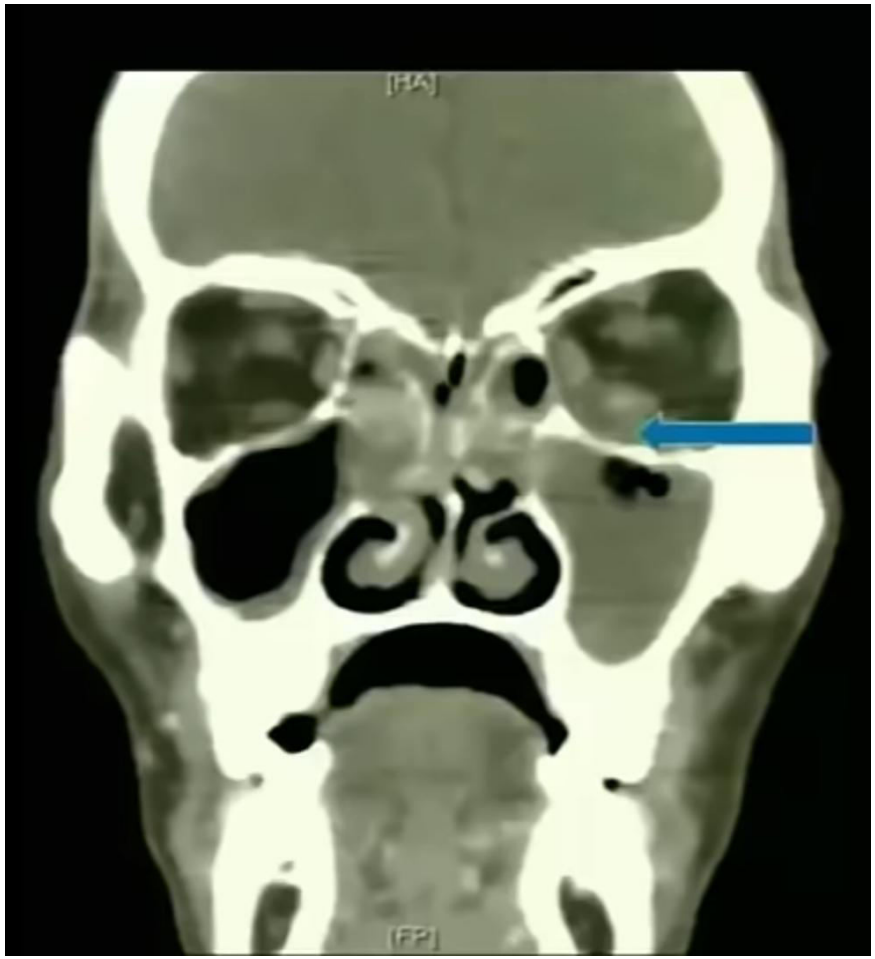
2) Infiltration to peri antral tissue

3)Bone erosion

•Nodular thickening & no fat plane

- Left maxillary sinus shows opacification
- Dark area on rt – normal fat plane
- Lt - peri antral infiltration and loss of fat plane
- Compare subcutaneous fat on rt & lt (infiltrated)

(loss of periantral fat plane & subcutaneous infiltration are suspects of mucormycosis)

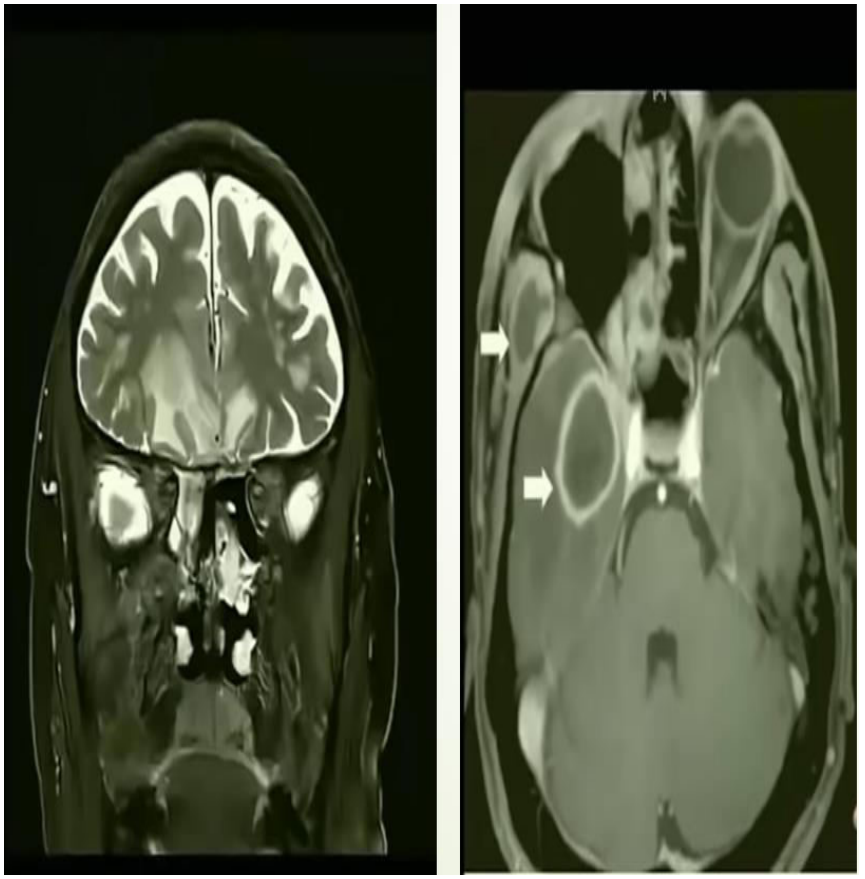


•CT showing left and right maxillary,ethmoid involvement
•Soft tissue ivolvement of left orbit – suggestive of orbital cellulitis

• Bilateral ethmoids involved
• Left orbital apex involved

MRI

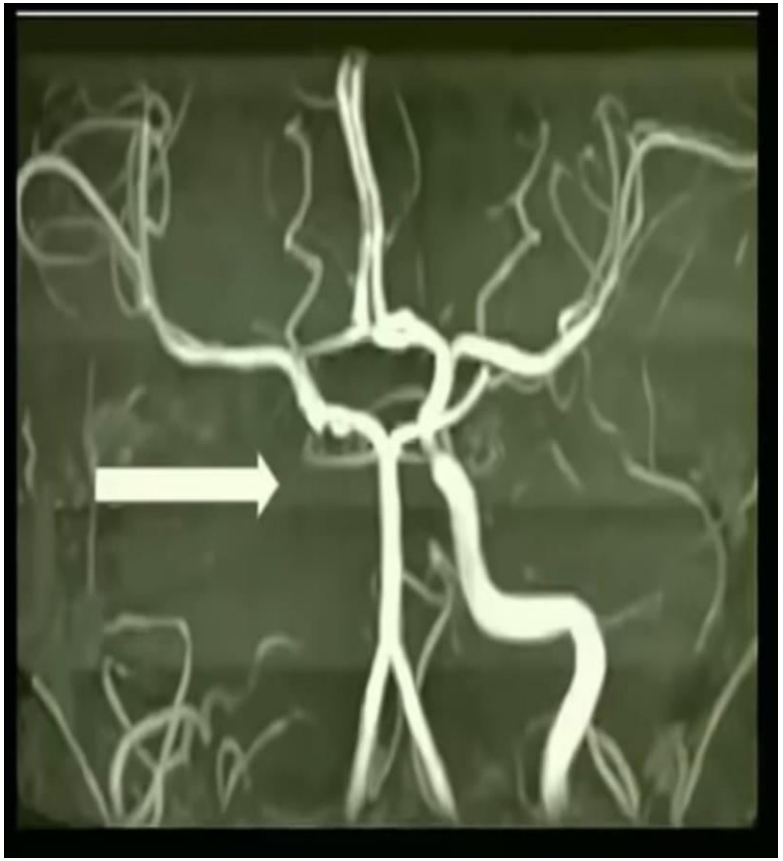
•Left side turbinate enhancing
•Rt mucosal thickening with non enhancing areas (Contrast enhanced T1 MRI)
•Rt infarcted ,non enhancing middle turbinate – BLACK TURBINATE SIGN



• T2 MRI- cerebral extension And Shows edema in brain
•Right ethmoid involvement
•Brain abscess – ring enchancing

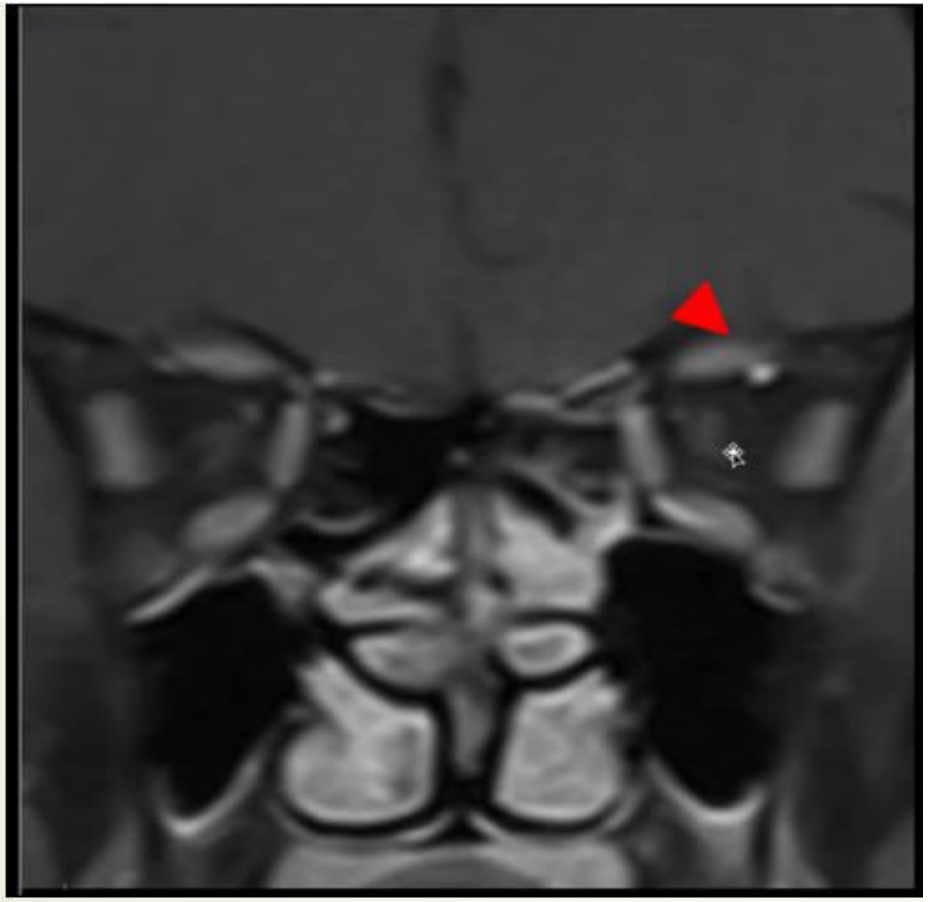
MRI

•CE MRI Showing right ethmoidal sinusitis
•Right orbital apex involved
•Right cavernous sinus showing – bulky and filling defects suggestive of thrombosis



• MR Angiography showing Rt ICA thrombosis

ALARMING RED FLAG SIGNS



1. Peri antral extension from maxillary sinus in to pterygopalatine fossa and cavernous sinus

2. Skull base osteomyelities through sphenoid sinus direct invasion to cavernous sinus (hypointense areas , fat not clearly visible)

3 . Look for prominent superior ophthalmic vein (cut off 3 mm) beyond it..indicates cavernous sinus invasion

STAGING

Stage 1: Involvement of nasal mucosa

1a : Limited to middle turbinate

1b : Involves inf turbinate or ostium of Naso lacrimal duct

1c : Involves nasal septum

1d : Bilateral nasal mucosal involvement

Stage 2 : Involves PNS

2a : one sinus

2b : two I/L sinuses

2c : > two I/L sinuses and or palate/oral cavity

2d : B/LPNS or involvement of zygoma or mandible

Stage 3 : Involves Orbit

3a : Naso lacrimal duct,medial orbit ,vision unaffected

3b : Diffuse orbital involvement, vision normal

3c : Central retinal artery or ophthalmic artery occlusion or superior ophthalmic vein thrombosis; involves sup and inf orbital fissure,orbital apex,loss of vision

3d : B/L orbital involvement

Stage 4 : Involvement of CNS

4a : Focal cavernous sinus involvement

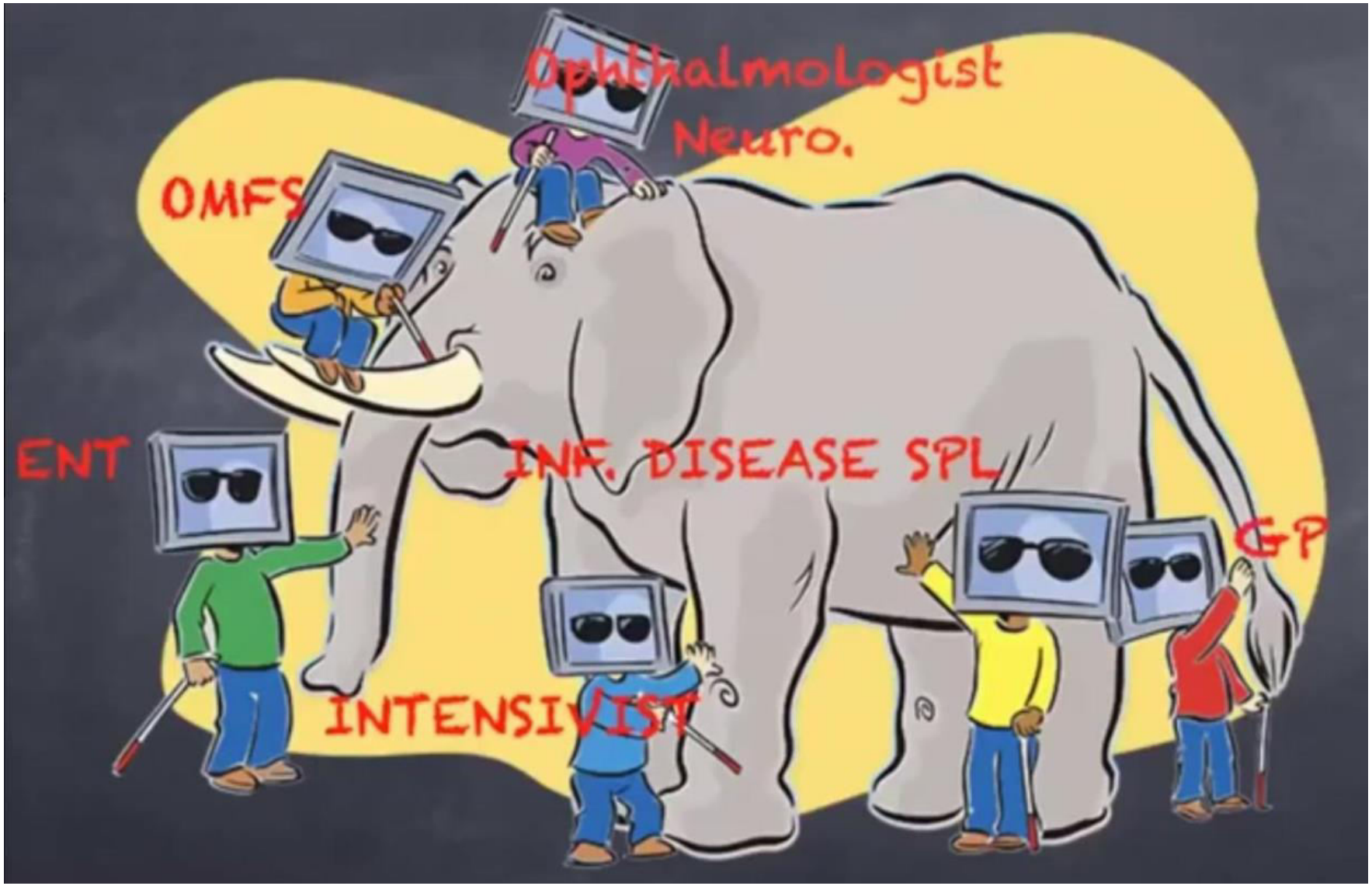
4b : Diffuse cavernous sinus involvement

4c : involves skull base, ICA occlusion, brain infarction

4d : Multifocal or diffuse CNS disease

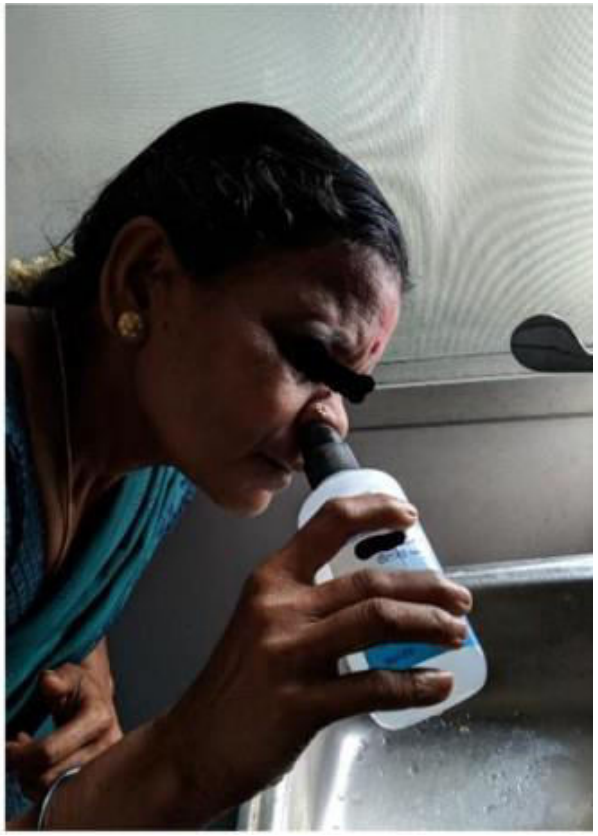
REFERENCE : Indian journal of ophthalmology

MANAGEMENT


Ophthalmologist
Neuro.
OMFS
ENT
INF. DISEASE SPL
GP
INTENSIVIST

Medical management

- General measures
- Anti-fungals currently used are – Amphotericin B, Isavaconazole,Posaconazole
- Ampotericin B is the drug of choice
- Anti fungals started immediately as induction therapy for probable and proven mucormycosis cases and continued as consolidation therapy after surgical debridement




NDC 60270-857-20
HYPERTONIC SALINE SOLUTION 7.2%
STERILE - PRESERVATIVE FREE
For Animal Use Only
NET CONTENTS: 1000 mL
VETTEK


500 ml
Povidone-Iodine Solution IP 5% w/v
बीटाडीन
Betadine®
Standardised
Microbicidal Solution 5%
Standardised

AMPHOTERICIN B

Lipid formulations

- 1) ABCD (AMPHOTERICIN B including colloid dispersion)
- 2) ABLC (AMPHOTERICIN B lipid complex)
- 3) Liposomal Amphotericin B

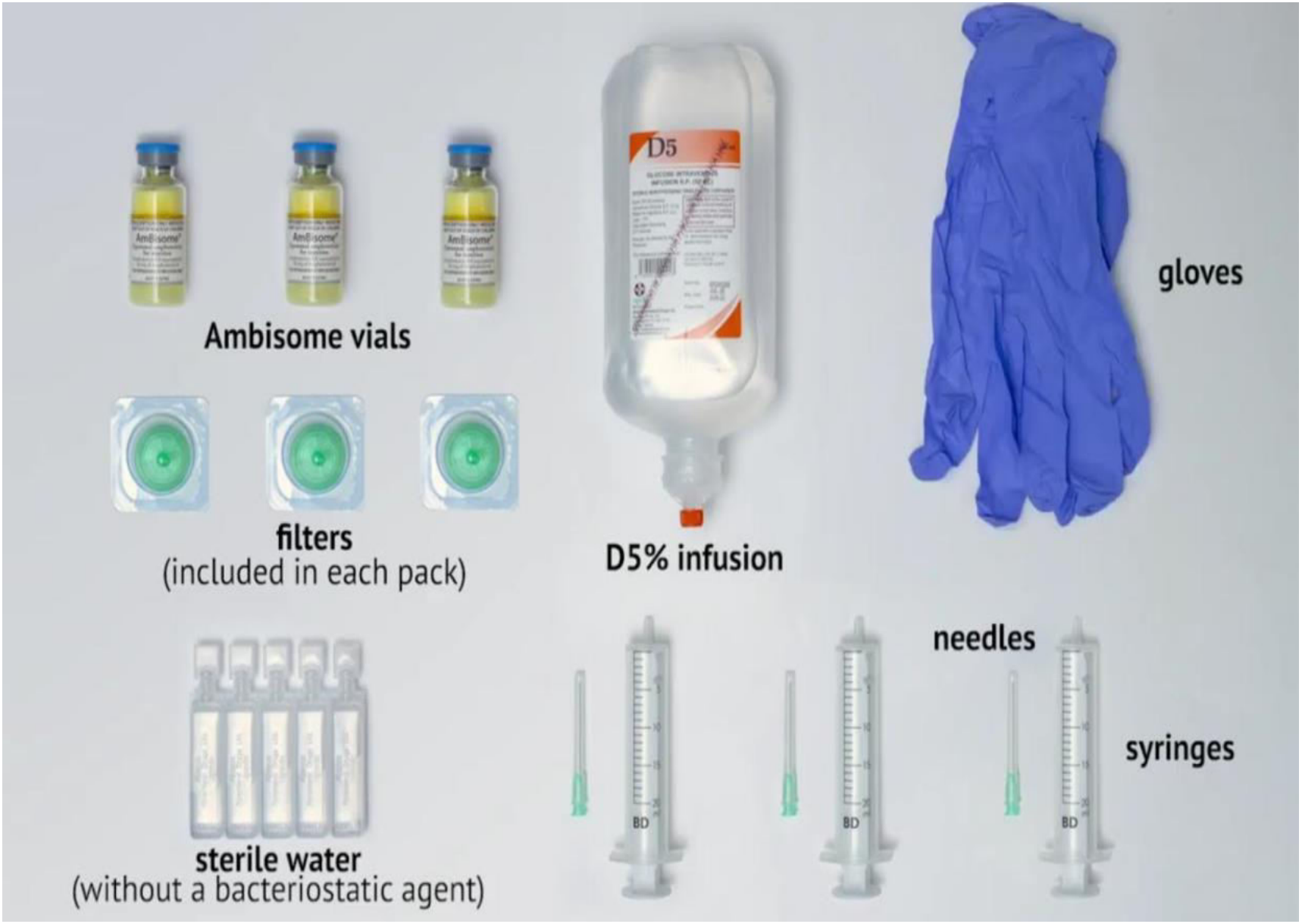
MONITORING OF ANTIFUNGAL TREATMENT

- Serum electrolytes (potassium and magnesium
- Complete Blood Picture
- Renal function tests
- Liver function tests

- Install PICC (peripherally inserted cental catheter)
- Maintain adequate systemic hydration by infusing 500 ml NS before and after AMP B infusion
- The duration of Anti- fungal therapy should be determined on individual basis, usually continued till the follow up biopsy specimens and culture from affected site and recovery from immunosuppression and near normalization of radiological images

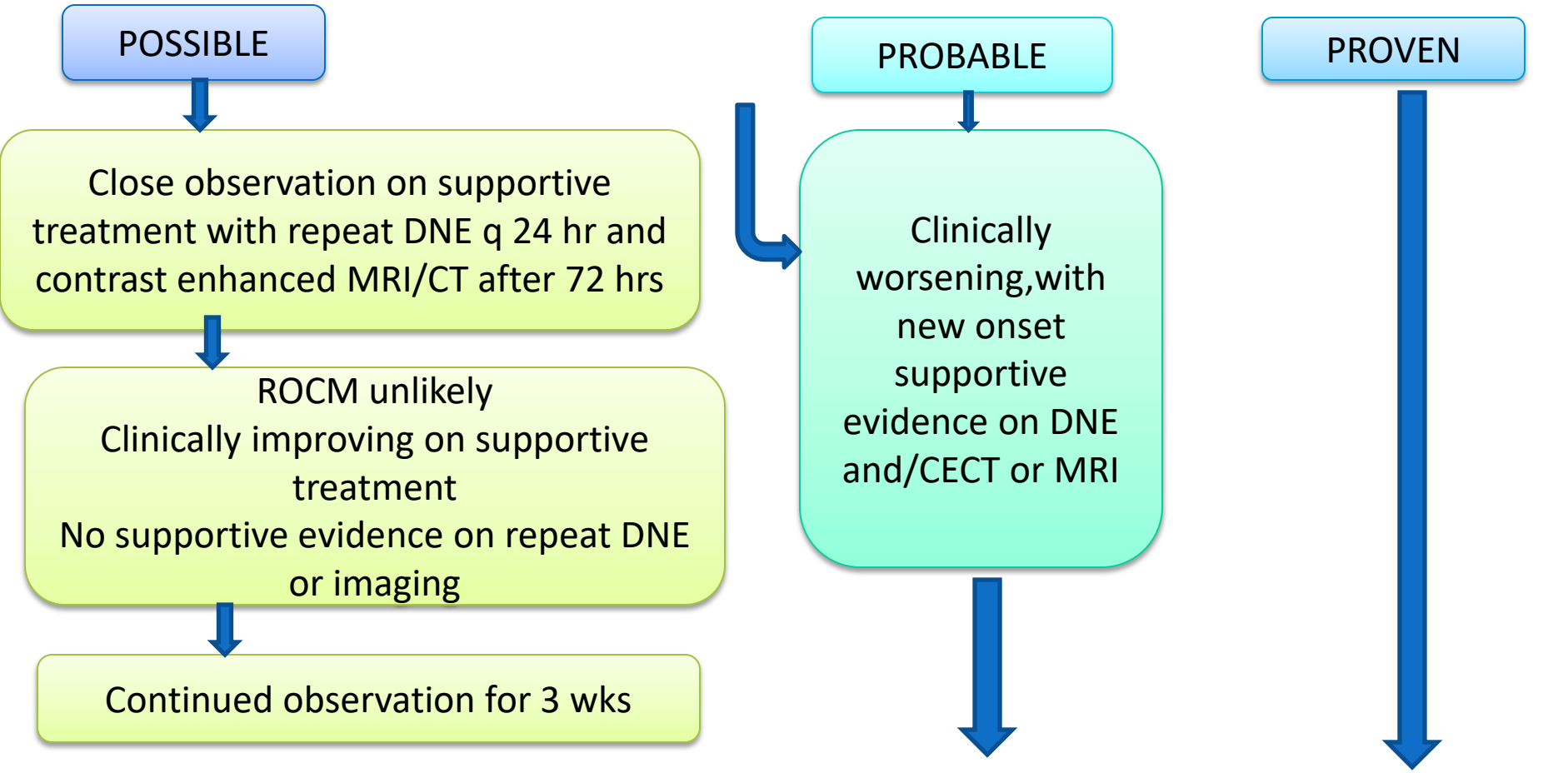
LIPOSOMAL AMP B

- 5-10 mg /kg/day as infusion in 5% D over 3-4 hrs
- Reconstitution : 12 ml of sterile water (not NS) is mixed with vial to yield 4mg/ml of preparation
- Shake vigorously for 30 sec to dispense content and make yellow translucent solution
- Further diluted in 500 ml 5% D
- The contents are injected via 5 micron filter which is provided with syringe
- Filter used for removal of precipitate and used only once for one vial


Ambisome vials
filters
(included in each pack)
D5
D5% infusion
gloves
sterile water
(without a bacteriostatic agent)
needles
syringes
BD
BD
BD

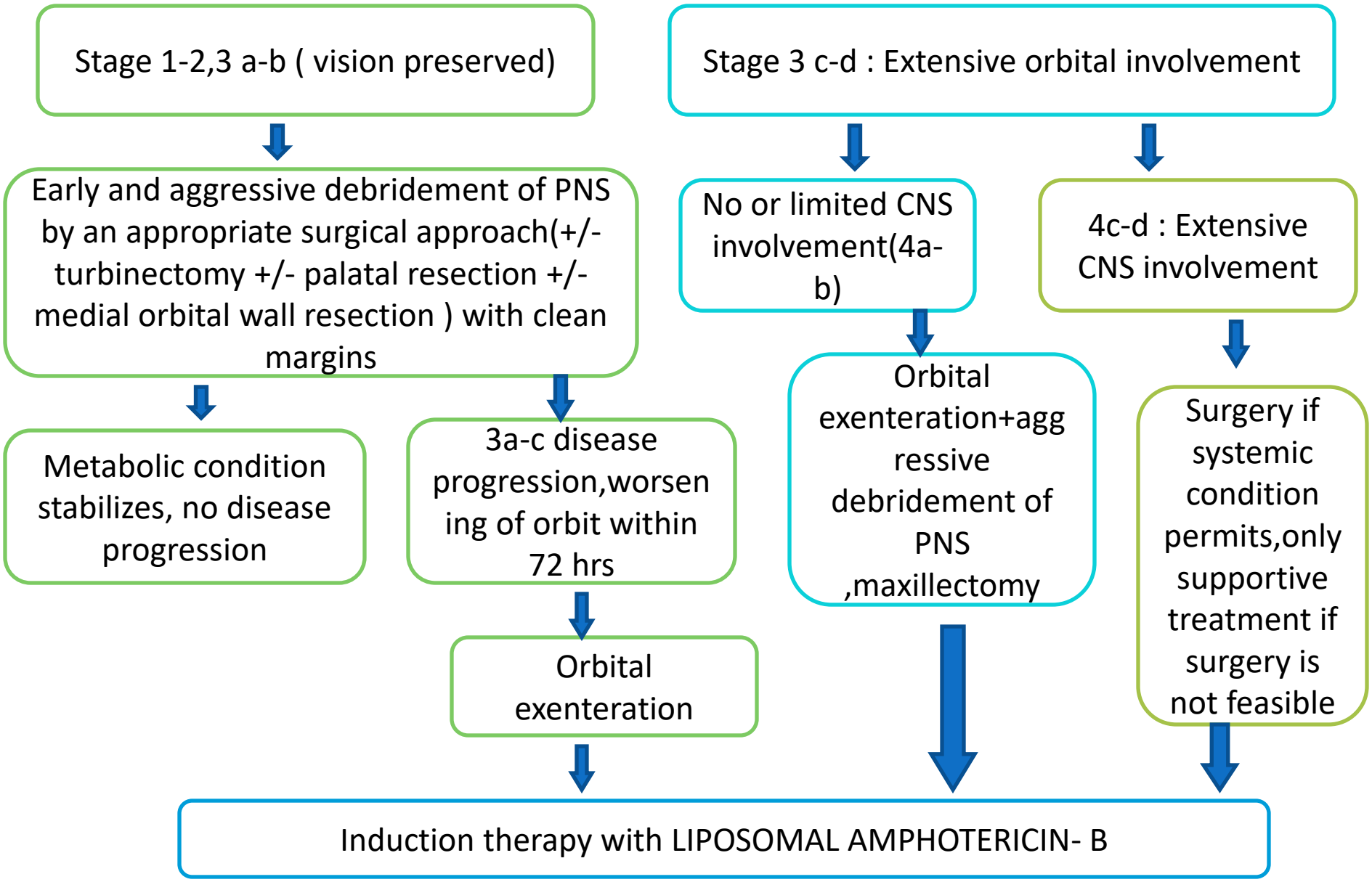
	CONVENTIONAL AMP B	LIPOSOMAL AMP B
ROUTE OF ADMINISTRATION	Poor absorption so given IV	IV
MOA	Binds to ergosterol in the cell membrane of fungus , increases the permeability of cell membrane and cell contents leak out leading to death of cell	Same as conventional AMP B
TEST DOSE	Test dose of 1mg in 50 ml of 5% dextrose given IV over 20-30 min	Same as conventional AMP B
TREATMENT DOSE	1 mg/kg/bodyweight in 500 ml 5% D over 3-4 hrs ,till cumulative dosage of 2 gms reached	5-10 mg /kg/day as infusion in 5% D over 3-4 hrs
SIDE EFFECTS	Nephrotoxicity,Hemotoxicity (anemia and thrombocytopenia),hypokalemia,hypomagnesia	Lower nephrotoxicity and anemia,so high dose can be given
INFUSION TOXICITY	High(due to release of pro inflammatory cytokines – fever,rigor,chills,nausea)	Low
MONITORING	S.electrolytes,CBP,LFT,RFT	

MANAGEMENT PROTOCOL



Reference - : Indian journal of ophthalmology

SURGICAL MANAGEMENT



Reference - AOIAP

- After surgical management, continue induction therapy with IV Liposomal AMP-B 5-10 mg/kg body wt. for minimum dose of 2 gms
- Followed by consolidation therapy – oral Isavuconazole 200 mg TID on day 1 and 2 ,200 mg OD from day 3 (or)
- Oral Posaconazole 300 mg BD on day 1, 300 mg OD from day 2 for 3-6 months or minimum of 6 wks following clinical and radiological regression

PREVENTION OF ROCM IN SETTING OF COVID-19

- Judicious and supervised use of systemic steroids & antibiotics
- No prophylactic Voriconazole for ICU patients
- Aggressive monitoring and control of DM
- Strict aseptic precautions while administering oxygen (sterile water for the humidifier, daily change of sterilized humidifier and tubes
- Personal and environmental hygiene
- Barrier mask covering nose and mouth
- Pre inform the red flag c/f of ROCM and to inform early to the doctor in post covid recovery patients


THANK YOU