Covid Diagnostic And Treatment Algorithm Ver 3/21 dt 26/5/2021

USUAL SYMPTOMS		SEVERE SYMPTOMS	
Fever >38 C i.e >100.4 F, coryza, sore throat, cough,		Dyspnoea	
Muscle pain		Chest pain	
Redness of eyes		Stroke	
Headache		Unilateral swelling of legs with pain	
Diarrhoea, nausea		Any febrile illness > 72 hrs without clinically overt localization	
Rash		Acute severe pain abdomen	
Loss of taste or smell		Altered mental status in elderly	

- Spo2 > / = 95%
- *Spo2 </= 94 % will need evaluation*
- Stable vital signs e.g. Pulse < 100-110/min (Note: each degree of fever can increase pulse by up to 10/min from the patient's baseline pulse)
- Home isolation can be done if
- Proper monitoring is possible and
- Regular contact with Physician is possible

- RR >24
- SpO2 90-93%
- If on O2, requiring <5 Lt/min (~ 40% FiO2) to maintain SpO2> 90%

- SpO2< 90%
- RR > 30
- If on O2, requiring>5L/min or any respiratory support (HFNC/ NIV/ Ventilation)
- BP<90/60,
- ARDS, end organ damage
- Severe MAS

Age < 60 with no comorbidities

Age < 60 with comorbidities

Age> 60

MILD

Category A

MILD

Category A With Risk Factors

MILD

Category A With Risk Factors

Moderate

Category B

Severe

Category C

INCREASED RISK WITH				PROBABLE INCREASED RISK WITH	
ADULTS		**CHILDREN**			
Chronic kidney disease		Who have neurologic/ genetic/ metabolic/ congenital heart disease		Use of corticosteroids/ immunosuppressants Immune deficiencies Thalassemia Solid organ malignancy Obstructive sleep apnoea Psychiatric disease Blood/bone transplant Overweight Pulmonary fibrosis Hypertension	
Solid organ transplant		Who have leukemia/ hematological malignancy especially with recent chemotherapy,			
Obesity/overweight		Cystic Fibrosis			
Heart failure		Type I diabetes			
Coronary artery disease		Complex neurological conditions			
Type I & II diabetes		Sickle cell disease			
Pregnancy					
Asthma					
Dementia					
Stroke					
HIV					
Smoking					

TESTS (Day 5/6)

- CBC*,CRP
- CXR-PA

TESTS (Day 5/6)

- CBC
- CRP
- CXR-PA/ NC HRCT CHEST (Day 6/7)
- RTPCR FOR COVID**

TESTS (Day 5/6)

- CBC
- CRP
- BIL/SGPT/SGOT/ PT(optional)
- CREATININE
- NC HRCT CHEST*** (Day 6/7)
- RTPCR FOR COVID

TESTS

- CBC,RDW
- CRP
- LFT,KFT
- D DIMER
- PT,APTT
- FBS,HBA1C
- ECG
- NCHRCT CHEST
- RTPCR FOR COVID

TESTS

- CBC,RDW
- CRP
- LFT,KFT
- D DIMER
- PT,APTT
- FBS,HBA1C
- ECG
- NCHRCT CHEST
- RTPCR FOR COVID
- NT PRO BNP
- ECHO

Symptomatic Outpatient Treatment WITH REST

Either Outpatient

Or Inpatient Treatment

WITH REST

Admit In Covid

Ward

Admit In Covid ICU

MUST DOS:

i. Physical distancing, indoor mask use while in vicinity of the patient and strict hand hygiene.
ii. Symptomatic management (hydration, anti-pyretics, anti-tussive , multivitamins)
iii. Stay in contact with treating physician
iv. Monitor temperature and oxygen saturation and pulse(by applying an Spo2 probe to finger)

SEEK IMMEDIATE MEDICAL ATTENTION IF:

a. Difficulty in breathing
b. Respiratory rate>24
c. High grade fever/severe cough, particularly if lasting for > 5 days
d. If Spo2 < 94% persisting for some time(check proper positioning of pulse oximeter, battery and if the nails are painted with nail polish)
e. A low threshold to be kept for those with any of the high-risk features.

- Consider 3 or 6 minute walk test; test Spo2 after walking for 6 min.
- Advice home pulse oximetry monitoring every 4h

Therapies on low certainty of evidence

- Consider inhaled Budesonide 800 mcg twice daily2(If symptoms persist beyond 5 days)
- May use Ivermectin (200 mcg/kg) or 12 mg once daily x 3 days

Admit if clinical course worsening or fever persists >7 days

Oxygen support

- Target Spo2 92-96%(88-92% in COPD patients)
- Non-rebreathing, face mask preferred
- Awake proning encouraged in all patients requiring supplemental oxygen(sequential position changes every two hours)

Anti-inflammatory therapy

- Start injection methyl prednisolone 0.5 mg per kg in 2 divided doses or Dexamethasone / Corticosteroids x 5-10 days
- Start prophylactic LMWH
- Consider Remdesivir if <10 days from symptom onset
- May add narrow spectrum antibiotics like Amoxyclav, Ceftriaxone

Respiratory Support

- Consider use of NIV(Helmet or face mask interface depending on availability) in patients with increasing oxygen requirements if work of breathing is low
- Consider use of HFNC in patients with increasing oxygen requirement
- Intubation should be prioritized in patients with high work of breathing/if NIV is not tolerated
- Use conventional ARDS net protocol for ventilator management

Anti-inflam,matory therapy

- Injection methyl prednisalone 1-2 mg per kg IV into 2 divided doses or dexamethasone x 5-10 days

ANTI-COAGULATION

- Weight based prophylactic LMWH(Enoxaparin 0.5 mg per kg per dose SC BD)

- Start Tocilizumab
- Consider antibiotics
- Consider experimental therapies
- May add narrow spectrum antibiotics like Amoxyclav, Ceftriaxone

MONITORING

- **Clinical monitoring:** respiratory rate hemodynamic instability
- **Radiology:** Serial chest X-Ray, HRCT Chest to be done only if there is worsening
- **Lab monitoring :**CRP and D-Dimer 24-72 hourly, CBC, KFT, LFT 24-48 hourly; IL-6 levels to be done if deteriorating

May need to do ECG after isolation /discharge to R/O cardiac problems like myocarditis,Ischemia

PATIENTS USUALLY DETERIORATE BETWEEN 6 TH TO 10 TH DAYS

PATIENTS WHO HAVE HIGH FEVER, INTENSE HACKING COUGH , BREATHING DIFFICULTY OR SENSE OF PRESSURE CHEST BEYOND 4-5 DAYS HAVE HIGH PROBABIITY OF DETERIORATION

IT IS IMPORTANT TO CONSIDER OTHER POSSIBLE ETIOLOGIES INCLUDING: other respiratory viral infections (e.g., influenza), community-acquired pneumonia, congestive heart failure, asthma or chronic obstructive pulmonary disease exacerbations, and streptococcal pharyngitis.(NIH)

DYSPNOEA TENDS TO OCCUR BETWEEN 4 AND 8 DAYS AFTER SYMPTOM ONSET ,ALTHOUGHIT MAY OCCUR AFTER 10 DAYS.WHILE MILD DYSPNOEA IS COMMON ,WORSENING DYSPNOEA AND SEVERE CHEST PAIN/ TIGHTNESS SUGGEST THE PROGRESSION OF PULMONARY INVOLVEMENT. IN STUDIES OF PATIENTS WHODEVELOPED ARDS, PROGRESSION OCCURRED AT A MEDIAN OF 2.5 DAYS AFTER THE ONSET OF DYSPNOEA.(NIH)

LABS DONE TOO EARLY WILL NOT SHOW MUCH DEVIATION FROM THE NORMAL AND HENCE CANNOT REFLECT THE PROBABILITY OF THE DISEASE ENTERING THE SEVERE/CRITICAL PHASE

- * Lymphocytopenia (lymphocyte count under 1.0 x 10_9 /L) is a risk factor for progression to severe disease. Neutrophil lymphocyte ratio >3.13 is an independent risk factor for severe disease. RDW>14.5% at diagnosis or a rise in RDW during hospitalization predicts increased mortality.
- ** A negative test for SARS CoV-2 PCR (especially from an upper respiratory sample) does not exclude SARS-CoV-2 infection: need to repeat testing if index of clinical suspicion is high, preferably from a lower respiratory tract specimen. Rapid antigen test has a specificity of 100% and sensitivity of 50-84%; if negative, PCR is needed to rule out infection. Serology for SARS CoV-2 may be considered for PCR negative individuals with late presentations 2 weeks after onset of symptoms or COVID related auto-immune syndromes. Govt rules need to be followed in decisions on testing.
- *** CT chest (without contrast) is more sensitive than RT-PCR for the diagnosis of febrile patients with COVID-19 and is indicated as a diagnostic aid in patients at high risk for clinical progression if RT-PCR testing is negative/not available/report is delayed. Ultrasonogram of chest (where expertise available) can be used if CT not possible. CTPA (CT Pulmonary Angiography) is the test of choice for suspected PE.

1. Patients treated on outpatient basis should be advised regarding home isolation, **warning signs** like severe headache, blurred vision, breathing difficulty, chest pain, severe weakness, pain abdomen, unilateral swelling of leg with pain and need for close follow up.

2. The NIH Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids in outpatients** to treat mild to moderate Covid infection in the absence of another indication **(AIII)**. There is currently a lack of safety and efficacy data on the use of these agents in outpatients with COVID-19.The Panel **recommends against** the use of **antibacterial therapy** (e.g., **azithromycin**, **doxycycline**) in the absence of another indication **(AIII)**. The NIH Panel also **recommends against** the use of **chloroquine** or **hydroxychloroquine** with or without **azithromycin (AI)**. There are insufficient data for the Panel to recommend either for or against the use of other agents for the treatment of outpatients with COVID-19.

3. **Budesonide:** Start if fever continues for more than 5 days or may be started as early as possible after symptom onset according to some. Dose is 800 micrograms twice daily till resolution of symptoms.

4. **Dexamethasone**: dose is 6 mg once daily iv/po for 7-10 days (or till discharge if earlier) . Alternatives are hydrocortisone 50 mg IV q8h or methylprednisolone 32 mg/day. Consider adding a single dose of Ivermectin 12 mg to prevent Strongyloides hyper-infection. In patients continuing to remain severely hypoxemic after 10 day course of dexamethasone, re-assess need for continued steroids after CTPA. Early initiation of oral steroids is not beneficial.

I. Start prophylactic dose **LMWH** (e.g. enoxaparin or equivalent) for all admitted patients. Dose of enoxaparin is 40 mg for Cat B and 1mg/kg for Cat C given sc q24h. *Contra-indications:* active bleeding or a platelet count of $<25\times10_9$/L.
A rising d-dimer >1mcg/ml, especially >6 times normal, suggests DVT/PE. Start therapeutic anticoagulation for proven or strongly suspected DVT or PE till excluded on venous doppler/CTPA. Prolonged a PTT is not a contra-indication to anticoagulation. Repeat PT, platelet count and d-dimer every 2-3 days in patients who do not show improvement. At discharge, consider starting patients at high risk (modified IMPROVE-VTE score>4 or score>2 with d-dimer >2 times upper limit, age>75, underlying malignancy) on DVT prophylaxis (eg. **rivaroxaban** 10 mg od for 4 weeks or equivalent).

II. **Remdesivir**: dose is 200 mg iv on day 1 followed by 100 mg once daily for 4 more days. Does not reduce mortality but reduces duration of hospital stay and improves oxygenation in patients requiring oxygen, but not on high flow O2/NIV/HFNC/mechanical ventilation. Benefit greater if started early in disease (<10 days from symptom onset). Avoid co-administration of HCQ probably reduces efficacy. No renal or hepatic dysfunction (eGFR <30 ml/min /m2 ,SGPT or SGOT >5 times ULN-not an absolute contradiction. NOT TO BE USED IN PATIENTS WHO DO NOT NEED OXYGEN OR IN HOME SETTINGS. The WHO Solidarity trial has showed that Remdesevir had little or no effect on hospitalized patient with Covid 19,as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.

5. Community acquired bacterial pneumonia (CAP) complicating COVID is uncommon, unlike influenza. Elevated Procalcitonin may help decide if antibiotics are indicated: use narrow spectrum antibiotics like **ceftriaxone or amoxicillin-clavulanate**. Blood cultures are not routinely recommended for suspected bacterial CAP. CAPA (Covid associated Pulmonary Aspergillosis) should be considered and looked for in patients on mechanical ventilation using serum AG (Aspergillus galactomannan) or BDG: serum 1-3 Beta d glucan, and ET fungal stain and culture.

6. **Tocilizumab :** administer single dose within 24 h of worsening in patients with CRP>75 requiring FiO2>0.4, HFNC rate >30 l/mt or higher levels of respiratory support. Use only when significantly raised inflammatory markers or not improving despite use of steroids. Dose is single infusion of 400 mg iv or 8 mg/kg (not to exceed 800 mg of total dose). A second dose may be considered if there is no improvement 24h after first dose. Avoid if infection present or suspected.

7. **Experimental therapies for COVID**:
   - Colchicine: consider for high risk patients >65 within 24 h of positive test. Dose is 0.5 mg bd for 3 days, then od till clinical illness resolves.
   - Convalescent plasma: consider plasma with high antibody titers for high risk patients presenting within 3 days of symptom onset (>75 y or >65y with co-morbidities). Dose is 200-250 ml followed by a second dose if needed 24 h later. No use after 7 days and are not of proven benefit
   -

RTPCR (CT)	*SCORE*	*VIRAL LOAD*	**D-DIMER**	*VALUE (MICROGRAM/ML)*	*SEVERITY OF INFLAMMATION*
LOWER THE VALUE HIGHER THE VIRAL LOAD	17-24	HIGH VIRAL LOAD		0.5	Normal
	25-35	MEDIUM VIRAL LOAD		<1	Mild
	>36	MILD VIRAL LOAD		>1	Moderate-Severe
CRP	*VALUE (MG/DL)*	*SEVERITY OF INFLAMMATION*	**IL-6**	*VALUE (MG/DL)*	*SEVERITY OF INFLAMMATION*
	<6	NORMAL		<7	NORMAL
	<26	MILD		<15	MILD
	26-100	MODERATE		16-100	MODERATE
	>100	SEVERE		>100	SEVERE

NEUTROPHIL TO LYMPHOCYTE RATIO	
MILD	MOD-SEVERE
<3.5	>3.5

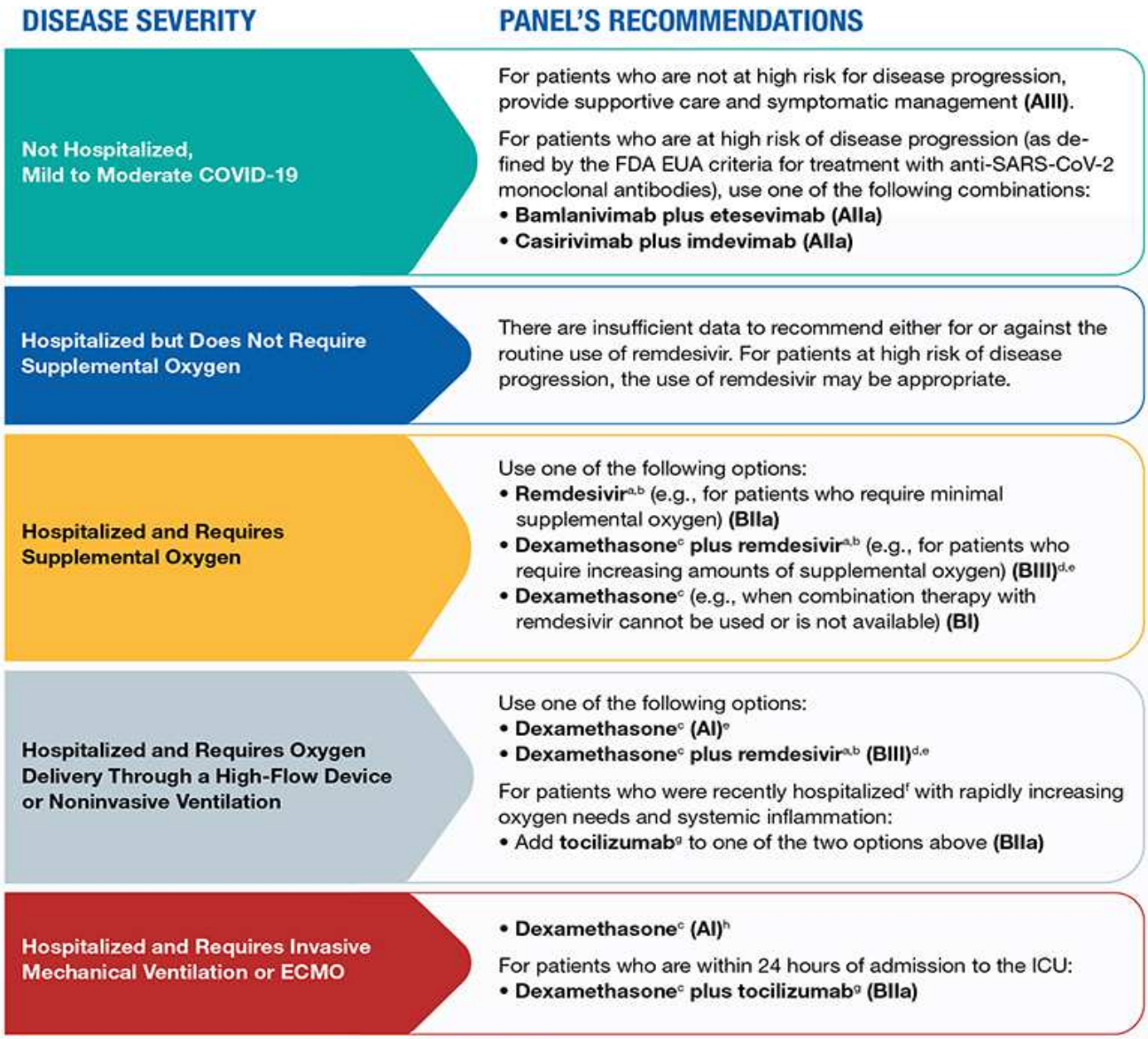
HRCT CHEST			
CT SEVERITY SCORE		*CO-RADS SCORE*	
SCORE	CT SEVERITY	CO-RADS-1	NO
<8	MILD	CO-RADS-2	LOW
9-15	MODERATE	CO-RADS-3	INTERMEDIATE
>15	SEVERE	CO-RADS-4	HIGH
		CO-RADS-5	VERY HIGH
		CO-RADS-6	VERY HIGH WITH PCR+

This is a SARS Covid 19 guideline procured from various sources like GOI, CDC, and hospitals like Apollo Hospitals. These are to help in decision making by clinicians, institutions or help the common people to understand categorization of patients according to severity and subsequent evidence based treatment. This is to be updated from time to time. This is to be used in consultation with physicians.

Gavista Health Foundation, as an issuer will not be responsible, if someone uses the same without consulting their physicians and without following latest Government guidelines.

Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnotes.



Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] The remdesivir dose is 200 mg IV for one dose, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.

[b] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.

[c] The dexamethasone dose is 6 mg IV or PO once daily for 10 days or until hospital discharge. If dexamethasone is not available, equivalent doses of other corticosteroids (e.g., prednisone, methylprednisolone, hydrocortisone) may be used. See the Corticosteroids section for more information.

[d] The combination of dexamethasone and remdesivir has not been studied in clinical trials.

[e] In the rare circumstances where corticosteroids cannot be used, **baricitinib plus remdesivir** can be used **(BIIa)**. The FDA has issued an EUA for baricitinib use in combination with remdesivir. The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.

[f] For example, within 3 days of hospital admission. See the Interleukin-6 Inhibitors section for more information.

[g] The tocilizumab dose is 8 mg/kg of actual body weight (up to 800 mg) administered as a single IV dose. Tocilizumab should not be combined with baricitinib and should be avoided in certain groups of patients who are at increased risk for complications. See the Interleukin-6 Inhibitors section for more information.

[h] The combination of **dexamethasone plus remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of remdesivir monotherapy in these patients.

Key: ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; ICU = intensive care unit; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally

AIIMS/ ICMR-COVID-19 National Task Force/Joint Monitoring Group (Dte.GHS)

Ministry of Health & Family Welfare, Government of India

CLINICAL GUIDANCE FOR MANAGEMENT OF ADULT COVID-19 PATIENTS

22nd April 2021

COVID-19 patient

Mild disease

Upper respiratory tract symptoms (&/or fever) WITHOUT shortness of breath or hypoxia

Home Isolation & Care

MUST DOs

- ✓ Physical distancing, indoor mask use, strict hand hygiene.
- ✓ Symptomatic management (hydration, anti-pyretics, anti-tussive, multivitamins).
- ✓ Stay in contact with treating physician.
- ✓ Monitor temperature and oxygen saturation (by applying a SpO2 probe to fingers).

Seek immediate medical attention if:

- Difficulty in breathing
- High grade fever/severe cough, particularly if lasting for >5 days
- A low threshold to be kept for those with any of the high-risk features*

MAY DOs

Therapies based on low certainty of evidence

- ➢ Tab Ivermectin (200 mcg/kg once a day for 3 days). Avoid in pregnant and lactating women.
  OR
- ➢ Tab HCQ (400 mg BD for 1 day f/b 400 mg OD for 4 days) unless contraindicated.
- ❖ Inhalational Budesonide (given via Metered dose inhaler/ Dry powder inhaler) at a dose of 800 mcg BD for 5 days) to be given if symptoms (fever and/or cough) are persistent beyond 5 days of disease onset.

*High-risk for severe disease or mortality

- ✓ Age > 60 years
- ✓ Cardiovascular disease, hypertension, and CAD
- ✓ DM (Diabetes mellitus) and other immunocompromised states
- ✓ Chronic lung/kidney/liver disease
- ✓ Cerebrovascular disease
- ✓ Obesity

Moderate disease

Any one of:
1. Respiratory rate ≥ 24/min, breathlessness
2. SpO2: 90% to ≤ 93% on room air

ADMIT IN WARD

Oxygen Support:

- ➢ Target SpO_2: 92-96% (88-92% in patients with COPD).
- ➢ Preferred devices for oxygenation: non-rebreathing face mask.
- ➢ Awake proning encouraged in all patients requiring supplemental oxygen therapy (sequential position changes every 2 hours).

Anti-inflammatory or immunomodulatory therapy

- ➢ Inj. Methylprednisolone 0.5 to 1 mg/kg in 2 divided doses (or an equivalent dose of dexamethasone) usually for a duration of 5 to 10 days.
- ➢ Patients may be initiated or switched to oral route if stable and/or improving.

Anticoagulation

- ➢ Conventional dose prophylactic unfractionated heparin or Low Molecular Weight Heparin (weight based e.g., enoxaparin 0.5mg/kg per day SC). There should be no contraindication or high risk of bleeding.

Monitoring

- ➢ Clinical Monitoring: Work of breathing, Hemodynamic instability, Change in oxygen requirement.
- ➢ Serial CXR; HRCT chest to be done ONLY if there is worsening.
- ➢ Lab monitoring: CRP and D-dimer 48 to 72 hrly; CBC, KFT, LFT 24 to 48 hrly; IL-6 levels to be done if deteriorating (subject to availability).

Severe disease

Any one of:
1. Respiratory rate >30/min, breathlessness
2. SpO2 < 90% on room air

ADMIT IN ICU

Respiratory support

- Consider use of NIV (Helmet or face mask interface depending on availability) in patients with increasing oxygen requirement, if work of breathing is LOW.
- Consider use of HFNC in patients with increasing oxygen requirement.
- Intubation should be prioritized in patients with high work of breathing /if NIV is not tolerated.
- Use conventional ARDSnet protocol for ventilatory management.

Anti-inflammatory or immunomodulatory therapy

- Inj Methylprednisolone 1 to 2mg/kg IV in 2 divided doses (or an equivalent dose of dexamethasone) usually for a duration 5 to 10 days.

Anticoagulation

- Weight based intermediate dose prophylactic unfractionated heparin or Low Molecular Weight Heparin (e.g., Enoxaparin 0.5mg/kg per dose SC BD). There should be no contraindication or high risk of bleeding.

Supportive measures

- Maintain euvolemia (if available, use dynamic measures for assessing fluid responsiveness).
- If sepsis/septic shock: manage as per existing protocol and local antibiogram.

Monitoring

- Serial CXR; HRCT chest to be done ONLY if there is worsening.
- Lab monitoring: CRP and D-dimer 24-48 hourly; CBC, KFT, LFT daily; IL-6 to be done if deteriorating (subject to availability).

After clinical improvement, discharge as per revised discharge criteria.

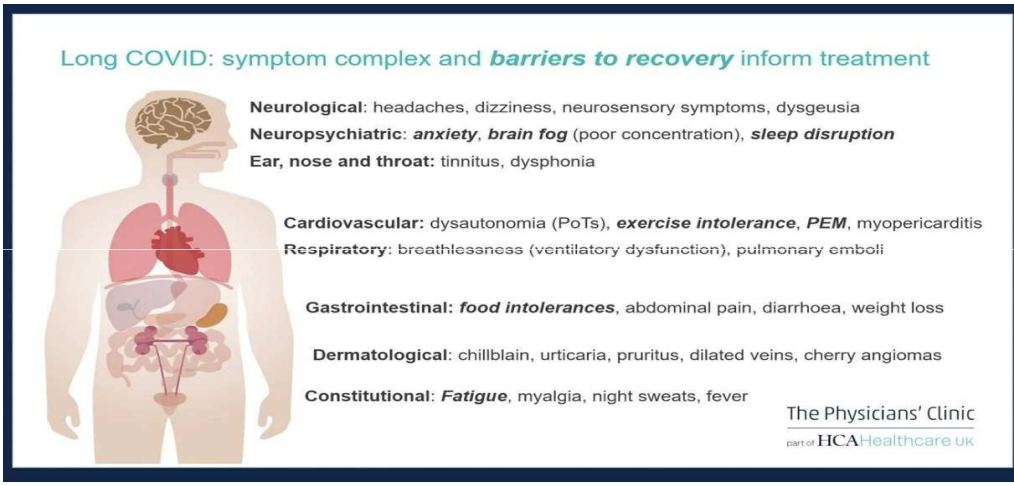
EUA/Off label use (based on limited available evidence and only in specific circumstances):

- ➢ Remdesivir (EUA) may be considered ONLY in patients with
  - Moderate to severe disease (requiring SUPPLEMENTAL OXYGEN), AND
  - No renal or hepatic dysfunction (eGFR <30 ml/min/m2; AST/ALT >5 times ULN (Not an absolute contradiction), AND
  - Who are within 10 days of onset of symptom/s.
    - ❖ Recommended dose: 200 mg IV on day 1 f/b 100 mg IV OD for next 4 days.
  - Not to be used in patients who are NOT on oxygen support or in home settings
- ➢ Tocilizumab (Off-label) may be considered when ALL OF THE BELOW CRITERIA ARE MET
  - Presence of severe disease (preferably within 24 to 48 hours of onset of severe disease/ICU admission).
  - Significantly raised inflammatory markers (CRP &/or IL-6).
  - Not improving despite use of steroids.
  - No active bacterial/fungal/tubercular infection.
    - ❖ Recommended single dose: 4 to 6 mg/kg (400 mg in 60kg adult) in 100 ml NS over 1 hour.
- ➢ Convalescent plasma (Off label) may be considered ONLY WHEN FOLLOWING CRITERIA ARE MET
  - Early moderate disease (preferably within 7 days of symptom onset, no use after 7 days).
  - Availability of high titre donor plasma (Signal to cut-off ratio (S/O) ≥3.5 or equivalent depending on the test kit being used).

Department of Medicine, AIIMS (ND)

LONG COVID

1.FIND OUT THE SYMPTOM COMPLEX



2, FIND OUT BARRIERS TO RECOVERY

Four key barriers to recovery include 1) poor gut health, 2) overexertion, 3) overworking, and 4) sleep disruption. Patients with any of these don't recover quickly.

Neuropsychiatric symptoms:

FIND OUT THE SYMPTOM:

- Headache
- Fatigue
- Sensory disturbance
- Cognitive sympotoms (brain fog)
- Palpitations
- Tremor
- Dizziness
- Myalgia
- Depression , anxiety
- Sleep disturbance
    - Insomnia
    - Excessive day time sleepiness

Source: The Physician's Clinic HCA Health Care UK

BE WARY OF WARNING SIGNS:

The pulsatile tinnitus symptom is a common symptom (It may be a sign of raised intracranial pressure).**SNOOP** mnemonic highlights causes of potentially life-threatening headaches:

Systemic signs

Neurologic symptoms

New **O**nset headache or change in character & patient > 50 yrs old

Onset in thunderclap presentation

Papilledema, Pulsatile tinnitus, Positional provocation

> ***TEST:***
> Autonomic function testing is important. Respiratory therapy for those with breathing issues. Some need GI imaging. Some do develop autoimmune issues, even a year later. Patients who have PTSD, they have "health-related PTSD", which does NOT get treated with CBT or other forms of psychotherapy. He recommends probiotics. Addressing sleep is crucial . If patients do not sleep, they do not recover.

Management of Migraine:

- MRI /CT
- Fluids
- Analgesic overuse to be avoided
- Vit B6 (Riboflavin) 400 mg
- Prophylaxis
    - Nortryptiline 5 mg initially
    - Topiramate
    - Propanalol
    - Candesartan
    - Botulinum toxin
    - Monoclonal antibodies

Treatment of sleep disruption:

- Sleep hygeine
- No alcohol/ caffeine
- Medication

Source: The Physician's Clinic HCA Health Care UK

- Magnesium 500-1000 mg at night
- Melatonin SR 2- mg at night
- Sedating antihistamines(Promethazine 10-20 mg at night- Avoid in elderly)
- Amitryptiline 10-20 mg at night

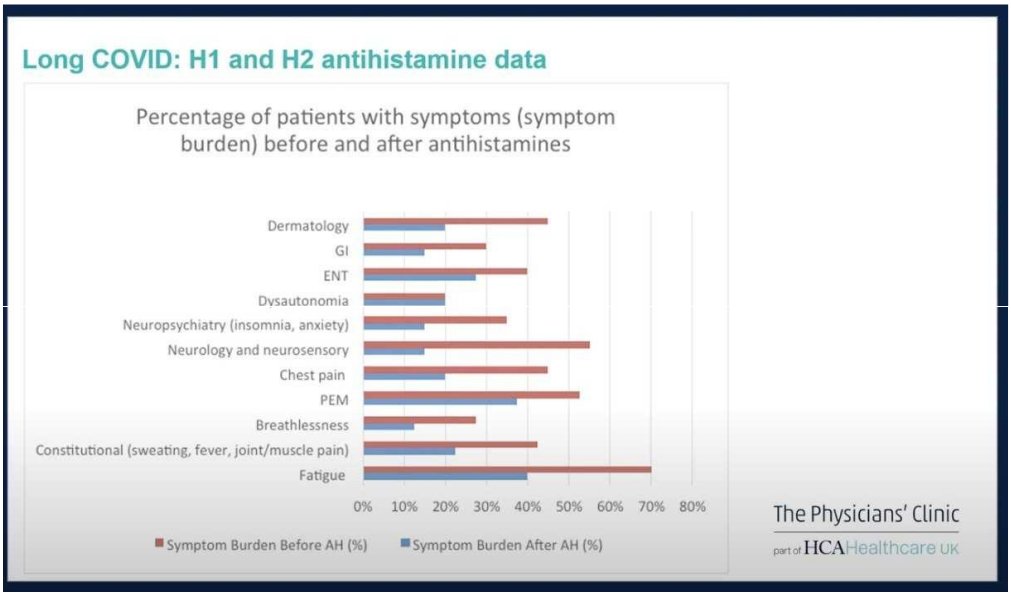
Breathlessness management:

- Respiratory physioptherapy
- Singing or swimmming

Disautonomia management:

- Salt and water loading
- Beta blockers / Ivabradine
- Breathing exercises

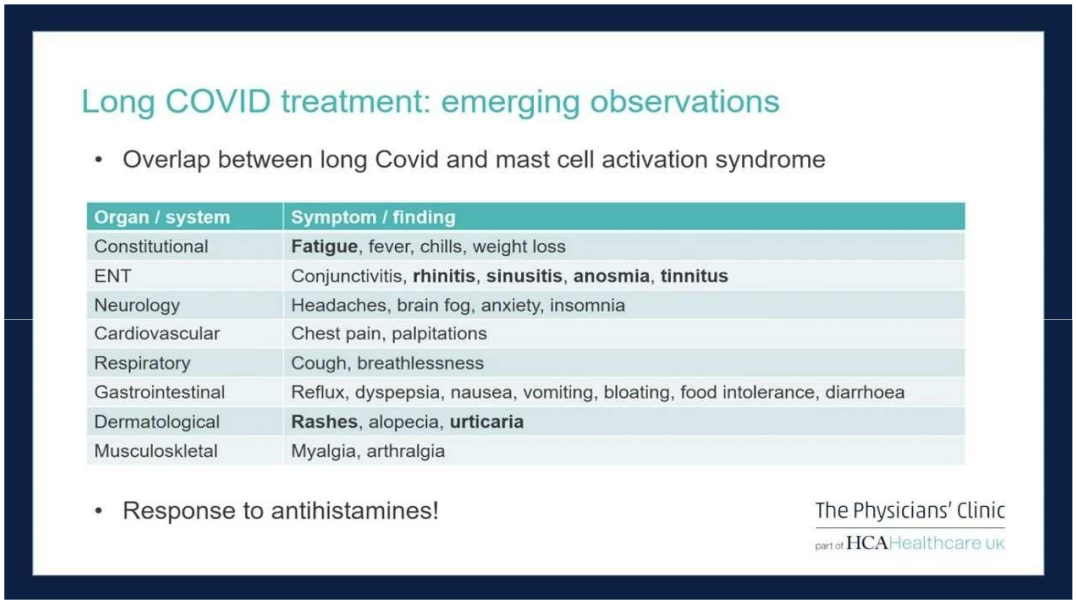
Treating patients with a combination of H1 and H2 antihistamines helps many symptoms, like Loratidine/ Fexofenadine plus Famotidine. (Famotidine has also been shown to alleviate even some breathing and neurological symptoms). These are safe, well-tolerated treatments.



Source: The Physician's Clinic HCA Health Care UK

The above chart showing a wide range of symptoms, including neurological and respiratory symptoms, responding to anti-histamine treatments: (some patients with SIBO, dysbiosis, or other GI issues should be careful/take good probiotics alongside this).Some experts opine to put the patients on loratadine, 10mg 2x daily, in combination with famotidine, 40mg, at night. Patients are assessed every 2 weeks - if they don't respond, Loratidine may be changed to Fexofenadine . Sometimes increasing the dose of famotidine for a period of time helps. In patients who respond and then stagnate, ketotifen may be introduced at night, which is sedating (good for sleep dysfunction patients) and is also considered a mast cell stabilizer.

In some patients with mild gut symptoms, can consider sodium cromoglicate; in patients with airway symptoms montelukast may be considered.



Patients may see an improvement between 1-12 weeks after starting this regimen. This implies the pathophysiology is more complicated than just histamine, because histamine responses are over the course of hours, not weeks.

Cardiac Complications:

1. ***UNDERSTAND PATHOPHYSIOLOGY:*** In acute Covid Thrombosis may happen

    - High risk of VTE (may be > 50 % in critically ill patrients)

Source: The Physician's Clinic HCA Health Care UK

- Very ill patients often have high D -dimer, deranged clotting , but relatively preserved platelet
- D-dimer remains elevated in the sickest patients for several weeks
- Treated with LMWH (discussed earlier)

Microvascular clotting is a feature of Long Covid.Patients have headaches, poor exercise tolerance, extreme lethargy. Many such patients have elevated VWF.

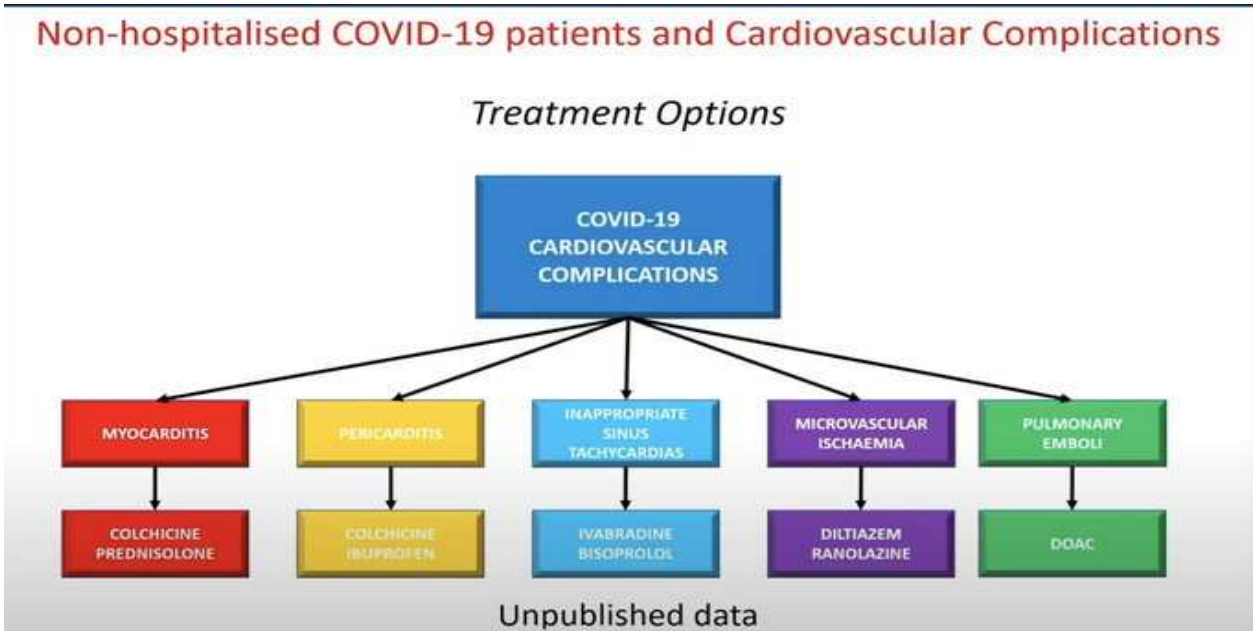
2. ***DIAGNOSIS:Cardiac MRIs are helpful.*** Even when they look normal from a functional standpoint, subepicardial late gadolinium enhancement can be identified, showing post-viral myocarditis.

TESTS:

- Blood tests
  - Cardiac Biomarkers-Natriuretic peptides are most helpful
  - D dimer
  - Inflammatory Biomarkers-FBC, CRP, ESR, LDH
- ECG, 24/48 hrs Holter
- ECHO
- Cardiac MRI with inflammatory sequence, perfusion images
- CTPA
- Oxygen desaturation on exercise can help distinguish between cardiac & respiratory causes: cardiac causes of breathlessness *do not* lead to oxygen desaturation, implies respiratory causes. A physiological stress echo may help if no respiratory issues are found

Pericarditis can sometimes be diagnosed with ECG or echo, but these tests are often normal, it requires specialist review as well. Natriuretic peptide tests help, are usually but not always elevated.

3. ***TREATMENT:***



Source: The Physician's Clinic HCA Health Care UK

4. Three anecdotal treatments may help in Long Covid in some cases:

1.Fluvoxamine 2. Statins 3. Anti-coagulants.

It is often seen, patients with normal cardiac/respiratory tests but low oxygen saturation. It seems reasonable to assume microvascular disease is responsible, in which cases low dose aspirin seems reasonable.

Source: The Physician's Clinic HCA Health Care UK

ROCM (Rhino Orbito Cerebral Mucormycosis)

RISK FACTORS	
Uncontrolled diabetes	
Use of steroids	
Prolonged ICU/hospital stay	
Co-morbidities	
Post organ transplant	
Cancer	
Voriconazole therapy	
Cut, scrape, burn, or other types of skin trauma.	

AREAS INVOLVED

- Sinus involved with the overlying skin
- Eyes
- Lung
- Brain

SIGNS & SYMPTOMS

- Blackening or discoloration over the nose
- Bloody nasal discharge
- Blocked nose
- Foul smell
- Toothache
- Blurred or double vision
- Proptosis/ sudden ptosis/ sudden loss of vision
- Fever
- Headache
- Altered mental status
- Seizures
- Chest pain
- Breathing difficulties
- Coughing of blood

Source : 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.

PREVENTION

- Oral hygiene care with mouthwash
- Betadine mouth gargle twice a day (1:3 ratio)
- While administering oxygen, water for humidification must be sterile
- Steroid usage must be limited to no more than necessary
- Strict blood glucose control.
- Unnecessary use of broad-spectrum antibiotics, antifungals should be stopped as this removes the normal commensal flora resulting in the growth of unwanted organisms due to lack of competition.

PROPHYLAXIS

Oral Posaconazole in high-risk patients

- >3 weeks of mechanical ventilation
- >3 weeks of supplemental oxygen
- >3 weeks of systemic steroids
- Uncontrolled diabetes mellitus with or without ketoacidosis
- Co-morbidities with immunosuppression)

DIAGNOSIS	
Direct microscopy	Direct microscopy of the endoscopy-guided nasal swab, paranasal sinus, or orbital tissue, by using a KOH mount for rapid diagnosis. Non-septate or pauci-septate, irregular, ribbon-like hyphae;,non-dichotomous branching) and greater hyphal diameter as compared to other filamentous fungi. Smears stained with Hematoxylin-Eosin, periodic acid-Schiff, and Grocott-Gomori's methenamine-silver stains can also

Source : 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.

	help • **Direct microscopy has about 90% sensitivity.**
Culture	Culture of the deep or endoscopy- guided nasal swab, paranasal sinus, or orbital tissue. Rapid growth of fluffy white, gray or brown cotton candy-like colonies. The hyphae are coarse and dotted with brown or black sporangia. Brain heart infusion agar, potato dextrose agar or preferably Sabouraud dextrose agar with gentamicin or chloramphenicol and polymyxin-B grow the fungus. • **Only about 50% of samples from cases of probable ROCM grow the organism on culture.**
Molecular diagnostics	Molecular diagnostics of the tissue sample (deep or endoscopy-guided nasal swab, paranasal sinus, or orbital tissue) or blood. Kits are not widely available commercially. There is a promising role of quantitative polymerase chain reaction. • **Molecular diagnostics have about 75% sensitivity.**
Histopathology	Obtaining the sample from clinically active parts of the lesion (not from grossly necrotic tissue) may help improve the diagnostic yield. Hematoxylin- Eosin, periodic acid-Schiff, and Grocott-Gomori's methenamine-silver special stain is diagnostic. • **Histopathology provides diagnostic information in about 80% of samples of probable ROCM.**
Imaging	Contrast-enhanced MRI and CT scan. • Nasal and paranasal sinus mucosal thickening with irregular pat chy enhancement is an early sign. Non-enhancement of turbinates manifests as an early sentinel sign on MRI – black turbinate sign. The fluid level in the sinus and partial or complete sinus opacification signifies advanced involvement of the paranasal sinuses. • Thickening of the medial rectus is an early sign of orbital invasion. Patchy enhancement of the orbital fat,lesion in the area of t the orbital apex, and bone destruction at the paranasal sinus and orbit indicate advanced disease. Stretching of the optic nerve and tenting of the posterior pole of the eyeball indicate severe inflammatory edema secondary to tissue necrosis. MRI and MR angiography help determine the extent of cavernous sinus involvement and ischemic damage to the CNS. • **The absence of paranasal sinus involvement has a strong negative predictive value for RO CM.** • **Contrast-enhanced MRI is preferred over CT scan.** • **Beware of renal compromised patients, Gadolinium contrast may cause fibrosis that is irreversible**

Source : 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.

CATEGORIZATION	
Possible	A patient who has symptoms and signs of ROCM in the clinical setting of concurrent or recently (<6 weeks) treated COVID-19, diabetes mellitus, use of systemic corticosteroids and tocilizumab, mechanical ventilation, or supplemental
Probable	When the clinical symptoms and signs are supported by diagnostic nasal endoscopy findings, or contrast-enhanced MRI / CT Scan,
Proven	Clinico-radiological features, coupled with microbiological confirmation on direct microscopy or culture or histopathology with special stains

TREATMENT PRINCIPLES

- Multidsciplinary team with surgical input is needed
- Lliposomal Amphotericin B is the definitive first step.
- In resource-constraint situations, Amphotericin B Deoxycholate or Amphotericin B Lipid Complex may be used in patients with good renal function. These have relatively lower efficacy and higher systemic toxicity.
- There is no convincing data to support combination antifungal therapy, and it is not recommended.
- Prolonged step-down oral antifungal therapy is warranted.

Source : Honavar SG. Code Mucor: Guidelines for th iagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis in the Setting of COVID-19. Indian J thalmol 2021;69:1361-5.

Possible ROCM

Typical signs and symptoms in the clinical settings of concurrent or recently treated (< 8 weeks) Covid 19,DM, use of corticosteroids/ Tocilizumab, immunosuppression, mechanical ventilation or oxygen inhalation

No evidence on Nasal endoscopy +/- CE CT/ MRI

Repeat Nasal Endoscopy after q 24 hrs and imaging after 72 hrs

ROCM UNLIKELY

Clnically improving on supportive treatment

No evidence on Nasal endoscopy +/- CE CT/ MRI

MONITOR X 3 WEEKS

PROBABLE ROCM

Supportive evidence clinically, on Nasal endoscopy +/- CECT/ MRI

No evidence on Culture /Histopathology/ Molecular diagnostics

PROBABLE ROCM

Clinically worsening with supportive evidence clinically, on Nasal endoscopy +/- CECT/ MRI

No evidence on Culture /Histopathology/ Molecular diagnostics

PROVEN ROCM

Supportive evidence clinically, on Nasal endoscopy +/- CECT/ MRI

Evidence on Culture /Histopathology/ Molecular diagnostics

TREATMENT

Immediate induction with liposomal Amphotericin B IV 5-10 mg/kg BW with strict metabolic control

In case of impaired renal function, Posaconazole IV 300 mg BID x 1day, then 300 mg OD OR Isavuconazole 200 mg TID x 2 days,then 200 mg once daily

Prepare the patient for surgery

Predominantly sino nasal involvement

Limited / no involvement of the orbits, vision preserved

Extensive Orbital involvement

Source : Honavar SG. Code Mucor: Guidelines for the Diagnosis, Staging and Management of Rh -Orbito-Cerebral Mucormycosis in the Setting of COVID-19. Indian J Ophthalmol 2021;69:1361-5.

Early and aggressive debridement of paranasal sinuses and medial orbital wall with clean margins

No / Limited CNS involvement

Extensive CNS involvement

Retrobulbar Amphotericin B inj 3.5 mg/ml +/- sinus irrigation with Amphotericin B 1 mg/ml with endoscopy/ image guided debridement

Disease progression ,worsening of orbital component in , < 72 hrs

Orbital extenteration + aggressive debridement of paranasal sinuses (Turbinectomy/ Palatal resecetion/ Orbital wall resection may be needed) with clear margins

Only supportive treatment if surgery not feasible

Orbital Exenteration

Metabolic condition stabilizes, no disease progression

+/- sinus irrigation with Amphotericin B 1 mg/ml with endoscopy/ image guided debridement

Continue therapy with Liposomal Amphotericin B IV 5-10 mg/ kg BW x minimum 4 weeks, followed by oral 1.Posaconazole 300 mg BID x 1 day, followed by 300 mg OD x 3 -6 months/ a minimum of 6 weeks following clinical & radiological regression.

2. Isavuconzole 200 mg TID x 2 days, then 200 mg OD x 3 -6 months/ a minimum of 6 weeks following clinical & radiological regression.

If refractory follow salvage therapy by ECMM

Source : 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.

UPDATES:

- Caption changed to **Covid Diagnostic And Treatment Algorithm Ver 3/21**
- Long Covid added
- Version 3 dated 26/5/2021
  Version 2 dated 20/5/2021
  Version 1 dated 7/5/2021

This is a SARS Covid 19 guideline procured from various sources like GOI, NIH/CDC, and hospitals like Apollo Hospitals. These are to help in decision making by clinicians, institutions or help the common people to understand categorization of patients according to severity and subsequent evidence based treatment. This is to be updated from time to time. This is to be used in consultation with physicians.

Gavista Health Foundation, as an issuer will not be responsible, if someone uses the same without consulting their physicians and without following latest Government guidelines.

USE MASK ,MAINTAIN PHYSICAL DISTANCING, FOLLOW DOCTOR'S GUIDANCE, **DO NOT SELF MEDICATE** : HELP THE HEALTH WORKERS TO SERVE YOU BETTER

Gavista Health Foundation (A section 8 company)

This will be appended with a Handbook on common Covid related topics that are regularly updated