MANAGEMENT PROTOCOL FOR COVID-19

Department of Health and Family Welfare
Government of West Bengal

INDEX

LABORATORY CONFIRMED COVID 19 PATIENT

MILD DISEASE

Uncomplicated URTI (&/or Fever) **WITHOUT** breathlessness/ Hypoxia

HOME ISOLATION / SAFE HOME

- Supportive Management
- Mask, Hand Hygiene, Physical distancing, droplet precaution
- Hydroxychloroquine (400 mg BD on Day 1, followed by 400 mg OD for 4 Days) **considering high risk groups with prior ECG**
  OR
  IVERMECTIN 12 mg OD for 5 Days with **DOXYCYCLINE** 100 mg BD for 7 days
- MONITOR: SpO_2, BP, Temp, Pulse, Sensorium
- Preferable Investigations: CXR PA, CBC, CRP, LFT, ECG, CBG, Serum Creatinine

Warning Signs

- **Difficulty in breathing**
- **Chest pain/ tightness**
- **Severe Cough**
- **Resting tachycardia**
- **SpO2 <94% (Room Air)**
- **6 minutes walking induce deoxygenation** (3 min for >60 years/ having co- morbidities)
- **As advised by physician**

REFER TO COVID HOSPITAL (WARD/ICU)

After clinical Improvement discharge as per revised discharge criteria

MODERATE DISEASE

Respiratory rate ≥24/min **AND/ OR** SpO_2< 94% on Room Air

ADMIT in COVID WARD

ANTIVIRALS

- **HCQ** 400 mg BD for 1-day f/b 400 mg OD for next 4 days
  Or
  Inj **REMDESIVIR** 200 mg Iv on day 1 f/b 100 mg IV daily for 5 days (Not to use both together)
  Or
  IVERMECTIN 12 mg OD for 5 Days with **DOXYCYCLINE** 100 mg BD for 7 days
- **CONVALESCENT PLASMA**

OXYGEN SUPPORT

- Target SpO_2 ≥ 95 % (88-92% in patients with COPD)
- Preferred Devices for oxygenation: non-re-breathing face mask,
- Conscious proning may be used in whom despite use of high flow oxygen hypoxia persist. (sequential position changes every 1-2 hours)

STEROIDS *(Indications:Increasing Oxygen requirement, increasing inflammatory markers, within 48 hours of admission)*

- IV methylprednisolone 0.5-1 mg/kg for 3-5 days
  OR
- Dexamethasone 0.1 to 0.2 mg/kg for 3-5 days

ANTICOAGULATION *(Prophylaxis for all high-risk patients, Therapeutic for suspected or documented Pulmonary Thrombo-embolism, increased PT, aPTT, raised D-dimer, prolonged immobilization, cancer, etc)*
Prophylactic dose of UFH or LMWH (Enoxaparin 40mg day SC)
Therapeutic dose (Enoxaparin 40 mg SC BD)

ANTIBIOTICS (Antibiotics should be used judiciously as per Antibiotic protocol)

Monitor

- CBC, LFT, KFT, D-dimer, Ferritin, Trop T, CRP, ECGCoagulation Profile.
- Change in oxygen requirement
- Work of breathing
- Hemodynamic instability

SEVERE DISEASE

Respiratory rate ≥ 30/min **AND/ OR** SpO_2< 90% on Room Air

ADMIT in COVID ICU

RESPIRATORY SUPPORT

- HFNC if work of breathing is LOW
- A cautious trial of NIV with helmet interface (if available otherwise face mask interface)/ CPAP with oronasal mask
- Consider Intubation if work of breathing is high/ NIV is not tolerated
- Lung protective ventilation strategy by ARDS net protocol
- Prone ventilation when refractory Hypoxemia

ANTIVIRAL

- Antiviral agents are less likely to be beneficial at this stage; use of Remdesivir to be decided on case to case basis

CORTICOSTEROIDS

- IV Methylprednisolone 1- 2mg/kg in 2 divided doses for 5-7 days OR
- Dexamethasone 0.2 to 0.4 mg/kg for 5-7 days

TOCILIZUMAB may be considered on a case to case basis after shared decision making

ANTICOAGULATION

- High-dose prophylactic UFH or LMWH (e.g. Enoxaparin 40 mg or 0.5 mg/kg BD SC), if not at high risk of bleeding

ANTIBIOTICS should be used judiciously as per Antibiotic protocol

INVESTIGATIONS

Essential investigations along with Cultures (Blood / Urine), FBS, PPBS, Ferritin, Trop-T/ Quantitative Troponins, Procalcitonin, CRP, LDH, D-Dimer, Coagulation Profile, NCCT Chest, USG Chest

SUPPORTIVE MEASURES

- Maintain euvolemia
- Sepsis/septic shock: manage as per protocol and antibiotic policy
- Sedation and nutrition therapy as per existing guidelines

EUA/ Off label therapies (use based on limited available evidence):

- **Remdesivir**(EUA) to be considered in Moderate to severe disease (requiring oxygen): Rule out renal or hepatic dysfunction (eGFR <30 ml/min/m2; AST/ALT >5 times ULN), Not to be combined with HCQ
- **Tocilizumab** (Off-label) may be considered in when all the below criteria are met: Moderate to Severe disease, significantly raised inflammatory markers (CRP &/or IL-6), Not improving despite use of steroids, Rule out active bacterial infections. The recommended dose is 4 to 8mg/kg (with a maximum dose of 800 mg at one time) in 100 ml NS over 1 hour (dose can be repeated once after 12 to 24 hours, if needed)
- **Convalescent plasma** (Off-label) may be considered when following are met: Early moderate disease, Increasing oxygen requirement
- **Ivermectin**Clinical trial is going on. Physicians should share clinical records and dataregarding use of Ivermectinwith state. **Ivermectin** and doxycycline combination can be used in mild-moderatediseases.

DISEASE EPIDEMIOLOGY

Current available evidence for Covid 19 suggests that the causative virus (SARS-CoV-2) has a zoonotic source closely related to bat-origin SARS-like coronavirus. It is an enveloped RNA beta coronavirus related to the Severe Acute Respiratory Syndrome (SARS) virus, and the virus has been shown to use the angiotensin-converting enzyme 2 (ACE2) receptor for cell entry.

The persons infected by the novel coronavirus are the main source of infection. Direct person-to-person transmission occurs through close contact, mainly through respiratory droplets that are released when the infected person coughs, sneezes, or talks. These droplets may also land on surfaces, where the virus remains viable. Infection can also occur if a person touches an infected surface and then touches his or her eyes, nose, or mouth.

The median incubation period is 5.1 days (range 2–14 days). The precise interval during which an individual with COVID-19 is infectious is uncertain. As per the current evidence, the period of infectivity starts 2 days prior to onset of symptoms and lasts up to 8 days. The extent and role played by pre-clinical/ asymptomatic infections in transmission still remain under investigation.

PATHOPHYSIOLOGY

Most patients with Covid-19 predominantly have a respiratory tract infection associated with SARS-CoV-2 infection. However, in a small proportion of cases, they can progress to a more severe and systemic disease characterized by the Acute Respiratory Distress Syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury and cardiac injury.It is also a hypercoagulable state with micro/macro thrombi being formed in various organs leading to organ damage.

CYTOKINE STORM

Cytokine storm is an acute hyperinflammatory response that may be responsible for critical illness in patients with Covid-19. Critically ill Covid-19 patients experiencing cytokine storm are believed to have a worse prognosis and increased fatality rate. IL-6 is mainly implicated in inflammatory and prothrombotic features of this condition.In SARS-CoV-2 infected patients, cytokine storm appears important to the pathogenesis of several severe manifestations of Covid-19.

Clinical characteristics of this entity are high rise of temperature, acute respiratory distress syndrome, thromboembolic diseases such as acute ischemic strokes caused by large vessel occlusion and myocardial infarction, encephalitis and acute kidney injury. It may ultimately progress to multi-organ dysfunction and death.

On laboratory investigations, features of increase in the inflammatory markers such as raised ESR and CRP, increase in the levels of IL-6, ferritin, LDH and D-dimer are often seen.

TOP SHEET FOR THE MANAGEMENT OF COVID-19 PATIENTS

PATIENT DETAILS

Name-	**Age-**	**Gender-**
Bed No.-	**Ward-**	**Date of Admission -**
Registration No.-	**Under-**	**Received By-**
Family Member Name-	**Relation-**	**Phone No.-**

TEST FORCOVID-19

Date	Method (RT-PCR / CB-NAAT / Other)	Test Center	Result

Symptoms: Fever, Malaise, Sore throat, SOB **Onset of symptoms:**

HIGH RISKFACTORS

Diabetes	Hypertension	IHD	COPD	Asthma
Chronic Kidney Disease	Chronic Liver Disease	HIV	Cancers	Cerebrovascular Disease
Immunosuppressive Drugs		Others		
Pregnancy	LMP	EDD		Fetal Status
List of Regular Medicines at Home				

PARAMETERSONADMISSION. DATE- TIME-

Temperature -	SpO2 -	Pulse Rate -	BP -
Breathlessness (Nil / Mild / Moderate / Severe)		Respiration Rate -	
Sensorium (Conscious / Drowsy / Stupor / Coma)			

BASIC TESTS DONE ON ADMISSION

Chest X-Ray	Time-	Normal / Abnormal	Findings -
ECG	Time-	QTc	Other Findings -
Complete Hemogram		**LFT**	
Creatinine	**Sugar**	**Na^+**	**K^+**

Signature of Staff Nurse **Signature of Doctor**

REGULAR MONITORING CHART

Date-			**Day –** 1st / 2nd / 3rd / 4th / 5th / 6th /7th / 8th / 9th / 10th /……	
	Morning	**Evening**	**Night**	**Observations**
Temperature				
Pulse				<100 / 100 - 120 / >120 per minute
Respiration				
BP				Syst<90, Diast<60 / Syst>100, Diast>70
Breathlessness				Nil / Mild / Moderate / Severe
SpO2				>95% / 95 - 90% / <90%
O2 Flow rate & Device				
Sensorium				Conscious / Drowsy / Stupor / Coma
Urine Output	ml	ml	ml	Total- ml in last 24hours
Auscultation				Breath Sound / Crepitation / Rhonchi
Medicines Given				Home Medicines / Insulin
Signature **Staff Nurse**				Appetite / Could Take Food and Medicines
Signature **Doctor on Duty**				Stable / Worsening / Ventilation / Referral / Discharge / Death

REPORT CHART FOR MODERATE / SEVERE PATIENTS (With Date and Time)

Blood Counts	Hb%	TC	Neutrophil	Lymphocyte	Platelet	
Biochemistry	LFT	Urea	Creatinine	Sugar (F/PP/R)	Na^+	K^+
ABG	pH / PaO2 / PaCO2 / HCO3			PaO2 /FIO2		
Other Tests	D-Dimer	P Time		APTT	CRP	
Other Tests	Ferritin	Trop-T				
Other Tests	Blood Culture	Urine Culture		Procalcitonin	Lactate	
Other Therapy	Antibiotics	Anti-Coagulant		Nor-Ad/ Dopamine	Corticosteroid	
Other Therapy	Tocilizumab	Covalesc. Plasma		Ventilation	NIPPV	

Signature of Staff Nurse **Signature of Doctor**

GENERAL PRINCIPLES

General principle for outdoor settings in all hospitals

1. Screening of patients with fever and respiratory tract symptoms in dedicated fever clinics
2. All patients attending fever clinic must wear a face mask, or may be provided with a mask
3. Maintain more than one meter distance from patient
4. Use appropriate PPE while seeing patients
5. Avoid face-to-face sitting with the patients

General principle for indoor settings in covid hospitals

1. All patients must always wear a 3-layer surgical mask after admission
2. No family member will be allowed in patient areas to meet the patient
3. Patient will not be allowed to carry any phone/mobile inside the ward along with him/her
4. A designated help line will communicate patient relatives about the patient's condition
5. Separate lifts should be used to transport the patients
6. Distance between two beds should be at least one meter.
7. All the paper works, e.g. writing notes in BHT or Treatment Cards should be done in a separate area.
8. Avoid moving and transporting patients out of their room unless medically necessary
9. Clean Environmental surfaces with detergents and 1% Sodium Hypochlorite solution
10. Manage Laundry, Food Service, Utensils and Medical Waste with safe routine procedures

Protective gears for the health care workers (HCWS)

1. **Health Care Workers (HCWs) should refrain from touching own Mouth, Nose or Eyes with potentially contaminated gloved or bare hands, and touching the surfaces.**
2. **HCWS must practice hand hygiene**
    - Before touching a patient
    - Before any clean or aseptic procedure is performed
    - After exposure to body fluid
    - After touching a patient, and after touching the patient's surrounding
    - Alcohol-based hand rub (ABHR) preferred if hands are not visibly soiled, Soap and water preferred when they are visiblysoiled
    - After examining each patient, they must wash their hands (with gloves on) with soap water or ABHR sanitizers
3. Full Set of PPE (Personal Protective Equipment) includes
    - N-95mask
    - Eye protection (Goggles) or facial protection (face shield)
    - Clean, non-sterile, coverall, long sleeved gown
    - Head Cover
    - Gloves
    - Shoe Cover
4. **Donning and doffing of PPEs to be done in separate areas with separate entry and exit**

5. Identify donning and doffing areas in each floor with hand washing facilities
6. **Advisory of Level of PPE in accordance with the level of Risk**

Area	HCW Category	Risk Level	Recommended PPE	Comment
• Triage Area inOPD • Doctors Chamber at OPD	• Doctor • Sister • SanitaryStaff	Moderate	N-95 Mask and Gloves	Aerosol Generating Procedure Not Allowed
• OPD	• Patient • PatientParty	Low	Triple Layer Medical Mask	Should Practice Hand Hygiene
• Emergency Dept Attending Non-SARI	• Doctor • Sister	Moderate	N-95 Mask and Gloves	Do
• Emergency Dept Attending SARI Pts.	• Doctor • Sister	High	Full Set of PPE	Aerosol Generating Procedure, only if absolutely needed
• Isolation Ward • COVID Ward	• Doctor • Sister	High	Full Set of PPE	Do
• Critical Care Unit	• Doctor • Sister • Technician	High	Full Set of PPE	Do
• Lift Service	• Liftman	Moderate	N-95 Mask and Gloves	Operating Lifts that Carry Patients
• Laboratory	• Doctor • Technician	High	Full Set of PPE	Sample Collection & Transport & Testing
• Sanitation	• Sanitary Staff	Moderate	N-95 Mask and Gloves	Cleaning Surfaces, Floor and Changing Linen
• Mortuary • ICU	• Dead Body Handling Staff	Moderate	N-95 Mask and Gloves	Dead Body Handling
• Administration • Maintenance PWD	• Administrator • Accountant • Engineering	Mild	Triple Layer Medical Mask	Administrative office Maintenance

CORRECT SEQUENCE OF DONNING AND DOFFINGOF PPE

CORRECT SEQUENCE FOR *DONNING* PERSONAL PROTECTIVE EQUIPMENT (PPE)

The type of PPE used will vary based on the level of precautions required; e.g., Standard and Contact, Droplet or Airborne Infection Isolation.

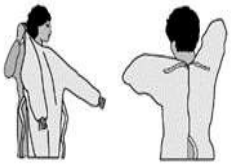
Remove hand jewellery and tie back hair.

Clean and dry hands thoroughly.

1. GOWN / APRON

Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back

Fasten in back of neck and waist



2. MASK OR RESPIRATOR

Secure ties or elastic bands at middle of head and neck

Fit flexible band to nose bridge

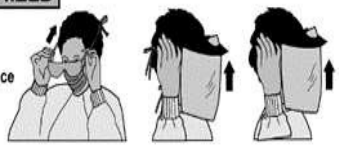
Fit snug to face and below chin

Fit-check respirator

3. GOGGLES OR FACE SHIELD

If you wear glasses put them on.

Place goggles or face shield over face and eyes and adjust to fit



4. GLOVES

Extend to cover wrist

Capital & Coast District Health Board
Ōpoko ki te Uru Hauora

Infection control January 2005. Developed using CDC Guidelines 2005

CORRECT SEQUENCE FOR *REMOVING* PERSONAL PROTECTIVE EQUIPMENT (PPE)

1. GLOVES

Outside of gloves are contaminated—DO NOT TOUCH!

Grasp outside of glove with opposite glovedhand; peel off

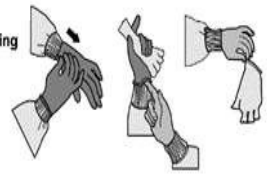
Hold removed glove in gloved hand

Slide fingers of ungloved hand under remaining glove at wrist

Peel glove off over first glove

Discard gloves in waste container

Clean and dry your hands thoroughly



2. GOGGLES OR FACE SHIELD

Outside of goggles or face shield are contaminated—DO NOT TOUCH!

To remove, handle by head band or ear pieces

Place in designated receptacle for reprocessing or in waste container

Clean and dry your hands thoroughly

3. GOWN / APRON

Gown front and sleeves are contaminated—DO NOT TOUCH!

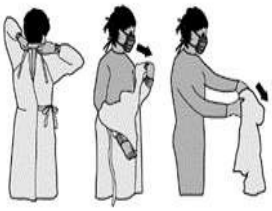
Unfasten ties

Pull away from neck and shoulders, touching inside of gown only

Turn gown inside out

Fold or roll into a bundle and discard

Clean and dry your hands thoroughly



4. MASK OR RESPIRATOR

Front of mask/respirator is contaminated—DO NOT TOUCH!

Grasp bottom, then top ties or elastics and remove

Discard in waste container

Clean and dry your hands thoroughly

Please visit the link below:
Donning and Doffing of PPE by Health-care workers by AIIMS New Delhi

https://youtu.be/8PSBOZUelTc

METHODS FOR SPECIMEN COLLECTION AND TRANSPORT FOR RT PCR

SPECIMEN COLLECTOR MUST WEAR FULL PPE

Specimen Collection

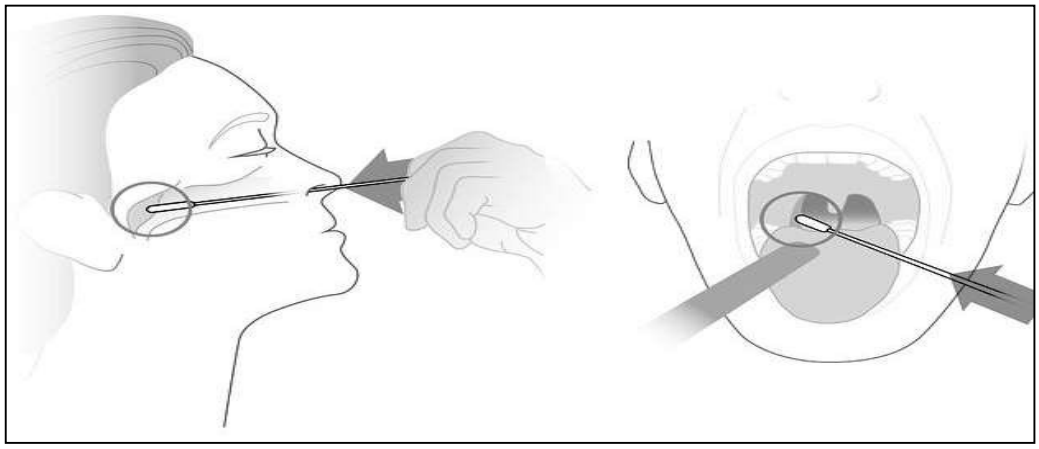
Preferred sample	Throat and nasal swab in viral transport media (VTM) and transported in cold chain.
Alternate	Nasopharyngeal swab, BAL or endotracheal aspirate which has to be mixed with the viral transport medium and transported in cold chain.

Nasopharyngeal Swab*:*

- Insert flexible wire shaft mini tip swab through the nares parallel to the palate (not upwards) until resistance is encountered indicating contact with the nasopharynx.
- Swab should reach the depth equal to distance from nostrils to outer opening of the ear.
- Gently rub and roll the swab.
- Leave swab in place for several seconds to absorb secretions.
- Slowly remove swab while rotating it.

Oropharyngeal Swab (Throat Swab): Insert swab in to the

1. Posterior pharynx and tonsillar areas.
2. Rub swab over both tonsillar pillars and posterior oropharynx
3. Avoid touching the tongue, teeth, and gums.



4. **Storage**
   - Place swabs immediately into sterile tubes containing 2-3 ml of Viral Transport Media.
   - Store specimens at 2 - 8°C for up to 72 hours after collection.
5. **Transport**
   - Send the sample specimen in Viral Transport Media to Testing Centre immediately
   - If delayed, store specimens at 2-8°C, and transport overnight on icepack maintaining proper cold chain.

METHODS FOR SPECIMEN COLLECTION AND TRANSPORT FOR RAPID ANTIGEN KIT

Rapid Antigen Test

Lateral flow assay
Rapid detection of SARS-CoV-2 (causing COVID-19) specific antigens
Nasopharyngeal swab used as sample for testing

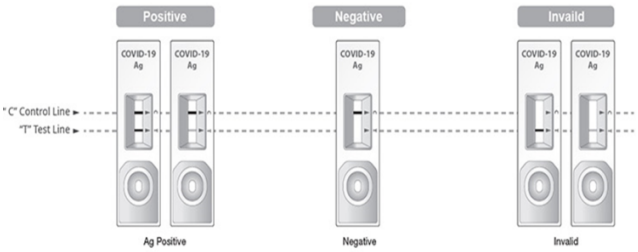
Sample collection, testing & data entry

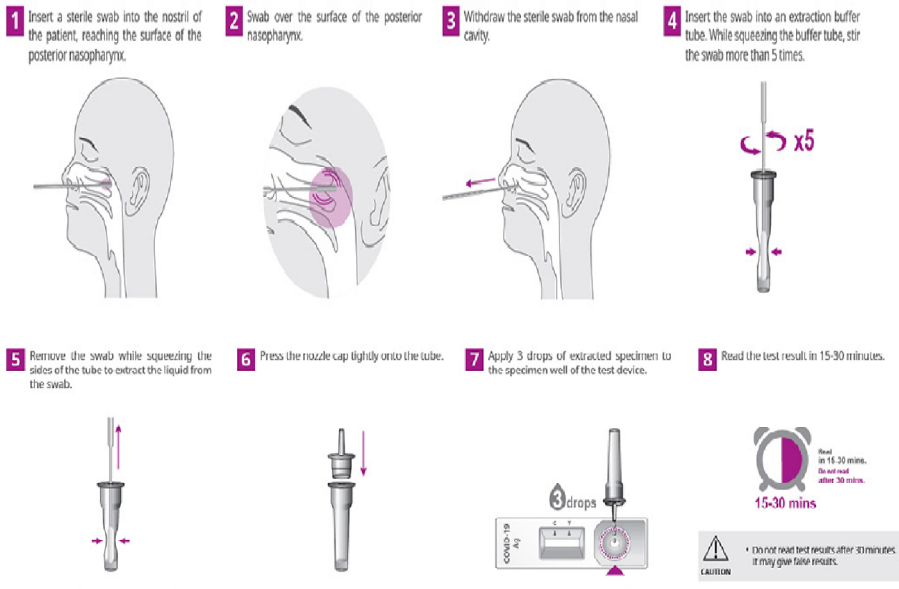
- Sample collection should be done by trained personnel wearing proper PPE.
- Only nasopharyngeal swab should be collected from each person. No other sample should be collected.
- For discarding of the kits and PPE, proper biomedical waste management bags should be available at the ATC.
- Clinical and demographic details of the patient being tested must be filled up in the Specimen referral form (SRF) for COVID-19 testing. Current version of the SRF available at icmr.gov.in must be used.

Interpretation

- **Positive:** If control and test band is visible. *No other confirmation is needed*
- **Negative:** If only control line is visible. *Negative can be false negative*

For symptomatic people who are negative by rapid antigen testing, nasal swab/throat swab should be collected in VTM for real-time PCR testing at the nearby lab. The VTM should be sent under cold conditions to an ICMR approved testing laboratory.





CASE DEFINITIONS

Suspect Case

A. patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset;

OR

B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset;

OR

C. A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

Probable Case

A. A suspect case for whom testing for the COVID-19 virus is inconclusive. **OR**

B. A suspect case for whom testing could not be performed for any reason.

Confirmed Case

A person with laboratory confirmed infection of COVID-19, by RT PCR or Rapid Antigen Test irrespective of clinical signs and symptoms

Mild disease

Patients with **uncomplicated upper respiratory tract infection**, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache **Without evidence of breathlessness** or Hypoxia (normal saturation).

Moderate disease

Pneumonia with no signs of severe disease

Adolescent or adult with presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO2 <94% (range 90-94%) on room air, Respiratory Rate more or equal to 24 per minute.

Child with presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO2 <94% (range 90-94%) on room air, Respiratory Rate more or equal to 24 per minute.Fast breathing (in breaths/min):< 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40

Severe disease

- Clinical signs of Pneumonia **PLUS** one of the following: **respiratory rate >30 breaths/min, severe respiratory distress, SpO2 <90% on room air.**
- Case with **Moderate Disease PLUS ARDS / Acute Respiratory Failure** and/or, **Sepsis with Multi-Organ Dysfunction Syndrome** and/or, **Septic Shock**

ILI :one with acute respiratory infection with fever >38C and cough with onset within last 10 days
SARI: case with acute Respiratory infection with fever >38C and cough with onset within last 10 days AND requiring hospitalization

SEVERE DISEASE

❖ ARDS(Acute Respiratory Distress Syndrome)

Onset: new or worsening respiratory symptoms within one week of known clinical insult.

Chest imaging (Chest X ray and portable bed side lung ultrasound): bilateral opacities, not fully explained by effusions, lobar or lung collapse, or nodules.

Origin of Pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g.echocardiography) to exclude hydrostatic cause of infiltrates/ oedema if no risk factor present.

Adults	Children
• **Mild ARDS**: 200 mm Hg<PaO_2/FiO_2 ≤300 mmHg(with PEEP or CPAP ≥5 cm H_2O)	• Bi-PAP or CPAP ≥5 cm H_2O via full face mask: PaO_2/FiO_2 ≤ 300 or SpO_2/FiO_2≤264 • Mild ARDS (invasively ventilated): OI ≥ 4 - < 8 or, OSI ≥ 5 - < 7.5 • Moderate ARDS (invasively ventilated): OI ≥ 8 - < 16 or, OSI ≥ 7.5 - <12.3 • Severe ARDS (invasively ventilated): OI ≥ 16 or, OSI ≥ 12.3
• **Moderate ARDS**: 100 mmHg < PaO2/FiO2 ≤200 mmHg (with PEEP ≥5 cm H_2O)	
• **Severe ARDS:** PaO_2/FiO_2 ≤ 100 mmHg with PEEP ≥5 cm H_2O)	

* OI = Oxygenation Index andOSI = Oxygenation Index using SpO_2

When PaO2 is not available, SpO2/FiO2 ≤ 315 mmHg suggests ARDS (including in non-ventilated patients) In absence of ABG facility at the hospitals, use SpO2/FiO2 ratio as described below:

PaO_2/FiO_2	SpO2/FiO2
<400	<512
<300	<357
<200	<214
<100	<89

❖ SEPSIS (SOFA Score ≥ 2)

SOFA Score: Please see Annexure 5

Sepsis	SOFA (Total Score 0 – 24)
Life threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection	1. PaO_2-FiO_2 Ratio (Score 0 – 4)
	2. Platelet Count (Score 0 – 4)
	3. Bilirubin (Score 0 – 4)
	4. Glasgow Coma Scale (Score 0 – 4)
	5. MAP & Vasopressor Requirement (Score 0 – 4)
	6. Creatinine and / or Urine Output (Score 0 – 4)
	Sepsis = SOFA ≥ 2 (Baseline score to be assumed as Zero if data not available)

Modified Sepsis-related Organ Failure Assessment (MSOFA)

Score	0	1	2	3	4
Respiration PaO_2(mmHg) /FiO_2 SPO_2/FiO_2 (%)	>400 >400	<400 <400	<300 ≤ 315	<200 ≤ 235 With Respiratory support	<100 ≤ 150 With Respiratory support
Liver	No scleral icterus or jaundice			Scleral icterus or jaundice	
Cardiovascular Hypotension *ug/kg/min for 1 hour	MAP≥70	MAP <70	*Dopamine <5 or *Dobutamine (any dose)	*Dopamine5.1-15 or *Adrenaline≤0.1 *Norepinephrine≤0.1	*Dopamine>15 or *Adrenaline>0.1 *Norepinephrine>0.1
CNS Glasgow Coma Scale	15	13-14	10-12	6-9	<6
Renal Creatinine (mg/dL) Creatinine (umol/L) Urine Output (mL/day)	<1.2 <106	1.2-1.9 106-170	2.0-3.4 177-301	3.5-4.9 309-433 <500	>4.9 >433 <200

❖ SEPTIC SHOCK

Adult	Children
Persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level < 2 mmol/L	Any Hypotension (SBP 2 SD below normal for age) **Or**, Any Two of the following:- 1. Altered mental state 2. Bradycardia or tachycardia (HR 160 bpm in infants and HR 150 bpm in children) 3. Prolonged capillary refill (>2 sec) or warm vasodilation with bounding pulses 4. Tachypnea 5. Mottled skin or petechial or purpuric rash 6. Increased lactate 7. Oliguria 8. Hyperthermia or hypothermia.

TRIAGE

Cases	Treatment at
Suspected Mild Case	**Home isolation**
Suspected Moderate / Severe Case (SARI)	**SARI ward**
Test Confirmed Mild Case	**Home isolation/ Safe Home**
Test Confirmed Moderate / Severe Case AND Test Confirmed Mild Case with High Risk*	**Designated Covid ward/ CCU/ HDU**

** [Patients with Age > 60 years; Chronic Lung Diseases; Chronic Liver Disease; Chronic Kidney Disease; Hypertension; Cardiovascular Disease; Cerebrovascular Disease; Diabetes; HIV; Cancers; on Immunosuppressive drugs.]*

MANAGEMENT OF MILD CASES

Patients with suspected or confirmed mild COVID-19 must be isolated to break the chain of transmission. Patients with mild disease may present to primary care/outpatient department, or detected during community outreach activities, such as home visits or by telemedicine.

- Mild cases can be managed at **Home isolation or Safe Home or Satelite Covid Centre**.
- Detailed **clinical history** is taken including that of co-morbidities.

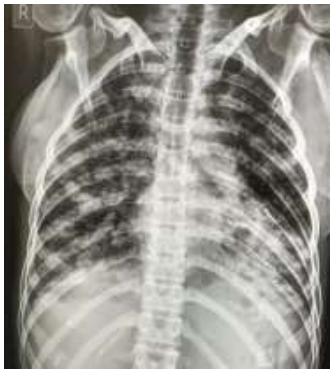
Following parameters should be observed by doctor / sister during daily rounds and recorded thrice daily / on worsening of symptoms

1. **Temperature**
2. **SpO_2 (By Pulse Oximeter)**
3. **Blood Pressure**
4. **Sensorium (conscious, drowsy or stupor)**
5. **Pulse**
6. Respiratory Rate
7. Urine Output
8. Chest Examination - Breath sound, crepitation andrhonchi

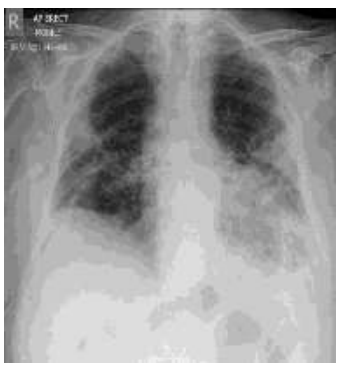
First seven features may be checked by the on duty sister.First five parameters are essential and must be recorded time to time in each shift and duly recorded in the top sheet.

Essential investigations for mild cases

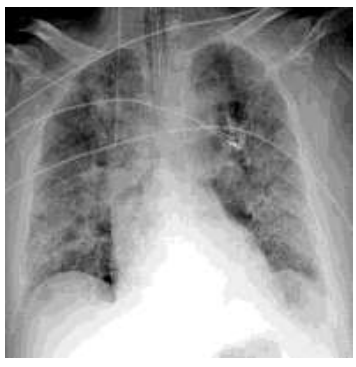
1. **Complete Hemogram**: common abnormalities are Leukopenia with Absolute Lymphocytopenia (On Admission and Daily)
2. **X-Ray Chest PA view**: (On admission / every 3rd day/ at worsening of symptoms):
    - In two third cases Chest X-ray may be normal.
    - Ground glass opacities and interstitial involvement are early changes.
    - Worsening of X ray feature is characterized by appearance of consolidation- bilateral/ multi-lobar
    - Bilateral involvement with lower lobe predominance and peripheral distribution is most common finding
    - Pleural involvement is not common
    - Chest X-ray is at its worst at 10-12 days from onset of symptoms.



Chest X-ray showing bilateral lung opacities



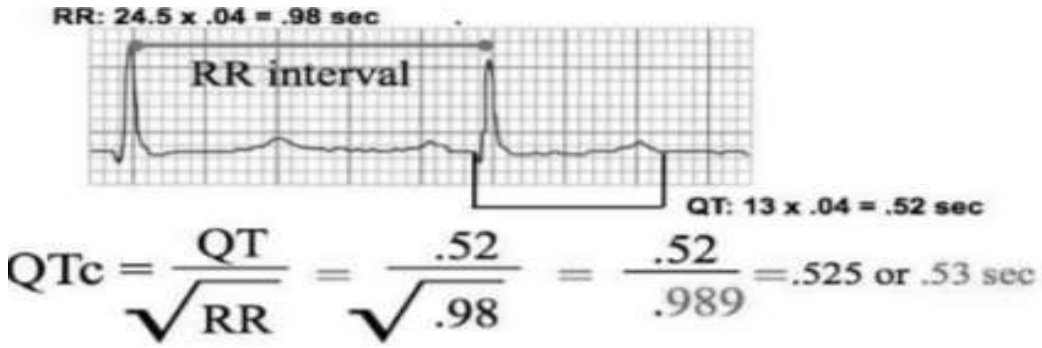
Chest X-ray showing extensive bilateral ground-glass opacities



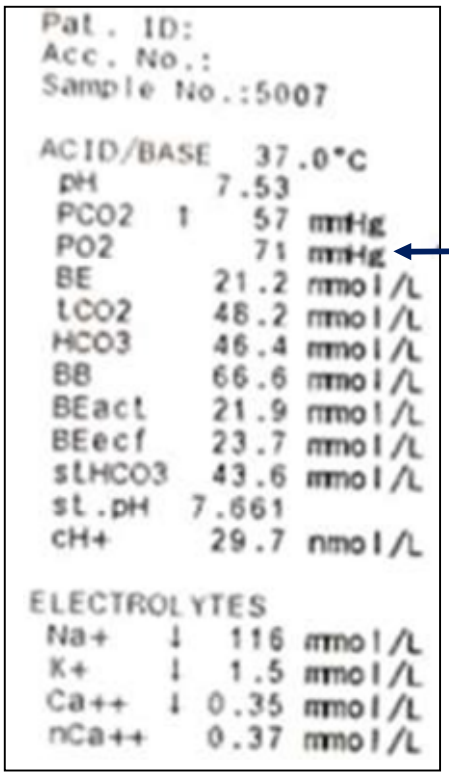
Chest X-ray showing bilateral, symmetrical peripheral consolidation with perihilar infiltrates

3. LFT: Raised Transaminases, Hyperbilirubinemia (Send on Admission / day 4 / day 7 / onWorsening)
4. Serum Creatinine: May be raised (Send on Admission / day 4 / day 7 / onWorsening)
5. Blood Glucose Level: Fasting, Post pandrial,
6. ECG: To look for ST-T changes suggestive of Myocarditis changes and to look for QTc prolongation. Hydroxychloroquine is to be administered cautiously, if QTc is >450 mSecs, and to be avoided if >500mSecs.

(To be done on Admission / on Worsening of symptoms)



7. ABG: (To be done in moderately or severely ill patients / on Worsening of symptoms)
Calculate PaO_2/FiO_2 Ratio to find the level of ARDS as describedabove.



PaO_2 in this ABG is 71 (as shown)

FiO_2 is 0.24, as the was getting Oxygen @ 24% by Nasal Cannula

PaO_2/FiO_2 Ratio in this ABG Report is

71/0.24 = 295.8

Suggestive of mild ARDS

8. Nasopharyngeal & Oropharyngeal Swabs for RT-PCR is not required to be repeated. May be done only if the patient is admitted as a suspect and not yet tested before admission**.**

Tests for mild cases on worsening

A. Chest X-Ray, ECG, Complete Hemogram and Blood Biochemistry for Sugar, LFT, Creatinine
B. ABG, CRP, D-dimer, Ferritin, Lactate, HRCT

Features for progression from mild disease to moderate disease

Clinical Suspicion:

1. **SpO_2 < 94% at Room Air** (For Obstructive Airway Diseases: SpO_2 < 90% at Room Air)
2. Stupor, Drowsiness or Confusion
3. SBP <90 mmHg AND/ OR DBP <60mmHg
4. Respiratory Rate>24/min
5. HR >100/min

Laboratory Markers/ parameters

6. Chest X-Ray showing Bilateral infiltrate (predominantly lower zones & periphery)/ Ground glass opacity
7. ST-T changes in ECG or high cardiac markers suggestive of Myocarditis (Trop-T positive)
8. Exacerbation of Co-morbid Conditions
9. Neutrophil : Lymphocyte Ratio ≥3.13
10. Development of Acute Kidney Injury
11. Raised Bilirubin or Liver Enzymes
12. Type 1 Respiratory Failure in ABG or PaO_2/FiO_2 ratio<300
13. Raised D-Dimer (>1000), Serum Ferritin, Lactate level (>2mmol/lit) or Procalcitonin

TREATMENT OF MILD CASE

Symptomatic Treatment

- Rest
- Vit C (500 mg BD), VitD3 (60K weekly), Zinc (50 mg OD).*
- Paracetamol for FEVER
- Antitussive for COUGH
- ORS for DIARRHOEA
- Metered Dose Inhalers for MILD BREATHLESSNESS
- Plenty of Fluids
- Nutritious Diet
- Laxative (For older person with constipation to avoid strain)

** Vit C, Vit D3, Zinc are micronutrient. They are immune modulator and required for general health and well being.*

Specific treatment for cases in high risk group

Tab. **Hydroxychloroquine** 400 mg BD on Day 1, followed by 400 mg OD for 4Days

Contraindications:

Children below 15 years, QTcin ECG >500 mSec, Retinopathy, Drug Interactions, Myasthenia Gravis, Porphyria, Epilepsy, G6PD deficiency, pregnancy, lactation.

If initial QTc> 450 mSec, perform basic biochemistry and ECG daily. Avoid Quinolones and Macrolides with Hydroxychloroquine, if possible. Monitor QTc closely if these are needed.

High risk group: Patients with

- Age > 60years
- Chronic Lung Diseases
- Chronic Liver Disease
- Chronic Kidney Disease
- Hypertension
- Cardiovascular Disease
- Cerebrovascular Disease
- Diabetes
- HIV
- Cancers
- On Immunosuppressive drugs

HCQ Prophylaxis	
• Asymptomatic household contacts of laboratory confirmed cases:	400 mg twice a day on Day 1, followed by 400 mg once weekly for next 3 weeks; to be taken with meals.
• All asymptomatic healthcare workers involved incontainment and treatment of COVID-19 andasymptomatic healthcare workers working in non-COVID hospitals/ non-COVID areas of COVID hospitals/ blocks. • Asymptomatic frontline workers, such assurveillance workers deployed in containment zones and paramilitary/ police personnel involved inCOVID-19 related activities.	400 mg twice a day on Day 1, followed by 400 mg once weekly for next 7 weeks; to be taken withmeals. The experts further recommended for its use beyond 8 weeks on weekly dosage with strict monitoring of clinical and ECG parameters which would also ensure that the therapy is given under supervision.

Specific Treatment (Experimental)

FAVIPIRAVIR: (Emergency use approval, Experimental: Not yet supported by quality RCT)
(NOT INCLUDED IN ICMR GUIDELINE; State recommendation- 'to avoid')

- **Mechanism of action:** It is a pyrazincarboxamide derivative that acts as an inhibitor of viral RNA dependent RNA polymerase causing chain termination and preventing RNA elongation.
- **Indications:** patients should satisfy following criteria:
    - Symptomatic COVID 19 infection confirmed by positive test for SARS CoV2.
    - Age above 18 yrs and below 75 yrs
- **Dose:** 1800 mg BD (9 tablets of 200mg each BD) on Day 1 followed by 800mg BD (4 tablets of 200 mg each BD) for a total duration of 7-14days
- **Contraindications:** Hyperuricaemia, severe hepatic &renal impairment, Pregnant and lactating mothers
- **Side Effects:** increased Uric Acid levels, diarrhea, decreased neutrophil counts, increase in AST/ALT.
- **Drug Interactions:** metabolised partly by Aldehyde Oxidase (AO) and partly by Xanthine Oxidase (XO). Precauitons for co-administration with Pyrazinamide, Repaglinide, Theophyline, Famciclovir**.**

IVERMECTIN(included in guideline in some countries both for prophylaxis and therapeutic use, **NOT INCLUDED IN ICMR GUIDELINE**; State recommendation-therapeutic use for clinical trial by expert under specific permission from state): Ivermectin, the well-known, effective, safe and affordable wide spectrum anti parasitc agent from since late-1970s, has been known to exert antiviral property against a host of viruses that cause dengue, Japanese Encephalitis, tick borne encephalitis, chikungunya, and even more recently Covid-19.While the antiviral potential of Ivermectin against SARS-Cov-2 may be attributed to it's inhibition of importin α/β1 mediated nucleo-cytoplasmic transport of the viral proteins, the potential benefit of ivermectin therapy may

rather/ also be explained by it's more general immune-modulatory role. It is selectively sequestered in pulmonary tissues, around three times of its plasma concentration, with long residence time.Following oral administration; it is well absorbed with plasma concentrations proportional to the dose.

However it is also recommended that all uses of ivermectin in prophylaxis and treatment of Covid-19 shall be deemed as "experimental" and all relevant clinical data regarding its use must be recorded in the prescribed data collection form in real time, and transmitted by email to the designated authority at rxivm.covid1@gmail.com.

- **Side effects:**It is usually well tolerated. Decreased leukocyte count (3%), eosinophilia (3%), and increased hemoglobin (1%) have been reported with the systemic use of systemic Ivermectin.
- **Caution:**Hepatic impairment, allergic disorders, HIV infection. Avoid in Pregnancy and children below 2 years. (Monitor LFT, hypersensitivity reaction etc)
- **Doses:**
  - **For Treatment in mild-moderate cases**: Tab Ivermectin12 mg once daily for 5 days PLUS Cap/ Tab Doxycycline 100 mg twice a day for 7 days
    Take Ivermectin with a fatty meal (say, half a cup of milk or half a tea-spoon of butter). Use in mild and moderate cases only.
  - **For prophylaxis**:
    Tab Ivermectin 12 Mg once daily on Day 1, Day 7 and followed by 12 mg once every 30 days. Take Ivermectin with a fatty meal.

Evidences:

1. Several observational studies in Bangladesh showed encouraging results in mild to moderate cases and showed increased recovery rate using Ivermectin.[Chowdhury et al, 2020]
2. In Latin American countries, Ivermectin has been approved in mild cases of Covid 19.
3. Australian study showed that Ivermectin can be taken as a preventive treatment by high risk individuals, or by those who test positive to minimize need for hospitalization [Borody et al, 2020]
4. In retrospective cohort study in USA, Ivermectin showed significantly lowered mortality rates when used in severe hospitalized cases. [Cennimo et al, 2020]
5. In an observational registry based study from 169 hospitals across different continents established the survival benefit of Ivermectin and it reduced the duration of hospital stay.[Patel et al, 2020]
6. Ivermectin and Doxycycline combination have already been recommended in several Indian states.
7. ICMR is yet to receive result of well designed randomized control trial. **References given at page 19*

Ivermectin and HCQ should not be used ideally together in case of prophylaxis and treatment as no in vitro or invivo studies have been conducted on the combined effect of HCQ and Ivermectin on SARS-Cov-2 infection.

DOXYCYCLINE and other tetracycline derivatives such as minocycline exhibit anti-inflammatory effects along with in vitro antiviral activity against several RNA viruses. Doxycycline is a strong and broad-spectrum inhibitor of MMPs. As lung immune injury/ARDS is prominent in patients with severe COVID-19, inhibiting MMPs may help repair the damaged lung tissue and enhance recovery. Also it provides coverage against

atypical bacterial pneumonia such as Mycoplasma pneumoniae and Legionella pneumophilia.
Contraindications: Pregnancy, children below 2 years

Antibiotics, especially of higher groups, have no role and should be avoided unless other co-infection is suspected. Doxycycline may be recommended and explained later. Doxycycline may be used for its various advantages as explained above, instead of giving other higher antibiotics.

When to refer to higher facility: Any patient developing ANY ONE **of the following:**

1. **SpO2 < 94% at Room Air**
2. **Confusion, Drowsiness**
3. **SBP <90 mmHg, DBP <60mmHg**
4. **X-Ray Chest PA- showing Bilateral infiltrate / Unilateral infiltrate / Ground glass opacity**
5. **Deranged Liver or Kidney Function**

When to discharge

1. **Mild / Very Mild / Pre-symptomatic cases can be discharged after 10 days of symptom onset with no fever for at least 3days**
2. Swab testing or Chest X-Ray is **not required** for discharge

Follow up

- All patients must undergo strict Home Isolation for 7 days after discharge
- First follow up visit within 14 days or when needed.

HOME ISOLATION OF MILD/ PRE-SYMPTOMATIC/ ASYMPTOMATIC CASES

Eligibility criteria for home isolation

1. **Mild symptomatic cases and pre-symptomatic or asymptomatic laboratory confirmed cases** as clinically assigned by the treating physician can opt for home isolation
2. Such cases **should have adequate facility at their residence for self-isolation** and also for quarantine of the family contacts
3. **A care giver should be available at their residence to provide care on 24 x 7 basis**
4. **Care giver and all close contacts of such cases should take Hydroxychloroquine prophylaxis** as per protocol and as prescribed by the treating medical officer
5. The patient will **agree to monitor his health**. For further follow up by surveillance teams, patient and the care giver will **regularly inform** his health status to the District Surveillance Team.
6. The patient will give an **undertaking of self-isolation** (Annexure) and will follow the guidelines
7. In addition to the guidelines available at **www.mohfw.gov.in/Guidelinesforhomequarantine.pdf**, required instructions for the care giver and the patient as in Annexure II should be also followed.
8. *Please follow the link:* https://www.wbhealth.gov.in/uploaded_files/corona/guideline_for_home_quarantine-bengali_final.pdf

What to monitor during home isolation (at least 12 hourly)

- Temperature
- SpO_2 (By Pulse Oximeter)
- Blood Pressure
- Pulse
- CBG (if diabetic: Fasting and post pandrial)
- **6 Minute Walk Test**

When to seek medical attention during home isolation

Immediate medical attention must be sought if any of the following serious signs/symptoms develop:-

1. **Difficulty in breathing**
2. **Persistent pain or pressure in the chest**
3. **Mental confusion or inability to arouse**
4. **Developing bluish discolorations of lips/ face**
5. Or as advised by physician

When to discontinue home isolation

Patient under home isolation will end home isolation

1. After 17 days from the onset of symptoms with at least 10 days from the remission offever
2. After 17 days from the date of sampling for pre-symptomatic or asymptomatic cases
3. **There is no need for swab testing by RT-PCR after the home isolation period is over**

Medicines

- Tab Ivermectin12 mg once daily for 5 days PLUS Cap/ Tab Doxycycline 100 mg twice a day for 7 days (Take Ivermectin with a fatty meal like half a cup of milk or half a tea-spoon of butter).
- Tab Paracetamol for fever
- Tab Vitamin C 500 mg twice daily*
- Tab Zinc 50 mg per day*
- Vitamin D360000 IU weekly*
- Supportive treatment for fever, cough, diarrhea etc

* These are not definite therapy for Covid 19 but these have effects on general well being as well as enhance immune status.

**Ref: Maharastra State Govt Covid19 Management Protocol*

Investigations:

- All routine investigations recommended for mild cases have to be sent

UNDERTAKING ON SELF-ISOLATION

I ……
S/W of ……,
Resident of……being diagnosed as a confirmed/suspect case of COVID-19, do hereby voluntarily undertake to maintain strict self-isolation at all times for the prescribed period. During this period I shall monitor my health and those around me and interact with the assigned surveillance team/ with the call center (1075), in case I suffer from any deteriorating symptoms or any of my close family contacts develops any symptoms consistent with COVID-19. I have been explained in detail about the precautions that I need to follow while I am under self-isolation. I am liable to be acted on under the prescribed law for any non-adherence to self-isolation protocol.

Signature: Date: Contact Number:

6 Minute Walk Test

- A 6 minute walk test is an established clinical test to look for cardio pulmonary exercise tolerance.
- American Thoracic Society recommends its use for prediction for mortality and morbidity in Heart failure, COPD and Primary Pulmonary Hypertension.
- A patient with pulse-oximeter attached to his finger is asked to walk in confines of his/her room.
- **Any drop in saturation below 93% or an absolute drop of more than 3 % or feeling unwell (light headed, SOB) while performing the tests are significant findings**.
- The test is used to unmask hypoxia
- Patients with positive 6 minute walk test may progress to become hypoxic and hence early intervention in form of admission to hospital or shifting to ICU and giving Oxygen and +/- steroids is recommended.
- **The 6 minute may be cut short for 3 minutes in patients above 60 years of age or having co-morbidities.**

Ref: Maharastra State Govt Covid19 Management Protocol

RED FLAG SIGNS

- **Resting tachycardia**
- **SpO2 < 94% at Room Air**
- **6 minute exercise induce deoxygenation**(3 minute walk test for patient more than 60 years of age or having comorbidities)
- **Neutrophil : Lymphocyte Ratio ≥3.13**

References for Ivermectin Use:

1. Chowdhury AT, Shahbaz M, Karim MR, Islam J, Dan G, He S. A comparative observational study on Ivermectin-Doxycycline and Hydroxychloroquine-Azithromycin therapy on COVID19 patients [Preprint] Available from: https:// www.researchgate.net/publication/342159343; 2020.
2. India e Trial Site News [Internet]. Ivermectin usage accelerates while the need for data is real: how about an ivermectin registry? [Internet]. Available from: https://www.trialsitenews.com/ivermectin-usageaccelerates- while-the-need-for-data-is-real-how-about-an-ivermectin- registry/; 2020 May.
3. Borody T, Daniels J. Phase II Double-Blind Randomized Placebo-Controlled Trial of Combination Therapy to Treat COVID-19 Infection.
4. Cennimo David J. What is the role of antiparasitic drug ivermectin in the treatment of corona virus disease 2019 (Covid-19)?.Updated: Jul 02, 2020. [Internet]. Available from: https://www.medscape.com/answers/2500114-197513/what-is-the-role-of-the antiparasiticdrugivermectin-in-the-treatment-of-coronavirus-disease-2019-covid-19.
5. Rajter JC, Sherman M, FattehN, Vogel F, Sacks J, Rajter JJ.ICON (Ivermectin in COvid Nineteen) study: use of ivermectin is associated with lower mortality in hospitalized patients with COVID-19 [medRxiv Preprint]. https://doi.org/10.1101/2020.06.06.20124461; 2020 Jun.
6. Patel A, Desai S, Grainger D, Mehra M. Usefulness of Ivermectin in COVID-19 Illness. 2020 Apr 19. Available at: SSRN 3580524.

MANAGEMENT OF MODERATE / SEVERE CASES

Same parameters like in mild cases should be observed during daily rounds by doctor, sister and recorded at least thrice a day or on worsening of symptom.

Investigations

All Routine Investigations Recommended for Mild Cases have to be sent

Additional investigations for moderate/ severe cases are as following:

1. Appropriate Cultures Blood / Urine (On Admission / on Worsening of symptoms)
2. For Diabetic patients - FBS, PPBS (as appropriate) [Laboratory /Glucometer]
3. Serum Ferritin
4. Trop-T/ Quantitative Troponins (When Suggestive)
5. Procalcitonin (To rule out secondary infection) - May be normal or mildly elevated
6. CRP
7. LDH
8. D-Dimer/ PT / INR / APTT / Fibrinogen / Platelets (To rule outDIC)
9. CT Scan Chest (Non-contrast) - If Chest X ray inconclusive or negative and suspicion ishigh
10. USG Chest: Where expertise available, can be used, as it may help sparing CT scan forall

Primary Findings on CT

- Ground-glass Opacities (GGO): usually bilateral, sub-pleural, peripheral opacities.
- Crazy Paving Appearance (GGOs and inter-/intra-lobular septal thickening)
- Air Space Consolidation may beseen
- Broncho-vascular thickening
- Traction Bronchiectasis may bepresent
- Thrombosed blood vessels, found as thickened vessel moving from centre to periphery

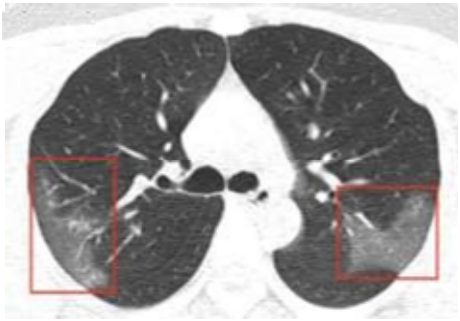
Temporal CT Changes

Four stages on CT have been described

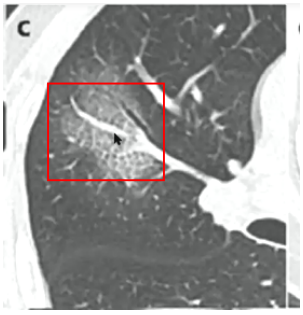
- Early / Initial Stage (0 - 4 days): Normal CT scan or GGO only
- Progressive Stage (5 - 8 days): Increased GGO and Crazy Paving Appearance
- Peak Stage (9 - 13 days):Consolidation
- Absorption Stage (>14 days): Abnormalities resolve at one month and beyond

CO-RADS Scoring: Level of suspicion Covid 19 infection

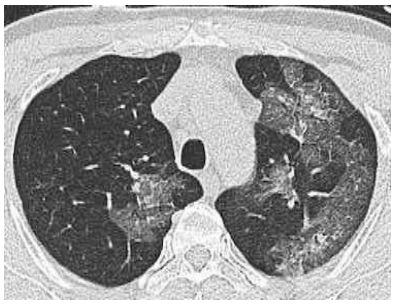
		CT Findings
CO-RADS 1	**No**	Normal/ non infectious abnormalities
CO-RADS 2	**Low**	Abnormalities consistent with infections other than Covid 19
CO-RADS 3	**Intermediate**	Unclear whether Covid 19 is present
CO-RADS 4	**High**	Abnormalities suspicious for Covid 19
CO-RADS 5	**Very High**	Typical Covid 19
CO-RADS 6	**PCR +ve**	



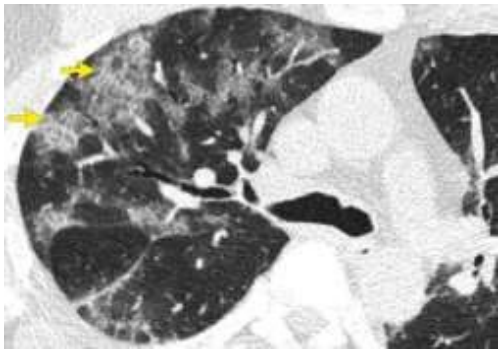
CT chest showing Bilateral Ground Glass Opacities (GGO) without Subpleural Sparing



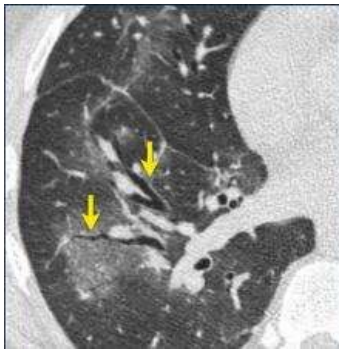
CT chest showing Peripheral Thrombo-embolism



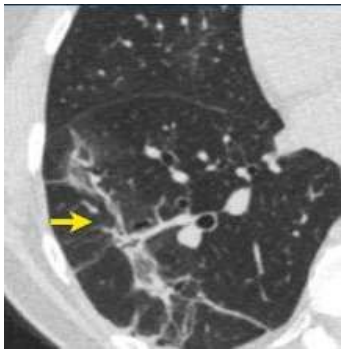
CT chest showing multifocal bilateral Ground-Glass Opacities with a posterior predominance.



CT chest showing thickened interlobular and intralobular lines with crazy paving appearance



CT chest showing bronchiectasis with a Ground Glass Opacities



CT chest showing sub-pleural bands and architectural distortion

Investigations to predict progression

- **CBC:** Monitor lymphocyte count. Lymphopenia is a risk factor for progression to severe disease. **Neutrophil Lymphocyte Ratio >3.13 is an independent risk factor for severe disease**
- **CRP:** Elevated levels of CRP may be seen in moderate to severe disease.
- **Liver Function Test:** Raised Transaminases, Hyperbilirubinemia, Acute liver failure in severe case
- **Renal Function Test:** Increased creatinine. Acute Kidney Injury in severe disease.
- **LDH:** Elevated LDH levels seen in moderate to severe disease. Marker of poor prognosis.
- **Ferritin:** Markedly elevated Ferritin level predicts poor outcome in patients with COVID-19.
- **D-Dimer, P-Time, APTT:** D-dimer >1mcg/ml predicts poor prognosis at an early stage. Increased D-Dimer, P-Time, APTT are markers of DIC/ Hypercoagulability and bad prognosis.

During the hyper-inflammatory state or Cytokine storm, which is expected to happen on Day 5 - Day 10, increase in the inflammatory markers such as raised ESR and CRP, increase in the levels of IL-6, ferritin, LDH and D-dimer etc are seen. So these parameters can be used to predict the progression.

SALIENT POINTS IN MANAGEMENT

Oxygen therapy

- Administer oxygen to all Severe Acute Respiratory Illness (SARI) patients and to patients with respiratory distress / hypoxemia /shock
- Start with nasal prongs @ 5L/min, or Simple Face Mask / Venturi Mask / Non-Rebreathing Mask @ 6-15L/min, as needed
- Titrate for target $SpO_2 \geq 95$ % (88-92% in patients with COPD)

Initial fluid management

- Conservative fluid strategy if no evidence of shock (**Fluid of choice: Ringer Lactate**)
- Cautious IV fluids
- Monitor for worsening of oxygenation during fluid therapy

Specific drug therapy for covid-19

Hydroxychloroquine:400mg BD on Day-1, followed by 400 mg OD on Day-2 to Day-5

IF THERE IS PROGRESSIVE WORSENING OF CONDITION

TOCILIZUMAB

Tocilizumab: (off label use, Experimental)

Tocilizumab is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R). Interleukin 6 (IL-6) is a cytokine that plays an important role in immune response and is implicated in the pathogenesis of COVID19 diseases.

Indications:Patients with moderate disease with progressively increasing oxygen requirements and in mechanically ventilated patients not improving despite use of steroids , Lung infiltrate on Chest Xray, Elevated inflammatory markers (Ferritin, CRP, IL6 > 5 times upper limit of normal)

Contraindications: Active infections(bacterial/fungal), Latent or clinical Tuberculosis, Pregnancy, lactation. Platelets <1lacs/cumm, Neutrophil <2000/cumm, ALT/AST >5 times upper limit of normal.

Dose: 4-8 mg /kg BW maximum 400 mg as a single one hour IV infusion in normal saline. This can be repeated after 12-24 hours, if necessary.

Adverse effects:upper respiratory tract infections, flu like symptoms, headache, high blood pressure, asymptomatic Liver enzyme elevation, skin rashes, gastritis and mouth ulcer.

Patients should be carefully monitored post Tocilizumab for secondary infections and neutropenia.

CONVALESCENT PLASMA

Convalescent plasma: (Emergency use approval, Experimental)

Convalescent plasma (Off Label) may be considered in patients with moderate disease who are not improving (oxygen requirement is progressively increasing) despite use of steroids. Convalescent plasma may confer clinical benefit including faster viral clearance when administered early in the disease course.

Special prerequisites while considering convalescent plasma include:

- ABO compatibility and cross matching of the donor plasma
- Neutralizing titer of donor plasma should be above the specific threshold (if the latter is not available, plasma IgG titer (against S-protein RBD) above 1:640 should be used)
- Recipient should be closely monitored for several hours post transfusion for any transfusion related adverse events
- Use should be avoided in patients with IgA deficiency or immunoglobulin allergy
- **Dose**: Dose is variable ranging

In event of the adverse transfusion event it is to be documented and the concerned blood centre should be informed. Only DCGI/ICMR approved centres may process convalescent Covid plasma. Any off-label convalescence Covid19 plasma use is to be approved by an expert review team along with the institutional ethics committee.

REMDESIVIR

Remdesivir (under emergency use authorization):

- **Indication**: Moderate to severe disease (on Oxygen). (Written informed consent should be obtained prior to administration)
- **Dose**: 200 mg IV on Day 1 , Then 100 mg IV OD for 4 days. (To be administered as an IV infusion over 30 – 120 minutes. Flush line with 30 ml NS after infusion is complete)
- **Contraindications**: SGPT >5 times upper limit, eGFR<30 ml/min or need for haemodialysis, Pregnancy/lactation, Child below 12 years, hypersensitivity.
- **Side effects**: anaemia, LFT abnormalities , AKI
- It should not be used later than 7-8days of onset of disease as it does not has any effect then.

Patient already on HCQs may continue with the same. Remdesivir should not be started in those cases as it may cause aggravation of side effects and may not have any advantage.

ANTICOAGULATION THERAPY

Anticoagulation therapy

Whom to start?

- **Venous Thrombo-Embolism (VTE) prophylaxis** for all high-risk patients i.e. patients with multiple co-morbidities and moderate/severe Covid 19 without any comorbidity
- **Therapeutic** for considering PE for patients with
    - Sudden onset of oxygenation deterioration, respiratory distress, and reduced blood pressure or imaging (CT angiogram) proved.
    - High Risk patients (increased PT, aPTT, D-dimer , FDP , prolonged immobilization, cancer, hospital admission >7 days etc.)
    - Signs of microthrombi induced organ dysfunction
    - Documented/suspected Macro-Thromboembolism

What to use? LMWH rather than oral anticoagulants, including switching patients who were taking a direct oral anticoagulant (DOAC) or vitamin K antagonist.

How long to continue?

During Hospital Stay: Prophylactic/Therapeutic dose as indicated

Post discharge: On the basis of individual risk/benefit ratio- Prophylactic dose to be given depending on:

- Duration of Hospital Stay
- Reduced mobility
- Previous VTE
- High D-Dimer level
- Malignancy
- Therapy can be extended upto 4-6 wks

How to estimate Risk Stratification in Hospitals?By serial estimation of D-dimer during Hospital admission:

- D-dimer <1000 microgram/dl: continue prophylactic dose
- D-dimer >2000 microgram/dl: imaging is warranted. If imaging not feasible and patient deteriorates clinically, give therapeutic dose
- D-dimer between 1000-2000mcg/dl: no clear guideline. Physician to apply his discretion

Dose of LMWH

- CrCl>30 ml/min: Enoxaparin 40mg SC /daily(consider BD dose in severe case)
- CrCl<30 ml/min: Enoxaparin 20mg SC/daily
- BMI >40: Enoxaparin 40 mg SC BID
- If anticoagulation contraindicated: mechanical device

How to monitor treatment depending on the dosage of Anticoagulants?

1. D dimer alternate daily (if possible)
2. Prothrombin time(INR) / aPTT
3. Platelet count

Use of antiplatelet drugs in patients already receiving them:

Platelet Count	Number of Antiplatelet Drugs	Further Treatment
<25,000	Two Drugs	Stop antiplatelets
25,000-50,000	Two Drugs	Stop Aspirin and Monitor Carefully
>50,000	Two Drugs	Continue management

Management of bleeding:

Clinically-overt bleeding is uncommon in the setting of COVID-19. However, when bleeding occurs in COVID-19-associated DIC, blood products support is to be given as follows:

- Platelet concentrate to maintain platelet count >50 000 in DIC patients with active bleeding or >20 000 in those with a high risk of bleeding or requiring invasive procedures.
- Fresh frozen plasma (FFP) (15-25 mL/kg) in patients with active bleeding with either prolonged PT and/or aPTT ratios (>1.5 times normal) or decreased fibrinogen (<1.5 g/L)
- Fibrinogen concentrate or cryoprecipitate to patients with persisting severe hypo-fibrinogenemia (<1.5 g/L)

Tranexamic acid should not be used routinely in COVID-19-associated DIC.

Post discharge: Anticoagulation therapy to continue in previously documented VTE.

STEROID THERAPY

Steroids have shown to decrease mortality by 33% in patients on ventilation and by 20% on patients on oxygen therapy.

What to use? 1.Methyl Prednisolone 2. Dexamethasone

When to use?

Moderate disease on Oxygen Therapy:

- If Oxygen requirement is increasing
- If inflammatory markers are increasing
- Preferably within 48 hours of admission

Severe Disease:

If not already given, use when oxygen requirement or inflammatory markers are increasing

Dose & Duration:

Moderate disease: 1. IV Methylprednisolone 0.5 to 1 mg/kg for 3 days **OR**

2. Dexamethasone 0.1 to 0.2 mg/kg for 3 days

Severe Disease: 1. IV Methylprednisolone 1 to 2 mg/kg for 5-7 days in 2 divided doses if not already given **OR**

2. Dexamethasone 0.2 to 0.4 mg/kg for 5-7 days in 2 divided doses if not already given

Precaution:

Larger doses and longer duration of steroid should not be used as it will delay the recovery from Covid-19 due to immunosuppressant.

Adjustments in different co-morbid conditions:

In case of patients with Diabetes mellitus, insulin dose needs to be titrated as steroid may increase/ alter glycemic status.

In case of hypertensive patients, antihypertensive drugs needs to be adjusted as steroids may alter blood pressure control.

Protocol for Rational Use of Antibiotics in the Management of Covid-19

[An Interim Guideline that shall be periodically updated]

General Principles:

1. Covid-19 being a viral disease, antibiotics *per se* have no role in it. Do not prescribe antibiotics routinely in Covid-19 unless bacterial co-infection is suspected.
2. Differentiate between infection and colonization clinically and based on infection markers, before considering antibiotic prescribing, switch or escalation.
3. In a Covid-19 patient who turned afebrile, a new onset fever may prompt suspicion of secondary bacterial infection. However, some Covid-19 patients show biphasic pattern of fever.
4. Consider using antibiotics to only those patientswith severe Covid-19 infection who have high oxygen demands and show signs of rapidly progressing respiratory failure. All patients with severe Covid-19 should not receive empiric antibiotics, if there is no clinical suspicion of and/or there is absence of biochemical or radiological markers of bacterial infections.

5. Antibiotics, when prescribed, should be done as per their PK/PD norm.
6. Consider empiric prescribing of antibiotics only in cases where bacterial infection cannot be excluded, e.g., COPD exacerbations with purulent sputum or radiological evidence of pneumonia, while awaiting Covid-19 test results. In case of confirmation of diagnosis as Covid-19, try to de-escalate antibiotic therapy as early as possible.
7. Consider antibiotic prescribing, guided by assessment of biomarkers of bacterial infection (total leucocyte count, C-reactive protein, pro-calcitonin), as per access to laboratory facility. However, C-reactive protein may be high in Covid-19 due to inflammation, and therefore may not be very reliable.
8. A CT-thorax, whenever available and/or feasible, may allow for a more exact determination of the typical infiltrate associated with bacterial lower respiratory tract infection as opposed to the ground glass opacities of Covid-19. However, chest X-ray may also help.
9. The choice of antibiotics should be guided by local antibiogram.
10. Microbiological tests (e.g., urine culture, blood cultures, sputum culture, as appropriate) should ideally be performed before initiation of any antibiotic treatment. However, a positive culture report does not necessarily prove presence of infection, unless this is accompanied by clinical signs and biochemical markers.
11. Once started, continuously re-evaluate antibiotic treatment intensively, and consider stopping it as soon as possible if the probability of bacterial super-infection is low, e.g.,
    - persistently low inflammatory biomarkers
    - negative culture tests
    - CT scan compatible with Covid-19 only

    Note that mere absence of fever should not be required as a criterion for stopping an antibiotic, since patients with Covid-19 often show persistent fever over several days.

    However, in general antibiotic therapy once started should be continued for a minimum of 5 days, or until the patient is afebrile for 48-72 hours; longer duration of therapy may be needed if initial therapy was not active against the identified pathogen or if it was complicated by extrapulmonary infections.
12. If parenteral antibiotic treatment is started, consider switch to oral antibiotics as soon as the patient is able to take oral medications.
13. For patients in ICU requiring mechanical ventilation, apply the standard measures to prevent ventilator-associated pneumonia (VAP) and other healthcare-associated infections.
14. Do not give antibiotics prophylactically to prevent bacterial pneumonia or other infections.
15. If during Covid-19 treatment, a secondary respiratory worsening occurs, do consider use of antibiotics after taking adequate respiratory samples and performing radiological diagnostics. Secondary worsening commonly seen at day 7–9 due perhaps to the hyper-inflammatory phase (adaptive immune reaction) rather than a bacterial super-infection. Other causes of respiratory worsening, e.g., cardiogenic failure, pulmonary embolism, fluid overload etc. should be ruled out.
16. Suspected Covid-19 patients may present with other infections such as urinary tract infections, skin and soft tissue infections, intra-abdominal infections etc. These should be considered in the differential diagnosis (especially in high risk patients) and be managed according to established guidelines. Antibiotic therapy used in such cases must be reviewed as more clinical information

becomes available and the duration of therapy should be kept short, not exceeding 5 days. If a given antibiotic treatment fails to demonstrate desired benefit, consider switch or stop. In the cases of failure of 5-day antibiotic treatment, also consider empiric/lab evidenced (based on fungal culture and galactomannan assay, where available) antifungal therapy with azoles (e.g., Fluconazole for Candida albicans and Voriconazole for Aspergillus) or echinocandins.

17. Empiric coverage for Staphylococcal infection should be reserved for high risk patients. Consider de-escalation once culturereport indicates absence of infection.
18. Standard infection control measures should be strictly followed at all times.
19. The reason for prescribing antibiotic, whether empiric or definitive, should be clearly documented in the clinical notes. Always provide summary clinical notes, mention about antibiotic usage if any, to all Covid-19 patients referred to another hospital.

Choice of Agents:

- If antibiotics are considered, a β-lactam antibiotic providing coverage for S. pneumoniae ± Staph. aureus should be the first option, e.g., Amoxicillin+Clavulanic acid or a third-generation cephalosporin+/- an anti-Staph agent.
- Avoid use of macrolides and quinolones because of their cardiac side effects—considering that other agents associated with cardiac side effects such as Hydroxychloroquine may be co-prescribed.
- If atypical coverage is considered necessary (e.g. COVID-19 not yet confirmed and suspicion of Legionella infection) consider prescribing Doxycycline. Avoid routine atypical coverage, given the low a prioriprobability of superinfection with atypical pathogens.
- In general, the empiric choice of specific antibiotics should ideally be dictated by local antibiograms and resistance patterns. In absence of the same, the following agents may be considered:

Suspected cases of community acquired pneumonia:

Mild to moderate cases use any of the following for 5 days:

- Co-Amoxiclav 500mg/125mg orally 8 hourly
- Doxycycline orally 200mg on first day and then 100mg once daily

Severe cases, use any of the following for 5-8 days:

- Co-Amoxiclav 1.2g intravenously8 hourly
- Ceftriaxone 2g intravenouslyonce daily
- Piperacillin-Tazobactam 4.5gm intravenously 6 hourly
- Imipenem-Cilastin 1g intravenously 6 hourly(only in cases of prior hospitalization or antibiotic use)
- Cefoperazone-Sulbactam 3gm intravenously 12 hourly(only in cases of prior hospitalization or antibiotic use)

If MRSA infection is suspected or confirmed in the severe cases, add any of the following for 5-8 days:

- Linezolid 600mg orally orintravenously12 hourly
- Ceftarolinefosamil: 600mg intravenously 8 hourly
- Teicoplanin: 6 mg/kg intravenously12 hourly for initial 3 doses, then once daily

Suspected cases of hospital-acquired pneumonia:

Mild to moderate cases, choose any of the following for 5 days:

- Co-Amoxiclav 500mg/125mg orally 8 hourly

- Doxycycline: 200mg on first day, then 100mg once daily, orally
- Co-trimoxazole: 960mg orally 12 hourly

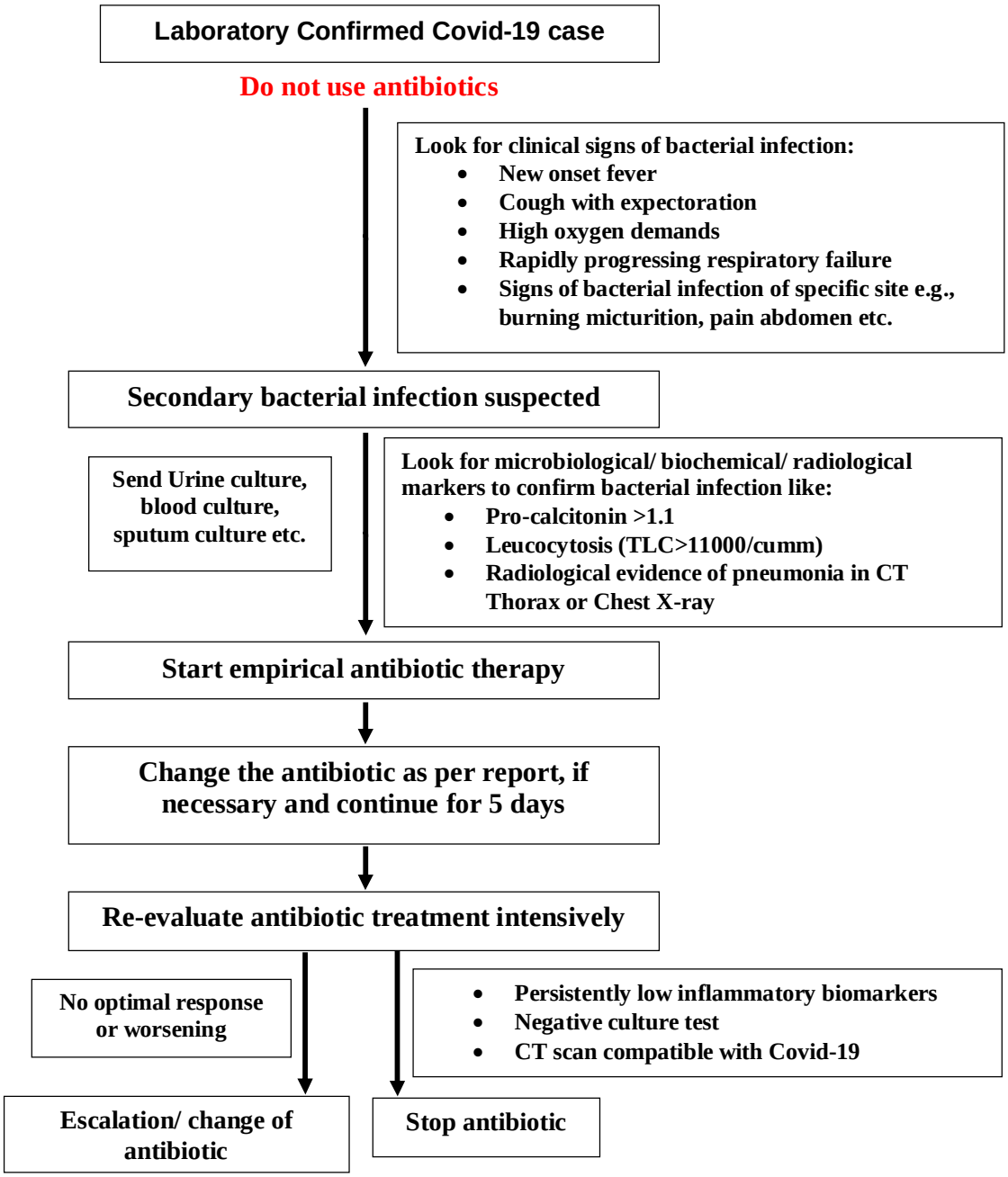
Severe cases (signs of sepsis or ventilator-associated pneumonia), choose any of the following for 5-8 days:

- Piperacillin-Tazobactam: 4.5g intravenously 6 hourly
- Meropenem 1gintravenously8 hourly

If MRSA infection is suspected or confirmed in the severe cases, add any of the following for 5-8 days:

- Linezolid: 600 mg orally or intravenously12 hourly
- Teicoplanin: 6 mg/kg intravenously 12 hourly for initial 3 doses, then once daily

Note: This document covers confirmed Covid-19 infections only. The suspected Covid-19 infection or SARI cases should be managed as per existing guidelines for community acquired pneumonia.



Continuation of chronic medications

- **ACE inhibitor /ARB**: Should be continued, if there is no hypotension or anycontraindication
- **Statins**: To be continued as same dose
- **Insulin**: To be continued as per blood sugar
- **Immuno-modulators**: Decisions to be individualized for prednisolone, biologics and others

Monitoring

- Monitor vital signs, SpO_2 and/or PaO_2 at regular intervals (every 2 hourly or onworsening)
- Check whether tolerating oxygen therapy. Do not delay intubation if worsening
- If **High Flow Nasal Cannula (HFNC)** is available, can consider a short trial of HFNC in selected patients under close monitoring on worsening of oxygenation. Decrease flow, if possible, to restrict aerosol generation. Do not delay intubation if worsening
- If HFNC not available, can consider a short **Non-invasive Positive Pressure Ventilation (NIPPV)** trial in selected patients under close monitoring. (Be careful about leaks, as high flow of NIPPV increases aerosol generation. Full face mask/ helmet interface preferred). Do not delay intubation if worsening.
- Air-borne precautions must during HFNC / NIPPV / Endotracheal intubation
- MDI with spacer preferred to nebulizers, if possible
- CBC / LFT / RFT / portable Chest X-ray / ECG / Lactate / Procalcitonin
- ABG 6 hourly or more frequently ifneeded
- D dimer, LDH, Ferritin on admission and on alternate days
- Early detection of myocardial involvement by Troponins, NT-proBNP and Echocardiography
- Other investigations as decided by treating team

Aerosol generating procedures

- Intubation, Extubation, Use of T piece or any other opencircuit
- High Flow Nasal Cannula (HFNC), Non-Invasive Positive Pressure Ventilation, BagMasking
- OpenSuctioning
- Bronchoscopy,Tracheostomy, GI endoscopy
- Cardio-Pulmonary Resuscitation(CPR)
- Nebulisation

Address comorbidities

Tailor management according to comorbidities

In case of already compromised lung (with/without Tuberculosis) with Covid-19, Oxygen requirement may increase or aggravate the disease so Tuberculosis should be excluded by sputum microscopy or Chest Xray if there is a history of cough/ fever for more than 2 weeks, treatment for TB should be initiated if newly detected.

MANAGEMENT IN CRITICAL CARE UNIT

General Supportive Care of critically ill Covid 19 patients

A. Nutritional Support: The same principles of nutrition in non Covid 19 critically ill patients should be applied to critically ill Covid 19 patients. Role of extra protein supplementation, Vitamin C or D supplementation or trace elements supplementation over and above the usual recommended daily doses is of uncertain value.

B. Fluid and Electrolytes Management: Prefer a conservative strategy of fluid management in patients of ARDS as long as hypotension and organ hypo-perfusion can be avoided. It is reasonable to target central venous pressure less than 4 mm Hg or Pulmonary Artery Occlusion Pressure less than 8 mm Hg.

C. Venous Thrombo-embolism Prevention: Routine pharmacologic Venous Thrombo-Embolism (VTE) prophylaxis is warranted, preferably with low molecular weight heparin (LMWH 40 mg SC once daily), unless there is a contraindication (e.g., bleeding, severe thrombocytopenia etc).

D. Sedation and Analgesia: Adequate sedation and analgesia must be provided for mechanically ventilated patients. Preferable to use Richmod Agitation Sedation Scale (RASS).

E. Glucose Control: For hyperglycemic critically ill patients keep blood glucose target of 140-180 mg/ dL. To achieve target blood glucose level in adult patients minimize the use of IVF that contains glucose and administer insulin only when necessary.

F. Stress ulcer prophylaxis: With Proton pump inhibitors or H2 Receptor antagonist

G. Ventilator Associated Pneumonia Precautions: This includes avoidance of intubation when possible minimizing sedation, maintaining and improving physical conditioning, minimizing pulling of secretions above endotracheal tube cuff, elevating the head of bed and maintaining ventilator circuits.

Criteria of critical care unit admission

1. Requiring Mechanical Ventilation
2. Hypotension Requiring Vasopressor Support
3. Worsening Mental Status
4. Multi-Organ Dysfunction Syndrome(MODS)

When to intubate

1. Worsening respiratory failure despite oxygen therapy or HFNC / NIPPV trial
2. Haemodynamic instability needing vasopressor support
3. Altered sensorium with threatened airway

(Although intubation is an individualized decision, keep a very low threshold for intubation at PaO2 / FiO2 ratio of ≤ 100)

How to intubate

- Full complement of PPE with face shield
- Ensure scene safety & check readiness of all essential drugs & equipment prior to procedure
- Most experienced team member to intubate
- Complete airway assessment prior to procedure

- Hemodynamic evaluation & optimization, if needed, prior to procedure
- Use **Heat and Moisture Exchanger** (HME) filter + Bacterial-viral filter in every oxygenation interface (Face Mask, Circuit, Endotracheal Tube (ETT), Catheter Mount, Laryngeal Mask Airway (LMA))
- Use closed system suctioning and Pre oxygenation with 100% O_2
- **Rapid sequence intubation** using induction agent (Propofol or Etomidate) and muscle relaxant (Succinylcholine or Rocuronium)
- Limit bag mask ventilation unless unavoidable
- Apply cricoid pressure only in case of ongoing regurgitation
- Use video laryngoscope with separate screen, if available
- In anticipated difficult airway, anesthesiologist may be called to intubate
- In unanticipated difficult airway, use LMA and simultaneously call for expert help
- Clamp ETT during unavoidable disconnections
- Use end-tidal CO_2 and CXR to confirm correct position of ETT
- After intubation, appropriate cleaning and disinfection of equipment and environment is mandatory.

Oxygen Therapy (See Annexure 1 for oxygen therapy)

- Administer oxygen to all Severe Acute Respiratory Illness (SARI) patients and to patients with respiratory distress / hypoxemia /shock / sepsis
- Target SpO2 during initial stabilization: 94-98% (88-92% in patients with documented hypercapnic respiratory failure)
- Target SpO2 after initial stabilization: 90-96% (88-92% in patients with documented hypercapnic respiratory failure)
- Always write an Oxygen prescription mentioning (a) Device (b) Flow rate (c) Target SpO_2.
- Check whether patient is tolerating oxygen therapy. Consider conscious proning as an add-on therapy in indicated patients. Do not delay intubation ifworsening ***(See Annexure 1 for oxygen therapy and Annexure 2 for protocol of conscious proning)***
- Conscious prone positioning should not be used as an rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise require intubation and mechanical ventilation
- If High Flow Nasal Cannula (HFNC) is available, consider a trial of HFNC in selected patients failing mask oxygen therapy under close monitoring. Do not delay intubation ifworsening. (***See Annexure 3***)
- Use ROX index ((SpO2/FiO2)/RR) to predict HFNC success (ROX Index ≥4.88 at 2, 6, 12 hrs: predictors of HFNC success and lower risk of intubation; ROX Index <2.85(at 2 hrs), <3.47(at 6 hrs), <3.85(at 12hrs): predictors of HFNC failure.
- If HFNC is not available, can consider a short Non-invasive Positive Pressure Ventilation (NIPPV / CPAP or Bilevel) trial in selected patients under close monitoring. Do not delay intubation ifworsening. NIPPV tolerance can be monitored by HACOR Score. ***(See Annexure 4)***
- Conscious proning may be tried with mask oxygen or any non-invasive respiratory support, either in the wards or Critical Care Unit, if the patient tolerates.***(Annexure 2 for protocol of conscious proning)***

COVID-19 AND ACUTE RESPIRATORY FAILURE

Invasive mechanical ventilation

- **Initial Mode:** Volume Control (can use Pressure Control, if Tidal Volume goals are met)
- **Initial Settings**
  - Tidal Volume (VT): 6ml/kg Predicted Body Weight (PBW)
  - Rate: to match baseline Minute Ventilation (not > 35)

PBW= In Males: 50 + 2.3 (Height in inches – 60);

In Females: 45.5 + 2.3 (Height in inches – 60)

- **Tidal Volume Adjustment:**
  - Check Plateau Pressure (Pplat)
  - Plateau Pressure Goal ≤ 30 cmH_2O
  - If Pplat > 30: decrease VT by 1ml/kg steps to minimum 4ml /kg
  - If breath stacking (auto PEEP) or severe dyspnea occurs, may increase VT to 7-8 ml / kg, if Pplat remains ≤30

Set PEEP according to PEEP-FiO_2 tables to achieve Oxygenation Goal (PaO_2 55 - 80 mmHg / *Preferably* SpO_2 90 - 96%)

Lower PEEP-Higher FiO_2 Combinations: (Start with minimum value for a given FiO_2)

FiO_2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
PEEP	5	5-8	8-10	10	10-14	14	14-18	18-24

Higher PEEP- Lower FiO_2 Combinations:

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5
PEEP	5	8	10	12	14	14	16	16	18
FiO_2	0.5	0.6	0.7	0.8	0.8	0.9	1.0	1.0	
PEEP	20	20	20	20	22	22	22	24	

STRATEGY

- Higher PEEP (> 10) in moderate to severe ARDS
- Lower PEEP (≤ 10) in mild ARDS and "Non-ARDS like" severe pneumonia
- Continue with higher PEEP, if PEEP responsive (Recruiters) and with lower PEEP, if PEEP non-responsive (Non-recruiters)

  PEEP Responsive (Recruiters): Keeping FiO_2 unchanged, *usually* oxygenation improves with increase in PEEP with minimal / no drop in mean arterial pressure, minimal / no rise in $PaCO_2$ and minimal / no rise in driving pressure)
- Try to keep Pplat ≤ 30 and Driving Pressure (Pplat – PEEP)<15
- **Conservative Fluid Management** in absence of tissue hypoperfusion. Avoid hypervolemia

Oxygenation Improving

- Reduce PEEP and FiO_2 gradually
- Shift to a partial assist /spontaneous mode, if tolerated
- Plan for protocolized liberation from ventilation (weaning)
- Smooth extubation with strict airborne precautions including N95 masks with eye protection or equivalent

Oxygen Not Improving

- Search for the reasons of failure and address them
- Ensure conservative fluid management
- Treat patient-ventilator dys-synchrony, if any
- Shift Volume limited mode to pressure limited mode
- Search for complications of disease and of ventilation

Oxygen Improving

- Optimize and persist with above mentioned approaches till patient is ready for liberation from ventilation

Oxygen Not Improving

- If acceptable gas exchanges not achievable without incurring Pplat> 30, consider rescue therapies, (vide below)

RESCUE THERAPIES

Prone Ventilation

- Most preferred rescuetherapy
- Consider in $PaO_2/FiO_2 < 150$ with a $FiO_2 \geq 0.6$ and PEEP ≥5 or $PaO_2:FiO_2 \leq 100$ with a $PaO_2 \leq 60$ despite optimization of ventilator settings on FiO_2 of1
- Consider early proning (within the first 36hours), 12-16 hours /day
- **Contraindications:** Shock (persistent MAP <65 mm Hg), Acute bleeding (multiple fractures/ trauma), spinal instability, pregnancy, raised ICP >30 mm Hg or CPP <60 mm Hg, Tracheal Surgery/ sternotomy in last 2 weeks
- **Criteria to end proning:** P:F ratio >200 with FiO_2<0.5, and PEEP <10 cm H_2O in ABG 4 Hr after re-supination.

Recruitment Maneuvers

- Consider in PEEP responsivepatients
- Preferred method: Sustained high-pressure inflation (35-40 cm H_2O of CPAP for 40seconds)
- Avoid staircase manoeuvres ((Incremental PEEP)
- Avoid routine use of recruitment manoeuvres

Neuromuscular Blockers

- Consider continuous infusion for up to 48 hrs in case of persistently high plateau pressures or severe dys-synchrony
- Can use intermittent boluses to facilitate lung protective ventilation, if needed

Pulmonary Vasodilators

- If available, a trial of inhaled prostacyclin or Nitric oxide may be considered, if other rescue strategies have failed

ECMO (Extracorporeal Membrane Oxygenation)

- Consider veno-venous (VV) ECMO, if available, only in selected patients, with refractory hypoxemia despite optimizing ventilation, proning and using other rescue therapies.
- Referral to ECMO Centre may beneeded

Ventilator Precautions / Maintenance

- Fresh ventilator circuit for every newpatient
- HME with Bacterial-Viral filter to be fitted incircuits
- Tubing and HME with Bacterial-Viral filters to change every 48 hours or when visibly soiled
- Use closed suction and avoid routine suctioning
- Avoid unnecessary disconnections. Clamp ET Tube for unavoidable disconnections
- Avoid nebulisation in intubated patients. Use in line MDI instead
- Use standby mode prior to disconnecting the ventilator from the patient to avoid mucus dispersion from the circuit
- Use an inspiratory bacterial and viral filter to assure non-contamination of the internal ventilator gas path
- Protect the expiratory valve with a hydrophobic bacterial filter
- Daily surface cleaning of ventilator during and after usage with disinfectant must.

REPRESENTATIVE STARTING VENTILATOR SETTINGS

	Volume Control	**Pressure Control**
Tidal Volume	4 - 8 ml / kg PBW	
Inspiratory Pressure		15 cmH_20 (Target VT: 4 - 8 ml/kg)
Rate	14 -18	14 -18
Flow (L/min)	20 -30	
Flow Pattern	Decelerating	Decelerating (default)
Inspiratory Time (Ti)		1 - 1.5 secs
I : E Ratio		1 : 1.5 to 1:3
FiO_2	1 (decrease subsequently)Target SpO_2: preferably90-96%	1 (decrease subsequently)Target SpO_2: preferably90-96%
PEEP (cm H_2O)	5-10 Target SpO_2 : preferably 90 - 96% Target PaO_2 : 55 - 80mmHg *For subsequent adjustments: Follow PEEP-FiO_2 tables*	5-10 Target SpO_2 : preferably 90 - 96% Target PaO_2 : 55 - 80 mmHg *For subsequent adjustments: Follow PEEP-FiO_2 tables*
Trigger Sensitivity (Pressure/Flow)	1-4	1-4
Inspiratory Pause	0-0.3 seconds	

COVID-19 AND SHOCK : HEMODYNAMIC SUPPORT

Fluid therapy

Strategy of Acute Resuscitation:

- Individualize, monitoring tissueperfusion
- Conservative strategy preferred to liberal
- Try to avoid hypervolemia

Choice of Fluids

- Buffered / balancedcrystalloids preferably **Ringer Lactate**
- Avoid Hydroxy Ethyl Starch (HES) / Dextran / Gelatine / Routine use ofAlbumin

Assess Fluid Responsiveness, Whenever Possible

- Use dynamic parameters, for assessing preload responsiveness (e.g. Passive Leg Raising), as feasible

Vasoactive agents

- **Vasopressor of Choice:** Noradrenaline (Vasopressin / Adrenaline if Nor-Ad notavailable)
- **Second line vasopressor:** AddVasopressin
- Mean Arterial Pressure Target : 60 - 65 mmHg
- Add Dobutamine in presence of cardiac dysfunction & persistent hypoperfusion despite fluids and Noradrenaline
- Avoid Dopamine
- Refractory shock despite fluids & vasopressors: Add IV Hydrocortisone (200mg/day as continuous infusion / intermittent doses)

COVID-19 AND OTHER ISSUES FOR INTENSIVE CARE SET UP

- Enteral nutrition
- Glycemic control
- Prevention of hospital acquired infections (VAP, CRBSI, CAUTI).
- Appropriate cultures to be sent. Care for invasive lines and change as per need.
- Early physical therapy
- Stress ulcer prophylaxis. PPI or H_2blocker
- Protocolised light sedation
- Pressure ulcer prevention by two hourly turning
- Deep vein thrombosis prophylaxis
- Protocolised liberation from ventilation
- Caution about premature extubation (especially without facilitative HFNC / NIPPV) and subsequent reintubation
- Not to use glucocorticoid routinely (if not indicated for some othercause)
- Use point-of-care Ultrasound as much as possible to avoid transfers out of CCU for investigations (e.g. CTscans)

RENAL REPLACEMENT THERAPY IN COVID-19 PATIENTS

Covid 19 related AKI is more common in patients admitted in ICU. Morality is more in chronic kidney disease patients, usually associated with co-morbidities & immune dysfunction. ESRD patients on maintenance hemodialysis may develop COVID 19 as they have comorbidities, travel twice or thrice in a week, get exposed to hospital environment Renal transplant & glomerular disease patients on immunosuppressants are also susceptible to COVID-19 infection.

AKI

Screening for renal involvement as early as possible by monitoring urine output, urine routine examination and blood for urea, creatinine, Na, K.

All patients with requirement of hospitalization will need screening for AKI with

- diabetes, hypertension IHD or COPD
- dyspnea, particularly with increasing oxygen demand and abnormal chest Xray
- hemodynamic instability
- admitted with COVID 19 in ICU

Early intervention with optimal fluid management, maintaining hemodynamic stability and avoiding nephro-toxic drugs are primary. Complicated patients may require multi - specialist opinion but one critical care consultant in ICU/CCU and one medical consultant in wards may make a summary of considered changes daily.

AKI on CKD

Diabetic, hypertensive, ischemic heart disease with compromised ejection fraction or already diagnosed chronic kidney disease patients may develop acute kidney injury.

A. Fluid management - more conservative.
B. Antibiotic and other drug choice need to be adjusted according to eGFR (CKD-EPI 2009 eGFR : Android based calculation)
C. Dialysis may be needed early if patients develop oliguria (refractory to fluid challenge or diuretics), volume overload, pulmonary edema, severe metabolic acidosis or uremic encephalopathy.
D. Fluid challenge and vasopressor support along with judicious use of diuretics some patients may come out of AKI.

Dialysis population: COVID patients already on dialysis, should be dialyzed in dedicated COVID unit and stay admitted as per ICMR Guideline for discharge in immune-compromised patients.

HD Modality

1. SLED is to be considered for hemodynamically unstable and multiorgan failure.
2. CRRT may be useful, but practiced only in few units.
3. Stable patients requiring HD may be managed by intermittent hemodialysis.
4. Acute Peritoneal dialysis may be done if there is crisis of resources, problem with access or need for avoiding anticoagulation.

SLED: Sustained low efficiency dialysis (SLED) is increasingly used as a renal replacement modality in critically ill patients with acute kidney injury (AKI) and hemodynamic instability. SLED may reduce the hemodynamic perturbations of intermittent hemodialysis, while obviating the resource demands of CRRT.

Dose of dialysis

May be decided based on the indication (volume overload vs need for solute clearance) haemodynamic status, presence of coagulopathy. COVID 19 patients have problem of increased access thrombosis, use of loading and hourly unfractionated heparin in patients without bleeding complication may be favored anticoagulation.

Managing resources: MT/ dialysis nurses team, nephrologist and dialysis management administrative head may take decision. (Already implemented in W.B.)

Medication

- No specific drug recommended.
- Injudicious antibiotic use should be discouraged.
- Patients on ACEI, ARB may continue if they are already taking unless there is hypotension, hyperkalemia and rising creatinine.
- Statins, anti-hypertensives and anti-diabetic to continue as per required modifications.

Safety of HCP involved in dialysis management:

1. Dialysis nurse, MT, residents in dedicated COVID unit must wear PPE, N95 MASK and face shield.
2. PPE Donning and Doffing areas should be identified in each facility
3. HCQS prophylaxis for MTS, HCPs in contact should be given as per ICMR Guideline.

COVID-19 AND CARDIAC ARREST: CARDIOPULMONARY RESUSCITATION

- In the event of a cardiac arrest, cardiopulmonary resuscitation should proceed with allmembers of the team wearing full PPE and N95mask.
- Practicing a test run of a COVID-19 patient's cardiac arrest isprudent.
- Bag-mask ventilation should be avoided (if feasible) and the ventilator can be used instead to deliver a respiratory rate of 10 beats perminute.
- "Crashes" should be avoided by close monitoring and anticipation. Aim for an elective, unhurried intubation
- Meaningful outcome in refractory critical illness and multiple organ failure is <5%:Assess futility of treatment early.

COVID-19 WITH CO-MORBID CONDITIONS

1. **Patients with one or more co-morbidity should be admitted as moderate disease in Covid ward/ hospital.**
2. **Treatment of co-morbidities should be continued as per guideline**

Diabetes	• **High chance of stress hyperglycemia** • **COVID can unmask latent Diabetes.** • **Use of steroids can aggravate hyperglycaemia.** • **HCQS can cause hypoglycemia** • **SGLT2 inhibitors, Glitazones should be used in caution, should not be newly started.** • **Patients admitted to ICU may need insulin for glucose control** • **Check blood glucose 3times/day** • **Never stopinsulin** • **In high fever, insulin dose may needto be increased** • **Target blood glucose between 110and 180mg/dl**
Obesity	→ **Obesity is an independent risk factor for mortality** → **Obesity increases dyspnea** → **Difficulty in intubation andprone ventilation** → **Do not initiate aggressive weight losing measures during Covid-19 infection.** → **No sudden change in pattern of diet or activity is advised. Yoga such as Surya Namaskar or simple asana is recommended.**
Hypertension	• **ACEi or ARB should be continued.** • **Patients already on these drugs may continue same without change ofdose** • **Good control of blood pressureis advised in patients**
Geriatric patients	• **Physical distancing most important for this age group** • **Non-essential travels outside home should be stopped** • **Strict hygiene in old age homes** • **Visitors at home to be discouraged** • **Elderly are more asymptomatic, Fever may not be present, atypical symptoms may be presentation.** • **In Chest Radiology multiple lobar involvement common, with slower recovery.** • **HCQs should be used with caution, QT interval should be monitored.** • **Routine vaccination should be continued.**

CVD	→ **SARS-CoV2 myocardial injury is a cause of mortality** → **Arrhythmia due to acute inflammation or cytokine storm** → **Vascular thrombosis in pulmonary or coronary vessels** → **Symptoms of AMI may be masked** → **Management of shock as in other cases** → **Anticoagulants may be used** → **ECMO in refractory cases** → **Monitor for heart failure** → **Drugs like HCQS may cause arrhythmia/ QT prolongation** → **Echocardiography preferred in severe dyspnea** • **Acute Coronary Syndrome** ➢ An acute COVID-19 cardiovascular syndrome is characterized by acute myocardial injury which is often associated with decreased left ventricular ejection fraction in the absence of obstructive CAD. ➢ Primary percutaneous coronary intervention (PCI) is the standard of care for STEMI (ST segment elevation myocardial infarction) patients only in high-risk cases during the COVID-19 pandemic, based on personal protective equipment (PPE) availability. ➢ In the absence of these resources, a fibrinolysis first approach should be considered. ➢ Regarding non–ST-segment elevation ACS and unstable angina, COVID-19 positive or probable patients should be managed medically
Hematology	• **Leukopenia** • **Lymphopenia** • **D-dimer is a prognostic marker** • **Serum ferritin is a marker of cytokine storm** • **Thrombocytopenia rare; but if patient on DAPT and Platelet count<50,000, one anti-platelet agent (Ecosprin) to be stopped**
Asthma/COAD	→ People with asthma/COPD at high riskof complications in Covid-19infection → Avoid crowded places → Do not stopinhalers → Avoid asthma triggers like dustorpollen → Use masks that arenon-allergic → Stopsmoking → Avoid spirometry study unless essential → Use of nebulizers in Covid-19patients increases aerosol generation

DISCHARGE

Test for viral clearance for discharge in moderate / severe cases

- Nasopharyngeal and Oropharyngeal Swab test for RT-PCR is not routinely required excepting in very severe cases with immunocompromised states, e.g. HIV, Transplant recipients and Malignancy. One negative report is required before discharge of such patients.

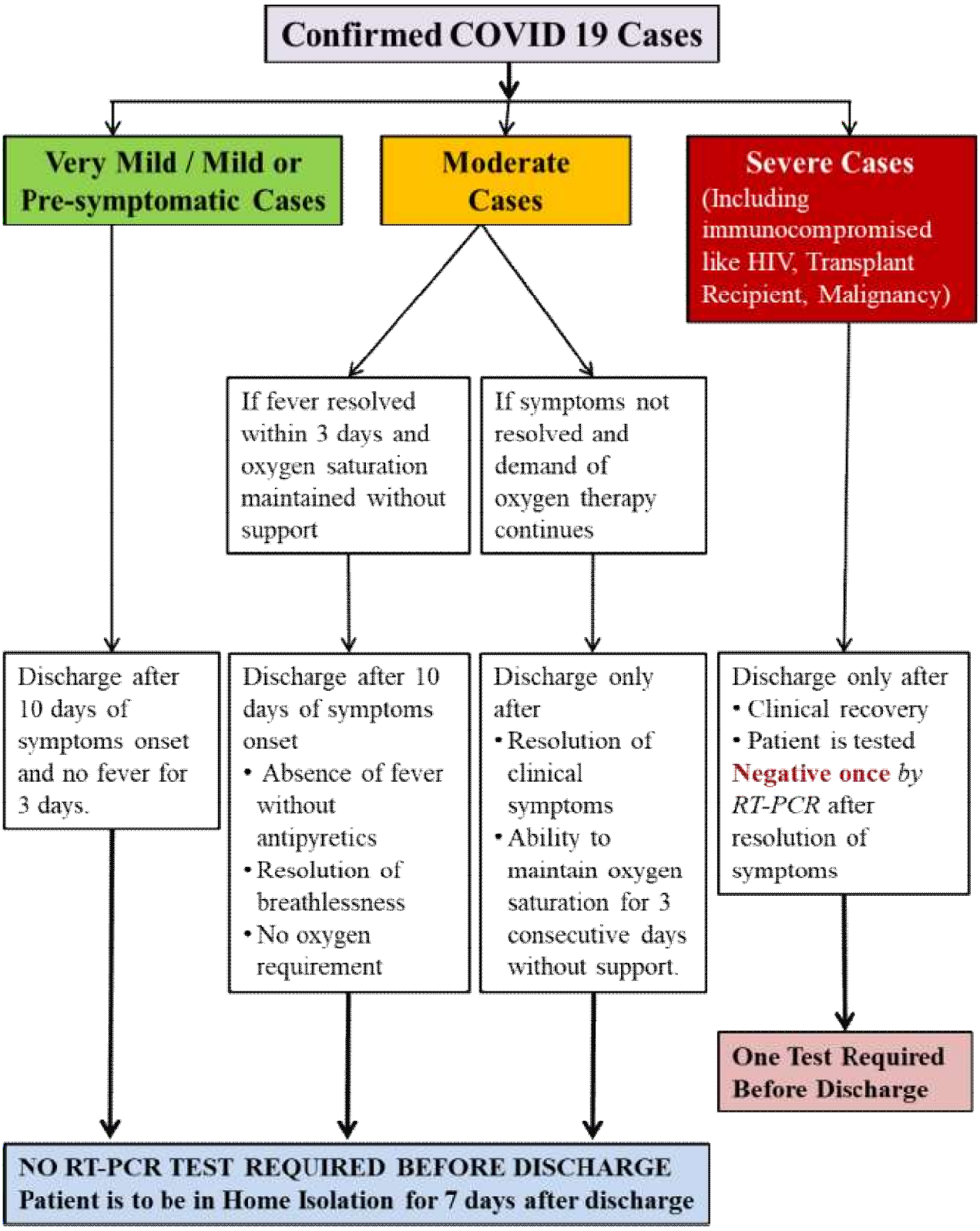
Discharge criteria in moderate / severe cases

- **Moderate case** whose symptoms resolve within 3 days and maintains SpO_2 above 95% for next 4 days can be discharged after 10 days of symptom onset if there is absence of fever without Paracetamol, resolution of breathlessness and no oxygenrequirement.
- **Moderate to severe cases** whose fever does not resolve within 3 days and demand of oxygen therapy continues can be discharged only after Resolution of clinical symptoms and ability to maintain oxygen saturation above 95% for 3 consecutivedays
- **Severe Cases** (including Immuno-compromised patients, HIV patients, Transplant recipient and Malignancy) can be discharged only after Clinical recovery and the patient's swab test becomes negative once by RT-PCR after resolution ofsymptoms.

FOLLOW UP

- All patients must follow strict **Home Isolation** for 7 days after discharge
- The first follow-up visit (physical/ telephonic) should be within 14 days after discharge or as required, preferably at the hospital where he/she underwent treatment.Severe cases requiring critical care support will require more stringent follow up.
- The patients, who had undergone home isolation, if they complain ofpersisting symptoms, will visit the nearest health facility or consult treating physician.
- Self-health monitoring at home - **temperature, blood pressure, blood sugar** (especially, if diabetic), **pulse oximetry** etc. (if medically advised)
- Post Covid pulmonary complication should be kept in mind as there is evidence of lung fibrosis or compromised lung function after Covid 19. Though scientists are not sure whether the lung changes are reversible or not, **SPO_2 by pulse oximeter** should be monitored routinely during follow up.
- If there is any respiratory distress complained by patients, necessary investigations should be advised. (Chest X Ray, HRCT Thorax, Pulmonary Function Test)
- Advice **nutritious diet, adequate sleep and rest**. **Avoid smoking and consumption of alcohol**.
- Continue **use of mask, hand & respiratory hygiene, physical distancing**.
- Patient should take regular medications as advised after discharge and also for managing co-morbidities, if any.
- If there is persistent cough / sore throat, do saline gargles and take steam inhalation. Look for early warning signs like high grade fever, breathlessness, Sp02 < 95%, unexplained chest pain, new onset of confusion, focal weakness and if present, contact nearby hospital/ physician.

DISCHARGE POLICY FOR COVID-19 CASES



COVID-19 AND PREGNANCY

General principles

- There is no data suggesting any increased risk of miscarriage or loss of early pregnancy.
- **COVID-19 is not an indication for Medical Termination of Pregnancy.**
- There is no recorded case of breast milk being tested positive for Covid19.
- Vaginal delivery is preferred. Caesarean Section should be done only in obstetric indications.
- If urgent delivery by Caesarean Section is needed, spinal anaesthesia is recommended to minimise the need for general anaesthesia. Always aim to keep the oxygen saturation above 94% during theprocedure.

Breast feeding

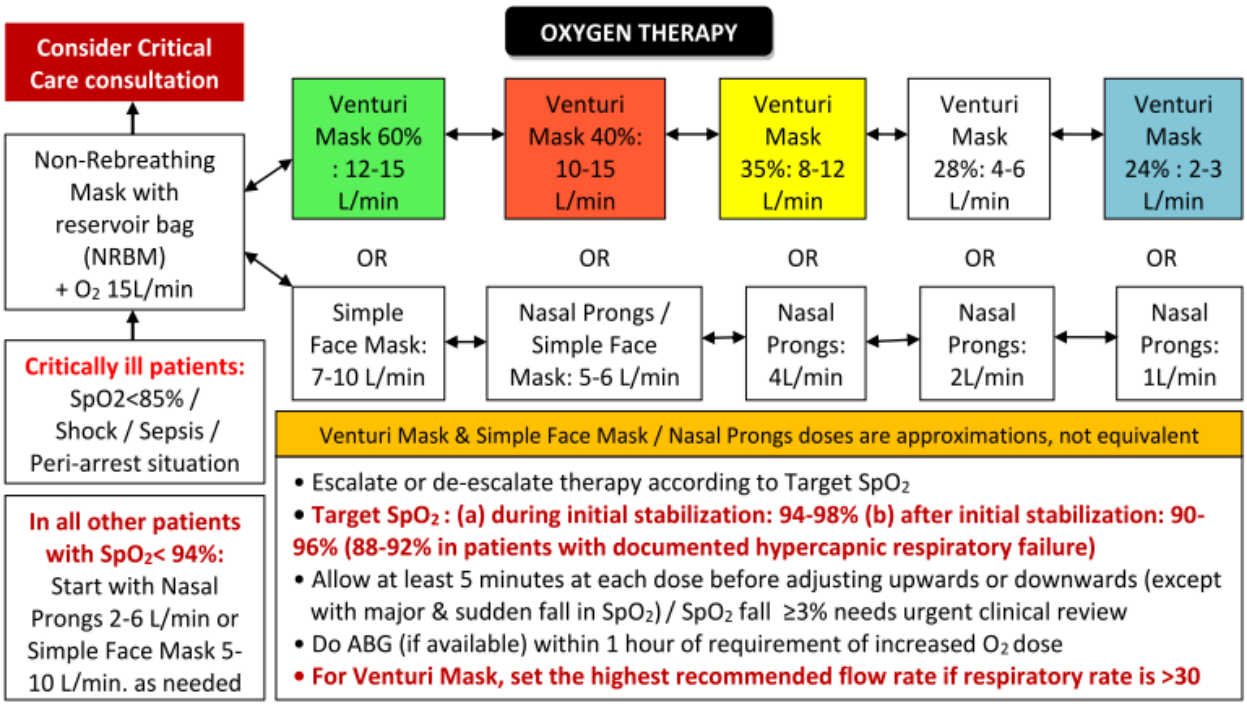
- Woman with Covid 19 can breastfeed if they wish to do so. They should
    - Practice respiratory hygiene and wear a mask
    - Wash hands before and after touching the baby
    - Routinely clean and disinfect surfaces
- If a woman with Covid19 is too unwell to breastfeed or admitted in ICU, she can be supported to safely provide her baby with breast milk in other ways, including by expressing milk, relactation or donor human milk.

Key Points

- If we follow the management protocol for all COVID-19 patients, the recovery rate is satisfactory and the death rate can be kept < 1% of all the affected persons.
- We should address the hypoxia or acute respiratory failure component and multi-organ involvement as early as possible in moderate to severely ill patients to save the maximum number of affected patients.
- The patient should be referred to Critical Care Unit in proper time on proper indications.
- During the course of treatment, we should always reassure the patient to alleviate his/ her fear or panic related to the disease.
- HCWs must write the appropriate treatment notes time to time in the management Top Sheet.
- Appropriate and adequate self-protection of the HCWs is of paramount importance during patient care.
- Any lack in safety measures and infection prevention is extremely undesirable.
- **Critical patients must be stabilized before being referred to Covid hospital or higher centre.**

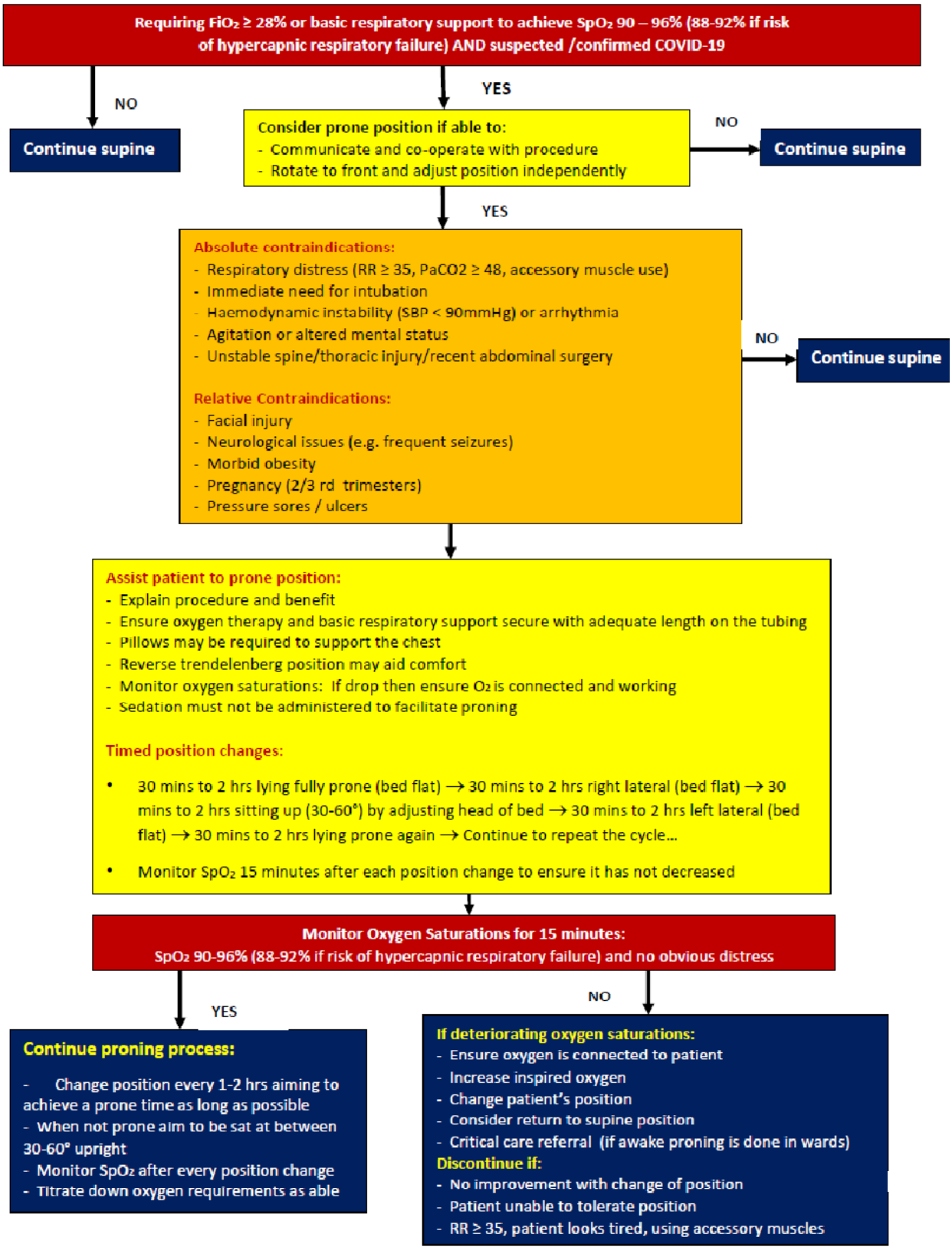
ANNEXURE

ANNEXURE 1: OXYGEN THERAPY

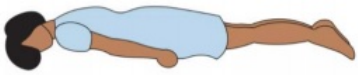


- **Each institute should ensure that all the four types of oxygen therapy devices mentioned above are continuously available in emergency, wards, OTs, CCU / HDU and during transport**
- **An oxygen prescription must be written in the daily orders by doctors in every case needing oxygen mentioning : (a) Device (b) Flow (L/min) (3)Target SpO_2**
- **Conscious proning may be tried as an add on to oxygen therapy *(see Annexure 2)***

ANNEXURE 2: PROTOCOL FOR CONSCIOUS PRONING



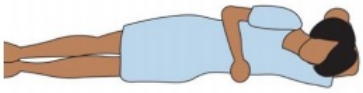
1. 30 minutes – 2 hours: laying on your belly
1. 30 minutos – 2 horas: acostado sobre su estómago (boca abajo)



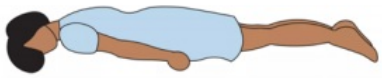
2. 30 minutes – 2 hours: laying on your right side
2. 30 minutos – 2 horas: acostado sobre su lado derecho

3. 30 minutes – 2 hours: sitting up
3. 30 minutos – 2 horas: sentado

4. 30 minutes – 2 hours: lying on your left side
4. 30 minutes – 2 horas: acostado sobre su lado izquierdo



Then back to Position 1. Lying on your belly!
Luego, vuelva a la posición 1. ¡Acostado sobre su estómago (boca abajo)!



ANNEXURE 3: HIGH FLOW NASAL OXYGEN (HFNO)

High Flow nasal Cannula is the preferred modality of non-invasisve assisted ventilation in Covid 19 patients. It is a simple machine, capable of generating high flows upto 80 L/min along with an oxygen blender to deliver accurate FiO_2, delivers humidified gases using disposable circuit.

1. Efficient supplemental Oxygen delivery. HFNCO therapy generates flow dependant FiO_2.
2. Delivering flows higher than the spontaneous inspiratory demand thus minimizing room air entrainment.
3. The flow rate must be titrated to match the patient's inspiratory demand and severity of respiratory diseases.
4. Decreases the anatomic dead space by washing out CO2 from upper airways
5. Reduces the work of breathing by optimally conditioning the delivered gas by warming and humidifying it to physiological conditions.

Indications: If patient continues to have RR>24/min or SPO_2< 92% on Oxygen by NRBM

Flow @ 30-60 L/ min, FiO_2 0.5-1.0

Mechanism:
Higher FiO2 and inspiratory Flow
Added PEEP
Improves dyspnea/ reduces work of breathing
Humidified O_2

HFNO improved ventilator free days and 90- day mortality in non-hypercapnic acute hypoxemic respiratory failure (FLORALI Trail, NEJM 2015)

ANNEXURE 4: HACOR SCORE

Variables	Values	Score
Heart Rate (H)	**≤120**	**0**
	≥121	**1**
Ph (A: Acidosis)	**≥7.35**	**0**
	7.30-7.34	**2**
	7.25-7.29	**3**
	<7.25	**4**
GCS (C: Consciousness)	**15**	**0**
	13-14	**2**
	11-12	**5**
	≤10	**10**
PaO_2/FiO_2 (O: Oxygenation)	**≥201**	**0**
	176-200	**2**
	151-175	**3**
	126-150	**4**
	101-125	**5**
	≤100	**6**
Respiratory rate (R)	**≤30**	**0**
	31-35	**1**
	36-40	**2**
	41-45	**3**
	≥46	**4**

- HACOR is a potentially useful bedside tool for the prediction of NIV failure
- It has been proved to be useful in hypoxemic respiratory failure
- A HACOR score >5 at 1hour of NIV highlights patients with a >80% risk of NIV failure regardless of diagnosis, age, and disease severity

ANNEXURE 5: SOFA SCORE

Variables	SOFA Score				
	0	1	2	3	4
Respiratory	PaO_2/FiO_2: > 400 SpO_2/FiO_2: > 302	PaO_2/FiO_2: < 400 SpO_2/FiO_2: < 302	PaO_2/FiO_2: < 300 SpO_2/FiO_2: < 221	PaO_2/FiO_2: < 200 SpO_2/FiO_2: < 142	PaO_2/FiO_2: < 100 SpO_2/FiO_2: < 67
Cardiovascular (doses in mcg/kg/min)	MAP ≥ 70 mm Hg	MAP ≥ 70 mm Hg	Dopamine ≤ 5 or ANY dobutamine	Dopamine > 5 Norepinephrine ≤ 0.1 Phenylephrine ≤ 0.8	Dopamine >15 or Norepinephrine > 0.1 Phenylephrine > 0.8
Liver (bilirubin, mg/dL)	< 1.2	1.2-1.9	2.0-5.9	6.0-11.9	> 12
Renal (creatinine, mg/dL)	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9	> 5.0
Coagulation (platelets x $10^3/mm^3$)	≥ 150	< 150	< 100	< 50	< 20
Neurologic (GCS score)	15	13-14	10-12	6-9	< 6