

**INTERIM CLINICAL GUIDANCE FOR CARE OF PATIENTS WITH
COVID-19 IN HEALTHCARE SETTINGS**

NEPAL MEDICAL COUNCIL

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INTERIM CLINICAL GUIDANCE FOR CARING OF PATIENTS WITH COVID-19 IN HEALTHCARE SETTINGS

I. PURPOSE OF THE GUIDELINES

The purpose of these clinical guidelines document is to help physicians, other healthcare workers and healthcare institutions to properly manage persons with suspected or proven Coronavirus Disease 2019 (COVID-19). COVID-19 is a respiratory tract infection caused by the betacoronavirus SARS CoV-2 (SARS coronavirus type-2). These guidelines are based on current knowledge in the available literature, expert consultations, and recommendations from WHO, CDC and other authorities. These guidelines are not meant to replace clinical judgment based on individual patient needs and do not exclude expert consultation and are subject to change based on new knowledge.

II. TARGET GROUPS

The intended target audience are physicians, nurses, other healthcare personnel, healthcare administration and policy makers involved in management of COVID-19 infection.

III. TRIAGING AND TRANSPORTATION OF PATIENTS PRESENTING TO THE HEALTHCARE FACILITY

III.A. Who should be screened?

All persons including children and adults presenting to the outpatient clinics (OPD) and Emergency Room (ER) should be screened at the entrance of the healthcare facility in a triage area.

III.B. How will the patients presenting to outpatient clinics (OPD) and Emergency Room (ER) be screened and handled?

1. **SCREENING QUESTIONNAIRE:** All individuals presenting to the OPD or ER entrance should be screened with the following questions:

a. Symptoms:

Do you have any of the following new symptoms?

- (Either one of) Cough? Fever? Shortness of breath? Or,
- (At least two of) Chills? Muscle pain? New loss of taste or smell? Diarrhea? Sore throat?

b. Travel history or contact with traveler:

Have you

- Recently returned from travel in, or been living in, an affected area in the past 2 weeks?
- Been in close contact in the past 2 weeks with someone returning from travel in an affected area?

c. Exposures:

Did you have exposure to any of the following?

- Close contact with anyone with the symptoms listed above, without alternative explanation
- Close contact with a person known or suspected to have COVID-19

2. TEMPERATURE: All persons presenting to the OPD or ER should be screened for fever with thermometer on the temple of head following non-contact method. A core body temperature of 38°C (100.4°F) (corresponding to surface temperature 37.5°C or 99.5°F) or higher is considered as fever.

(If not a no-touch thermometer, it should be cleaned with 60-70% alcohol or an alcohol swab.)

III.C. Case Definitions

The criteria for treating someone as a suspected case is subject to change depending on the dynamics of the epidemic and prevalence of cases inside and outside the country.

The case definitions for COVID-19 *for clinical purposes at hospitals* will be as follows:

Suspected case

- A.** A patient with fever or cough or shortness of breath, or either two of chills, muscle pain, new loss of taste or smell, diarrhea or sore throat in the last 14 days
AND
Has 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
Has history of contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset; (see definition of contact below)
OR
Is a healthcare worker who provides direct care to patients
- B.** A patient with fever or cough or shortness of breath, or either two of chills, muscle pain, new loss of taste or smell, diarrhea or sore throat in the last 14 days
AND
Has no alternative explanation of the symptoms

Probable case

- A.** A suspected case for whom testing for the COVID-19 virus is inconclusive.
OR
B. A suspected case for whom testing could not be performed for any reason.

Confirmed case

A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

Definition of Contact: A contact is a person who experienced any one of the following exposures during the infective period of a probable or confirmed case:

1. Being within 2 metres of a probable or confirmed case for more than 15 minutes without wearing proper personal protective equipment; OR
2. Having unprotected direct contact with infectious secretions or excretions of the patient (e.g., being coughed on, touching soiled handkerchief with a bare hand) and not washing hands immediately afterwards; OR
3. Additionally, for healthcare workers, not wearing eye protection if the person with COVID-19 was not wearing a cloth face covering or facemask, OR not wearing all recommended personal protective equipment (i.e. gown, gloves, eye protection, respirator) while performing an aerosol-generating procedure
4. Other situations as indicated by local risk assessments.

Definition of a confirmed case's period of infectivity to contacts:

For confirmed symptomatic cases, the period is considered to start from 48 hours before the onset of symptoms, and last until 14 days after the onset of symptoms.

For confirmed asymptomatic cases

- If there is history of known exposure to a suspected or confirmed case or exposure to a situation potentially leading to the infection (such as attending a mass congregation), the period of infectivity will be considered to start at 48 hours after such exposure and end 14 days after the test sample was taken.
- If there is no known history of such exposure, the period of infectiveness to contacts will be considered to start 10 days prior to taking the test sample, and end 14 days after the sample was taken.

III.D. How and where will a suspected case be handled and transported?

1. All suspected cases should be given a surgical mask and asked to perform hand hygiene with hand sanitizer, and then escorted by a healthcare worker (HCW) to a separate designated area for isolation of suspect cases.
2. The HCW should be wearing proper personal protective equipment (PPE) such as an N-95 mask (or surgical mask when N-95 mask is not available), face shield, gloves, and, if direct contact is expected, gowns.
3. A separate space away from other patients, families and visitors ("Fever" clinic) need to be designated for isolation and evaluation of symptomatic suspected cases. If necessary, a temporary structure such as a tent should be erected in a separate area away from the entrance of the emergency department or the outpatient clinics.
4. If there are more than one suspected cases, they should be separated at least by 6 feet distance between them. A protective barrier should be placed between two suspected cases, when possible.

5. Standard precautions (hand hygiene and use of gloves as necessary) and droplet precautions (surgical mask, face shield or goggles, gown) need to be strictly implemented in the designated area for isolation.
6. For details of the appropriate use of personal protective equipment and other infection control practices in fever clinics or elsewhere in the hospital, please refer to the most recent version of the Nepal Medical Council's "Interim Guidance on Infection Prevention and Control Practices when COVID-19 is Suspected: 1st Update (June 2020)".

III.E. How will a suspected case be disposed after initial evaluation?

1. Suspected COVID-19 cases with no symptoms or mild symptoms do not require hospital admission *for clinical reasons* unless other underlying risk factors for progression exist, such as DM, immunocompromised patient, cardiovascular disease, chronic respiratory conditions, etc.
2. All suspected patients need to be kept in isolation to contain virus transmission until the infection is ruled out.
3. **Please note that depending on the public health policy adopted by the government at a particular time, in the broader public health interest, even asymptomatic or mildly symptomatic suspected cases of COVID-19 may be required to be admitted to isolation units in hospitals or elsewhere.**
4. If the patient does not meet criteria for a suspected case for COVID-19, and there is no other reason for the patient to be admitted, they can be discharged from the hospital.
5. Refer to Appendix 1 for initial triage, evaluation and management flow chart.

IV. CLINICAL PRESENTATION

IV.A. What is the clinical presentation of COVID-19?

- The incubation period for COVID-19 is estimated to be 2-14 days from the time of exposure, with median incubation period being 4-5 days.
- The illness spectrum ranges from asymptomatic infection to acute respiratory distress syndrome (ARDS) and multiorgan dysfunction. (See Section VI.A below.)
 - The commonest symptoms are fever or chills, cough, shortness of breath, myalgia, fatigue, diarrhea and nausea. Although fever eventually occurs in close to 90% of those with symptoms, it may be absent in close to half of them at initial presentation.
 - Less common symptoms such as new loss of sensation to smell (anosmia) or taste (dysgeusia), sore throat, sputum production, headache, dizziness, anorexia, etc. have been reported.
 - Findings such as deep venous thrombosis including fatal pulmonary embolism, multisystem inflammatory syndrome ("cytokine storm"), chilblain-like lesions on digits ("COVID toes"), etc. appear to be more common than in other respiratory viral illnesses.

- According to the *Report of the WHO-China Joint Mission on Coronavirus Disease 2019*, approximately 80% of (symptomatic) confirmed cases do not progress to severe disease or critical disease. In those who develop severe or critical COVID-19, the worsening from mild to moderate illness usually occurs after around 7-10 days from the onset of symptoms.
- Higher risk of severe disease has not been noted in pregnant women. Children are not noted to be at higher risk except infants less than one year of age.
(See section VI.J for details.)

V. DIAGNOSIS

V.A. Who should get tested for SARS CoV-2?

Please refer to the most recent COVID-19 testing guidelines issued by the Ministry of Health and Population (MoHP), Government of Nepal for testing in different groups or populations.

- **In the absence of adequate testing resources**, suspected cases can be tested in the following order of testing priorities (See Appendix 1 Triage and Management Algorithm):
 1. Highest Priority group:
 - Hospitalized patients with symptoms of potential COVID-19 infection, including fever, cough, shortness of breath, chills, muscle pain, new loss of taste or smell, diarrhea or sore throat.
 - Healthcare workers with symptoms
 - Workers or residents in congregate living settings, such as prisons, with symptoms
 - Symptomatic elderly ≥ 60 years of age
 - Symptomatic individuals with underlying chronic conditions, such as diabetes mellitus, heart disease, lung disease, kidney disease or immunocompromising conditions
 - Symptomatic pregnant women
 2. Second Priority group:
 - Individuals with symptoms, who do not meet the above criteria, regardless of history of exposure to suspected or confirmed COVID-19 cases or history of travel to areas affected by COVID-19
 - Symptomatic or asymptomatic contacts of confirmed cases or travelers from areas with reports of cases, who may or may not be in quarantine facilities
 - Individuals without symptoms, who have been referred for testing by clinicians or prioritized for testing by public health agencies for any reason, including but not limited to preoperative screening, sentinel surveillance, public health monitoring or screening of other asymptomatic individuals
- **Please note that the testing criteria can be expanded by the public health authorities depending on the dynamics of the epidemic and the available testing capacity nationally or locally.**

V.B. What type of diagnostic tests will be performed for suspected cases?

1. ALL SUSPECTED CASES:

- Collect upper respiratory tract specimen, preferably nasopharyngeal swab or, if nasopharyngeal swab cannot be collected, oropharyngeal swab, for RT-PCR.
- If initial testing is negative but the suspicion for COVID-19 remains high, resampling and testing from multiple respiratory tract sites (nasopharynx, oropharynx, turbinates, sputum if readily available) should be performed in 24-48 hours.
- When repeated tests are negative but the suspicion for COVID-19 remains high, can consider doing a validated antigen-based test, if available.
- Infection control precautions for COVID-19 should continue while repeat evaluation is being performed.
- Patients who were initially screened while asymptomatic and reported negative and subsequently develop symptoms concerning for COVID-19 should undergo repeat RT-PCR testing.
- Based on evidence available so far, antibody based serological tests alone cannot be recommended for diagnostic purpose in acute care setting. Antibody based tests should only be used for epidemiological studies and surveillance purposes.

2. HOSPITALIZED PATIENTS:

- If upper respiratory specimens are negative and clinical suspicion remains, collect specimens from the lower respiratory tract when readily available (expectorated sputum or endotracheal aspirate) in ventilated patient) for COVID-19 virus testing by RT-PCR and bacterial stains/cultures.
- However we recommend against doing sputum induction or bronchoalveolar lavage just for the purpose of getting specimen for testing for COVID19 because of high risk for healthcare worker infection.
- Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. DO NOT delay antimicrobial therapy to collect blood cultures.

V.C. When and how should be follow up molecular testing performed for confirmed cases?

- For confirmed cases, repeat molecular testing can be used to assess for virological recovery and readiness for discontinuing infection control precautions or for discharge from hospital, provided testing resources are adequate. Timing of follow up tests is recommended based on whether they have developed symptoms or not.
 1. Symptomatic patients:
 - Repeat testing is suggested once they meet the symptom-based criteria:
 - i. At least 72 hours have passed since
 - a) resolution of fever without use of antipyretics, and

- b) improvement in respiratory signs and symptoms (cough, shortness of breath and oxygen requirement)
- ii. At least 10 days have passed since the onset of symptoms
 - If the first repeat test is negative, a second test should be done after 24 hours. However if the first test is positive, another test should not be done before 72 hours.
- 2. Asymptomatic patients:
 - Repeat testing can be performed once at least 72 hours have passed since the date of the first positive test for COVID-19.
 - If the first repeat test is negative, a second test should be done after 24 hours. However if the first test is positive, another test should not be done before 72 hours.
 - If the patient develops symptoms, the strategy for symptomatic patients above should be used.
- See Discharge Criteria in Section VI.M for information regarding discontinuation of infection control precautions and isolation at home after discharge.

V.D. How will the specimens be collected and transported?

- Use appropriate PPE for specimen collection including droplet and contact precautions for upper respiratory specimens.
- Follow airborne precautions for obtaining lower respiratory tract specimens (PPE, eye shield, gloves & N-95).
- Avoid sputum induction to minimize risk of aerosol transmission.
- Follow the guidance from the National Public Health Laboratory regarding processing and transporting of the collected specimen.)
- See figure in Appendix 7.

V.E. What type of imaging study should be offered initially?

- Chest X-ray should be done in all hospitalized patient with fever and cough or shortness of breath. Ground glass opacities and patchy infiltrates are common findings in patients infected with COVID-19.
- Chest X-ray should also be offered to the non-hospitalized patients whose respiratory symptoms are worsening.
- CT scan of the chest can be performed in patients suspected of COVID-19; however, CT scan is unlikely to give further useful information in most circumstances. CT should only be done in patients with worsening condition at the discretion of the clinicians and availability.

V.F. What other routine tests should be ordered initially?

1. No additional tests are needed for patients with asymptomatic or mild cases of COVID-19.
2. For moderate, severe or critical COVID-19 cases, the following tests are recommended:

- complete blood count and differential count (CBC/Diff)
 - Leukopenia and lymphopenia are expected in 85% of COVID-19 patients
 - renal function and electrolyte tests to assess kidney injury
 - liver function tests
 - Patients may have increased ALT/AST & Bilirubin
 - Where available, tests can be sent for D-dimer level, lactate dehydrogenase level, quantitative C-reactive protein, troponin, ferritin, procalcitonin, etc.
 - Samples should be sent for cultures of blood, sputum, and, if indicated, urine, before starting antibiotics for any reason or if bacterial sepsis suspected.
3. Depending on epidemiology and availability and indications for testing, other tests may be performed to rule out alternative causes of fever such as typhoid, tuberculosis, and tropical diseases such as scrub typhus, dengue, leptospirosis, malaria, kala-azar, etc.

VI. TREATMENT

VI.A. How will the severity of illness be classified?

We recommend following the classification of COVID-19 patients as suggested by the National Institutes of Health (USA) COVID-19 Treatment Guidelines Panel:

1. **Asymptomatic or Presymptomatic Infection:** Individuals who test positive for SARS-CoV-2 but have no symptoms.
2. **Mild Illness:** Individuals who have any of various signs and symptoms (e.g., fever, cough, sore throat, malaise, chills, headache, muscle pain, diarrhea) without shortness of breath, dyspnea, or abnormal imaging.
3. **Moderate Illness:** Individuals who have evidence of lower respiratory disease by clinical assessment or imaging and the oxygen saturation (SpO_2) $>93\%$ on room air at sea level.
4. **Severe Illness:** Individuals who have respiratory frequency >30 breaths per minute, $SaO_2 \leq 93\%$ on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 (or if arterial blood gas test is not available, SpO_2/FiO_2 ratio ≤ 315), or lung infiltrates $>50\%$ on chest x-ray or CT.
5. **Critical Illness:** Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction

VI.B. Who is at high risk of developing severe illness?

Patients diagnosed with COVID-19 who are at high risk for poor outcomes, including ARDS and death, are those who meet any 1 of the following criteria:

- Age ≥ 60 years
- Any one of the following medical conditions:

- Obesity
 - Cardiovascular disease, excluding hypertension as the sole cardiovascular diagnosis
 - Diabetes with HbA1c level >7.5%
 - Chronic pulmonary diseases, including asthma
 - End-stage renal disease
 - Advanced liver disease
 - Blood disorders (e.g., sickle cell disease)
 - Cancer
 - Neurologic or neurodevelopmental disorders
 - Post–solid organ transplantation, on immunosuppressive therapy
 - Use of biologic agents for immunosuppression
 - Undergoing treatment with chemotherapy or immunotherapies for malignancy
 - Within one year post–marrow transplant
 - Undergoing treatment for graft-versus-host disease
 - HIV infection, with CD4 cell count <200 copies/mm³
 - Surgery during incubation period
 - Any one of the following clinical findings:
 - Oxygen saturation (SaO₂) ≤93% on room air; <90% if known chronic hypoxic conditions or receiving chronic supplemental oxygen
 - Respiratory rate >24 breaths/min
- Note: Low socioeconomic status and being a victim of racism have been identified as risk factors for severe COVID-19 infection especially in the USA. While these findings have not been validated in the context of Nepal, these risk factors should be taken into account on a case by case basis while designing management plan in Nepal.
- Laboratory finding: elevated D-dimer level (>1 µg/mL), admission absolute lymphocyte count of <0.8, elevated levels of lactate dehydrogenase, troponin, C-reactive protein, creatine phosphokinase, ferritin and IL-6, and prolonged prothrombin time.

VI.C. How will asymptomatic or presymptomatic infection with SARS-CoV-2 be managed?

- Those with asymptomatic and presymptomatic infection *need to be isolated* as transmission of the virus from asymptomatic or presymptomatic cases accounts for close to half of the transmission of SARS-CoV-2 in the community.
- Persons with asymptomatic or presymptomatic infection with SARS-CoV-2 do not need to be admitted to a hospital *for clinical reasons* however, given the tradition of relatively larger and multigenerational households in Nepal and the significant risk of household transmission of this particular virus, public health authorities may require such patients to be admitted to hospitals or isolation facilities if safe and appropriate arrangements for isolation cannot be made at their own homes.
- It is not clear what proportion of patients with asymptomatic or presymptomatic infection will develop clinical disease.

- Those with presymptomatic or asymptomatic infection will need to be monitored for onset of symptoms or rise in temperature. Psychosocial evaluation and support may be indicated. (See below in Section VI.K)
- No additional laboratory testing or specific treatment is recommended for persons with asymptomatic or presymptomatic infection.
- For criteria for discontinuation of isolation precautions, please see [section VI.M Discharge Criteria].

VI.D. How will mild COVID-19 be managed?

- Patients with mild COVID-19 infection generally do not require hospital admission *for clinical reasons* unless other underlying risk factors for progression exist, such as DM, immunocompromised patient, cardiovascular disease, chronic respiratory conditions, etc. However, they need to be monitored closely since rapid worsening of clinical status can occur.
- Patients need to be kept in isolation. For criteria for discontinuation of isolation precautions, please see [section VI.M Discharge Criteria].
- Please note that, given the tradition of relatively larger and multigenerational households in Nepal and the significant risk of household transmission of this particular virus, public health authorities may require patients with mild COVID-19 to be admitted to hospitals or isolation facilities if safe and appropriate arrangements for isolation cannot be made at their own homes.
- If the patient is kept in isolation at home or at another designated location, they should be counseled about signs and symptoms of progression and if they develop any of these symptoms, they should return to designated hospital immediately.
- Psychosocial evaluation and support may be indicated. (See below in Section VI.K)
- No specific laboratory tests are indicated in patients that are otherwise healthy at baseline.
- Monitor vitals including SpO₂ at least every 6 hours. Inform treating doctor if SpO₂ drops by >2%.
- Use symptomatic treatment such as antipyretics (preferably paracetamol) as needed for fever. No specific antiviral or immunomodulatory therapy is recommended in mild COVID-19 disease.

VI.E. How will moderate COVID-19 be managed?

- Patients with moderate COVID-19 should be admitted and closely monitored in a hospital.
- If the hospital doesn't have intensive care facility, clinicians should consider referring patients with moderate illness to a hospital with intensive care facility.
- Laboratory tests as listed above in [Section V. Diagnosis] should be performed, for assessment and monitoring of severity and for prognostic value.
- Chest X-ray or ultrasound should be performed, and CT scan may sometimes be indicated.

- Monitor vitals including SpO2 at least every 6 hours. Inform treating doctor if SpO2 drops by >2%.
- There are insufficient data to recommend any antiviral or immunomodulatory therapy in patients with moderate COVID-19. Such treatment should ideally be offered only in the setting of clinical trial. Given the emerging evidence of potential benefits of Remdesivir, a 5-day course (200 mg on day 1, and 100 mg once daily on subsequent days) can be considered in patients with moderate COVID-19 if they have two or more risk factors for developing severe illness. (See section VI.B above)
- When bacterial superinfection is suspected, appropriate empiric antibiotics should be started. (See below in Section VI.K)
- Deep vein thrombosis prophylaxis should be considered in all patients when there is no contraindication for anticoagulation.
 - Patients should be advised to ambulate within the isolation unit at least every few hours when awake.
 - For pharmacologic prophylaxis, one of the following may be used: Enoxaparin, Dalteparin, Fondaparinux or Unfractionated Heparin. (See Table 1)
 - Avoid nebulization, if possible, or use dry nebulization protocol (See Appendix 4) as a non-aerosol generating option.
 - Psychosocial evaluation and support may be indicated. (See below in Section VI.K)

Table 1: Parenteral Anticoagulation for adults with COVID 19 hypercoagulopathy				
Anticoagulation Agent (AC)	VTE Prophylaxis		VTE Treatment	
	Cr Cl >30 ml/min	Cr Cl <30 ml/min	Cr Cl >30 ml/min	Cr Cl <30 ml/min
Enoxaparin	40mg/day SC	30mg/day SC	1mg/kg BD SC	1mg/kg OD SC
Dalteparin	5000 units OD SC	Use alternative AC	200 U/kg OD SC, or 100 U/kg BD SC	Use alternative AC
Fondaparinux	2.5 mg OD SC	Use alternative AC	<50kg: 5mg OD, 50-100kg: 7.5mg OD, >100kg- 10mg OD SC	Use alternative AC
Unfractionated Heparin (UFH)	5000 units 8-12 hourly SC		†80 units/kg bolus (maximum dose: 10,000 units), then 18 units/kg/hour IV (maximum initial infusion: 2,000 units/hour) APTT needs to be monitored with 6hrs of starting infusion and then regularly for dose adjustment DO NOT USE treatment dose of UFH if there is no facility to measure APTT	
†Enoxaparin is the preferred anticoagulant for prophylaxis and treatment of hypercoagulopathy. Avoid use of unfractionated heparin especially for VTE treatment if other options available. *In case of previous heparin-induced thrombocytopenia (HIT) or suspected HIT, use Fondaparinux. *VTE- venous thromboembolism, SC- subcutaneous, IV- intravenous, Cr Cl- creatinine clearance				

VI.F. How will severe COVID-19 be managed?

- Patients who are hypoxemic (SPO₂ <93% in room air) but not in respiratory distress (RR <30, not using accessory muscles of respiration), supplemental oxygen via nasal cannulae (upto 4-6 litres/minute) or non-rebreathing mask with reservoir (10-15 litres/minute) should be given to keep SPO₂ between 93 to 96% (or 88 to 92% if having chronic respiratory diseases). These patients need to be closely monitored for worsening saturation or respiratory distress and planned to be shifted to ICU as early as possible.
- FiO₂ level from various oxygen delivery devices can be estimated using the FiO₂ estimation chart. (See appendix 3)
- Consider using facemask or venturi mask instead of nasal cannula when using >4 litres/minute oxygen.
- Patients should use medical mask over the nasal cannula if they can tolerate.
- **Ask for ICU review if oxygen requirement is >4 litres/minute or >28% FiO₂ via venturi mask to keep SpO₂>93%. These patients need to be closely monitored for worsening saturation or respiratory distress and planned to be shifted to ICU as early as possible, depending on ICU doctor's assessment of the patient.**
- **Awake self-proning or repositioning:** For patients admitted to the ward, 'awake self proning or repositioning' should be considered if they require supplemental oxygen (SpO₂< 93%). This should only be attempted in those who are alert, able to communicate and with stable hemodynamics. Monitor patients carefully to look for signs of deterioration.
(See appendix 5)
- Deep vein thrombosis prophylaxis should be considered in all patients when there is no contraindication for anticoagulation.
 - Patients should be advised to ambulate within the isolation unit at least every few hours when awake.
 - For pharmacologic prophylaxis, one of the following may be used: Enoxaparin, Dalteparin, Fondaparinux or Unfractionated Heparin. (See Table 1)
- Laboratory tests as listed above in [Section V Diagnosis] should be performed, for assessment and monitoring of severity and for prognostic value.
- Chest X-ray or ultrasound should be performed, preferably at bedside. CT scan may sometimes be indicated, only if it changes the management significantly. (See *Interim Guidelines for Radiology Practice During COVID-19 Pandemic* published by Nepal Radiologists' Association for infection control measures during radiological tests.)
- There are insufficient data to recommend any antiviral or immunomodulatory therapy in patients with severe COVID-19. Such treatment should ideally be offered only in the setting of clinical trial. Given the emerging evidence of potential benefits of Remdesivir, a 5-day course (200 mg on day 1, and 100 mg once daily on subsequent days) can be considered in these patients. (See below Section VI.J)

- An adult (≥ 18 years-old) patient with critical (severe or immediately life threatening) COVID-19 may be offered convalescent plasma therapy provided there are no contraindications.
(See details below in “Section VI.J.2”.)
- When bacterial superinfection or viral coinfection is suspected, appropriate empiric antimicrobials should be started. (See below in Section VI.K)

VI.G How will critical COVID-19 be managed?

- Critically ill patients have associated acute respiratory distress syndrome (ARDS), septic shock that may represent virus-induced distributive shock, cardiac dysfunction, elevations in multiple inflammatory cytokines that provoke a cytokine storm, and/or exacerbation of underlying co-morbidities
- They may also experience cardiac, hepatic, renal, and central nervous system disease in addition to pulmonary disease.
- **Indications for ICU admission** (any one of the following):
 - Respiratory failure requiring ventilatory support such as NIV / HFNC or mechanical ventilation
 - Presence of shock or multi-organ failure
 - $\text{PaO}_2/\text{FiO}_2 < 200$ mmHg, or $\text{SpO}_2/\text{FiO}_2$ ratio ≤ 235 if ABG not available, with worsening respiratory distress
- Ask for ICU review if oxygen requirement is >4 litres/minute or $>28\%$ FiO_2 via venturi mask to keep $\text{SpO}_2 < 93\%$. These patients need to be closely monitored for worsening saturation or respiratory distress and planned to be shifted to ICU as early as possible depending on ICU doctor’s assessment of the patient.
- **Oxygen Therapy and Monitoring:**
 - Monitor oxygen saturation continually during oxygen therapy
 - Give supplemental oxygen therapy immediately to patients with severe acute respiratory infection (SARI) and respiratory distress, hypoxemia or shock.
 - Target oxygen saturation:
 - 93% - 96% for patients without chronic respiratory disease
 - 88% - 92% for patients with chronic type II respiratory failure
- **Proning:**
 - Consider awake proning for >12 - 16 hours a day in patients who require supplemental oxygen but are not yet intubated. Awake proning can also be done in patients who are on high flow nasal cannula (HFNC) or non-invasive ventilation (NIV).
 - Pre-requisites for awake proning- patient should be alert/ able to communicate, hemodynamically stable and not in respiratory distress.
 - Monitor patient closely during awake proning for signs of deterioration.
(See Appendix 5)
- **High Flow Nasal Cannula (HFNC) or Non Invasive Ventilation (NIV):**
 - For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy and no indication of urgent intubation, use HFNC over

conventional oxygen therapy. When HFNC is not available, NIV can be used with close monitoring and assessment for worsening respiratory failure at short intervals.

- Adopt airborne precaution when using HFNC/NIV as it can generate aerosols. Use viral filter or high efficiency particulate air (HEPA) filters wherever possible in NIV circuit.
- Patients should use surgical mask over the high flow nasal cannula or NIV mask if tolerated.
- Proceed to endotracheal intubation with airborne precaution if patient is not improving or has respiratory distress.
- **Endotracheal Intubation:**
 - If worsening respiratory distress with $SPO_2 < 90\%$ despite oxygen supplementation with 10-15 litres/minute via non-rebreathing facemask, and/or failure of HFNC/NIV to achieve target oxygen saturation, AND
 - $PaO_2/FiO_2 < 150$
- **Mechanical ventilation:**
 - If patients have indications for mechanical ventilation, intubate them without delay with airborne precautions. Use Rapid Sequence Intubation (preoxygenation, sedation, neuromuscular blocking (NMB) agents, intubation) technique to minimize bag-mask ventilation and to minimize aerosol generation
 - Non-invasive ventilation (NIV) or high flow nasal cannula (HFNC) are not preferred because of concerns with aerosol generation and may have worse outcome compared to invasive ventilation by delaying intubation.
They may only be considered in COVID-19 patients when there is shortage of ventilators.
 - In case of severe crisis and ventilator shortages in the country, anesthesia workstations can be used for ventilation of patients with COVID-19.
 - Full airborne precautions measures should be adopted when performing Bag and Mask Ventilation or endotracheal intubation or any other aerosol generating procedures. Viral filters should be used when available. (Refer NMC to Interim Guidance for Infection Prevention and Control When COVID-19 is Suspected, June 2020)
- **Antiviral and immunomodulatory treatments:**
 - There are insufficient data to recommend any antiviral or immunomodulatory therapy in critically ill COVID-19 patients. Such treatment should ideally be offered only in the setting of clinical trials. Given the emerging evidence of potential benefits of Remdesivir, a 5-10 day course (200 mg on day 1, and 100 mg once daily on subsequent days) can be considered in these patients. (See below in Section VI.J)
 - When bacterial superinfection or viral coinfection is suspected, appropriate empiric antimicrobials should be started. (See below in Section VI.K)

- **Convalescent plasma therapy:**
 - An adult (≥ 18 years-old) patient with critical (severe or immediately life threatening) COVID-19 may be offered convalescent plasma therapy provided there are no contraindications.
(See details below in “Section VI.J.2”.)
- **Treatment of co-infections:**
 - At initial presentation, if bacterial pneumonia or sepsis is suspected, start empiric antimicrobials to treat likely pathogens causing severe pneumonia and sepsis as soon as possible, preferably within 1 hour of initial assessment for patients with sepsis.
 - **When a viral etiology such as SARS-CoV-2 is identified, empiric antibiotic therapy should be deescalated or stopped on the basis of microbiology results and clinical judgement.**
- **Fluid management:**
 - Use restrictive fluid management strategy ensuring patient’s tissue perfusion.
 - In patients with severe acute respiratory illness, when there is no evidence of shock, aggressive fluid management may worsen oxygenation.
 - Closely monitor fluid intake and output.
- **Deep Vein Thrombosis (DVT) prophylaxis:**
 - Pharmacologic DVT prophylaxis should be considered in all admitted patients where there is no contraindication for anticoagulation.
 - One of the following may be used: Enoxaparin, Dalteparin, Fondaparinux or Unfractionated Heparin.
 - Increased incidence of arterial and venous thrombosis has been noted in severe/ critical COVID 19 patients. In case of rising D-dimer (>6 times the normal limit), worsening hypoxia not fully explained by worsening chest x-ray or in case of high suspicion of DVT/ pulmonary embolism or thrombosis of central venous or arterial line, treatment dose of anticoagulation may be needed. Consider venous Doppler ultrasound and echocardiogram to assess for right heart strain when available. If no alternative explanation for the worsening signs and symptoms, consider therapeutic anticoagulation.
(See Table 1, for anticoagulant dosage)

VI.H. How will ARDS secondary to COVID-19 be managed?

(Refer to Appendix 6 for management of refractory hypoxemia and ventilator adjustment.)

- Recognize severe hypoxemic respiratory failure and prepare to provide advanced oxygen/ventilatory support when a patient has worsening respiratory distress and is failing to respond to standard oxygen therapy ($\text{PaO}_2/\text{FiO}_2 < 150$ mmHg).
- Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions and using full PPE.
- Implement mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure < 30 cmH₂O)

- **Prone ventilation:**
 - Early proning without pulmonary vasodilator trial is recommended in adult patients with severe ARDS due to COVID-19, which is a departure from the typical practice for ARDS from other causes. In patients with severe ARDS (PaO₂/FiO₂ <150 mmHg), prone early, within 12 hours of FiO₂ >75%, for 12–16 hours per day.
 - Spinal cord injury and open chest are absolute contraindications.
 - Prone positioning may be associated with several complications; hence, experienced team should carry out or supervise the management of proned patients. Several sessions of prone positioning may be needed.
- Titrate PEEP and FiO₂ as per ARDSnet’s protocol. (**Appendix 6**)
- Adopt permissive hypercapnia (Target pH > 7.2)
- Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.
- Use in-line catheters (Closed Suction Catheter) for airway suctioning, and clamp endotracheal tube when disconnection is required. Consider paralysis during airway manipulation.
- Use Ventilator Bundle (**Table 2**) strictly.

Table 2: Ventilation Bundle

Head-of-bed elevation 30 - 45° Daily sedative interruption Daily spontaneous breathing trial Deep vein thrombosis prophylaxis Stress ulcer prophylaxis (in patients with high risk of gastrointestinal bleeding) Subglottic secretion drainage in patients likely to be ventilated for more than 48 hours
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- **Sedation and neuromuscular blockade:**
 - Avoid continuous sedation and neuromuscular blockade when possible.
 - Sedation should be given in case of ventilator dyssynchrony.
 - Intermittent boluses of neuromuscular blocking agents can be given if there are some ventilator dyssynchrony.
 - If persistent dyssynchrony, high plateau pressures or if prone ventilation then continuous NMBA may be need for upto 24 hrs.
- **Extracorporeal membrane oxygenation (ECMO) therapy:**
 - Consider ECMO if resources are available, in patients with refractory hypoxemia in spite of management including lung protective mechanical ventilation and prone positioning.

VI.I. How will Septic Shock secondary to COVID-19 be managed?

1. Recognition of septic shock

- a. Recognize septic shock when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP) ≥ 65 mmHg AND lactate is ≥ 2

mmol/L, in absence of hypovolemia. If lactate measurement is not available use clinical assessment for tissue perfusion status e.g. capillary refill time, change in mental status, urine output.

2. Resuscitation of patients with septic shock

- a. Give 500 mL crystalloid fluid (such as Normal saline or Ringer's lactate) as rapid bolus in first 15 minutes and reassess for signs of fluid overload after each bolus.
- b. Fluid resuscitation may lead to volume overload and respiratory failure, particularly with ARDS. If there is no response to fluids or if patient develops signs of volume overload (e.g. jugular venous distension, crackles on lung auscultation, pulmonary oedema on imaging, B lines on Lung USG, or hepatomegaly in children), then reduce or discontinue fluid administration.
- c. Do not use hypotonic crystalloids, starches, or gelatins for resuscitation.

3. Vasopressors

- a. Administer vasopressors when shock persists during or after fluid resuscitation. The initial blood pressure target is MAP \geq 65 mmHg in adults and improvement in markers of perfusion.
 - Norepinephrine is considered first-line treatment in adult patients; vasopressin and/or epinephrine can be added to achieve the MAP target. Because of the risk of tachyarrhythmia, reserve dopamine for selected patients with low risk of tachyarrhythmia or those with bradycardia.
- b. Vasopressors (i.e. norepinephrine, vasopressin, epinephrine and dopamine) are most safely given through a central venous catheter at a strictly controlled rate, but it is also possible to safely administer them via peripheral vein (lower concentration solution) and intraosseous needle.
- c. Monitor blood pressure frequently and titrate the vasopressor to the minimum dose necessary to maintain perfusion targeting MAP of 60-65 mmHg and also prevent side effects.

4. Antimicrobials: When bacterial superinfection or viral coinfection is suspected, appropriate empiric antimicrobials should be started. (See below in Section VI.K)

VI.J. What antiviral or other COVID-19 specific treatment should be offered to COVID-19 patients?

1. Antiviral Drugs

- At the time of this update, there are no proven safe and effective antiviral drugs for treatment of COVID-19. Antiviral drugs are not needed for most of the COVID-19 patients. Antivirals should be reserved only for hospitalized patients with moderate to severe COVID-19 illness. Although there are reports of several therapeutic options, all currently available drugs are being evaluated in clinical trials. Because of the safety concerns, authorities such as WHO, IDSA, NIH, and European CDC recommend the use of these drugs under investigational settings only. Treatment decisions with antiviral

drugs should be made by the health care provider based on their discussion with the patient and their legal guardians.

- All antiviral drugs for treatment of COVID-19 are currently being investigated in clinical trials in other countries. Nepal is also in the process of participating in clinical trials, such as World Health Organization (WHO) SOLIDARITY Clinical Trial. Clinicians treating patients with COVID-19 infection are encouraged to contact NHRC (Nepal Health Research Council) for further information.
- a. **Remdesivir:** Remdesivir is a direct acting antiviral drug that inhibits viral RNA synthesis of SARS-CoV, MERS-CoV, and SARS-CoV-2. In the preliminary report of a double-blind, randomized, placebo-controlled trial of intravenous Remdesivir, patients treated with Remdesivir had a shorter median recovery time compared to placebo group, although mortality was not significantly different. Another randomized, open-label phase 3 trial without placebo control involved 397 hospitalized patients with SpO₂ ≤94% on room air and radiological evidence of pneumonia (severe or critical COVID-19) and not requiring mechanical ventilation, who were treated with either 5 or 10 days of with Remdesivir. The clinical status was not different at day 14 between the two groups after adjustment for baseline clinical status.

Remdesivir will likely be available through clinical trials and/or expanded access and compassionate use mechanisms in Nepal. If / when available, it should only be used in those 18 years of age or older with severe or critical COVID-19. The recommended dose is 200 mg intravenously on day 1, followed by 100 mg once daily, for 10 days total in patients on mechanical ventilation or ECMO, and 5 days total in other patients (with extension to 10 days if there is no clinical improvement). It is contraindicated if alanine aminotransferase (ALT) level greater than 5 times the upper limit of the normal range and should be discontinued if ALT rises above this level during treatment or if there are other signs of liver injury. The pharmacokinetics of remdesivir in setting of renal impairment are uncertain, and its cyclodextrin vehicle can potentially cause toxicity in renal impairment. Therefore, it is not recommended if estimated creatinine clearance by Cockcroft-Gault formula is <30 ml/minute per 1.73 m².

Based on lab studies, without verification on clinical setting, the US FDA has warned against using remdesivir alongside hydroxychloroquine or chloroquine because it may result in lower antiviral activity for remdesivir.

- b. **Chloroquine/Hydroxychloroquine:** We do NOT recommend treatment with hydroxychloroquine or chloroquine for COVID-19, either alone or in combination with azithromycin. Reports from randomized controlled trials have shown no benefit from use of hydroxychloroquine or chloroquine as pre- or post-exposure prophylaxis, nor as treatment in COVID-19. WHO has withheld use of these drugs in its SOLIDARITY Clinical Trial, and the USA FDA has also revoked the emergency use authorization for these drugs in COVID-19. If chloroquine or hydroxychloroquine is used for another indication in patients with COVID-19, clinicians should closely monitor the patients for adverse effects, especially prolonged QTc interval. Hydroxychloroquine should NOT be used with azithromycin because of the increased potential for cardiac arrhythmias.

- c. **Favipiravir (T-705 or Avigan)**: Favipiravir is an inhibitor of viral RNA-dependent RNA polymerase. Favipiravir has been approved in Japan and China for the treatment of novel influenza virus infections. It has also been used for postexposure prophylaxis and treatment for Ebolavirus infection. However, it is a mutagen and has potential for both teratogenicity and embryotoxicity in humans. An open-label trial in China comparing oral favipiravir plus inhaled interferon compared with a historical cohort of patients receiving lopinavir/ritonavir showed that patients receiving favipiravir+interferon had median shedding of virus of 4 days compared with 11 days in the lopinavir/ritonavir group. Currently, its use in COVID-19 can be recommended only as an investigational agent.
- d. **Lopinavir/ritonavir (Kaletra)**: This combination of two protease inhibitors cannot be recommended alone in the absence of supporting evidence. Based on a modified intention to treat analysis, treatment with lopinavir/ritonavir failed to show or exclude a beneficial effect on mortality although failure of clinical improvement was lower in the lopinavir group. A more recent study done in Hongkong showed a combination of lopinavir/ritonavir with ribavirin and interferon beta-1b shortened duration of viral shedding and hospital stay in patients with mild to moderate COVID-19.

2. Convalescent Plasma Therapy (CPT)

- Based on success reports from retrospective analyses, CPT is currently being evaluated as a treatment option under clinical trials for patients with severe COVID-19. The CPT should be used only for patients with severe or immediately life-threatening COVID-19 infection. Based on recommendations from WHO, FDA and European Commission, Nepal is also in the process of launching CPT as an investigational therapy.
- An adult (≥ 18 years-old) patient with critical (severe or immediately life threatening) COVID-19 may be offered convalescent plasma therapy provided there are no contraindications. Informed consent should be obtained prior to initiating therapy. Generally, 200 ml of ABO compatible COVID-19 convalescent plasma should be administered over 1-2 hours. The patient should be closely monitored for possible transfusion related adverse events such as fever, pruritus, haemolytic and non-haemolytic transfusion reactions, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), delayed posttransfusion purpura, etc. and managed accordingly.
- **Refer to the MOHP’s “Interim Guidelines for Use of Convalescent Plasma for COVID-19” for details. Please contact NHRC (Nepal Health Research Council) or NPHL (Nepal Public Health Laboratory) for further information.**

3. Host Modifiers/Immune-Based Therapy

- **Dexamethasone**: On June 16, 2020, the Chief Investigators of the RECOVERY (Randomized Evaluation of COVID-19 thERapY) trial released a statement that said that they had randomized a total of 2104 patients to receive dexamethasone 6 mg once per day (either by mouth or by intravenous injection) for ten days and 4321 patients randomized to usual care alone. In their study, “dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88];

$p=0.0003$) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; $p=0.0021$). There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75]; $p=0.14$).” The study suggests that 1 death would be prevented by treatment of around 8 ventilated patients or around 25 patients requiring oxygen alone. Since these results have only been released through a press release so far without a formal peer review of the manuscript and publication in a medical journal, it would not be appropriate for us to recommend treatment with dexamethasone to COVID-19 patients even though the results seem to be promising. Until peer-reviewed journal publication of the study is available, we advise clinicians to follow emerging evidence regarding use of dexamethasone in COVID-19. We strongly urge that at this point, if dexamethasone is used in a COVID-19 patient, only the low dose of 6 mg once a day (by mouth or intravenous injection) should be used, and it should not be used in those who do not require respiratory support, i.e. those without severe or critical COVID-19, unless there is another indication for the drug.

- There are insufficient clinical data to recommend either for or against the use of the following agents which are being studied in clinical trials for treatment of COVID-19.
 - a. Interleukin-6 inhibitors (e.g., sarilumab, siltuximab, tocilizumab): Studies have suggested that the pathogenesis of SARS and MERS-CoV involves release of proinflammatory cytokines including interleukins-6 (IL-6). Treatment with IL-6 inhibitor tocilizumab has shown to reduce mortality in one study. There were no deaths reported in 21 severe and critically ill patients who received tocilizumab and no serious adverse events were reported in the study. However, these findings are currently being verified in randomized clinical trials. Patients receiving tocilizumab for other indications are often at an increased risk of serious infections including bacterial, viral, invasive fungal infections and tuberculosis, and hepatitis B reactivation. Cases of anaphylaxis, severe allergic reactions, severe liver damage and hepatic failure, and intestinal perforation have been reported after receiving tocilizumab.
 - b. Systemic interferon, in particular interferon β -1a, is also being evaluated as an adjunct drug with lopinavir/ritonavir or favipiravir in clinical trials. Use of interferons as a single agent for treatment of COVID-19 is not recommended.

In a phase 2, prospective, multicenter, open label, randomized trial from Hong Kong, 127 patients were randomly assigned (2:1) to a 14-day combination of lopinavir 400 mg and ritonavir 100 mg every 12 hours, ribavirin 400 mg every 12 hours, and 3 doses of 8 million international units of interferon beta-1b on alternate days (combination group) or to 14 days of lopinavir 400 mg and ritonavir 100 mg every 12 hours (control group). The combination group had a significantly shorter median time from start of study treatment to negative nasopharyngeal swab than the control group. In this study, those with mild disease were included. Pregnant or lactating mothers were excluded. In our assessment, these data are somewhat promising, however evidence from further studies of double antiviral therapy with interferon beta-1b as a backbone are needed to recommend such combination therapy in COVID-19 patients.

4. Vaccines

- Currently there is no proven vaccine against COVID-19. Multiple potential COVID-19 vaccines are under development and being evaluated in clinical trials. Nepal is currently not participating in any vaccine trials. However, when a vaccine appears safe and has proven efficacy, they will be evaluated at the time.

VI.K. What other adjunct treatment considerations are there?

- Systemic corticosteroids: Use of systemic corticosteroids (except low dose dexamethasone in severe or critical COVID-19) for treatment of COVID-19 pneumonia without ARDS is not recommended. Please see above in section VI.J.3 regarding discussion of the possible use of dexamethasone in COVID-19. Systemic corticosteroid can be considered in patients with severe ARDS with high ventilatory support or if required for septic shock, adrenal crisis or comorbidities such as COPD exacerbation or asthma exacerbation.
- Antimicrobials:
 - a. The rates of bacterial superinfection of COVID-19 appear to be low (10-20%), but when present increase mortality risk. Anecdotal reports suggest less MRSA superinfection than is often seen with influenza. **Unnecessary antibiotics carry risks of fluid overload and drug-resistance, as well as the possibility that antibiotics may become a limited resource.**
 - b. In patients who meet the definition of sepsis/septic shock, antibiotics should be started within an hour of presentation or recognition of signs of sepsis. The initial antibiotic regimens should be chosen based on the type of patients.
 - c. Empiric antimicrobial coverage of a presumed pulmonary source of infection:
 - In patients **without** risk factors for MRSA or *Pseudomonas* (i.e., community acquired infection, no prior multi-drug resistant organisms): Ceftriaxone or Amoxicillin-clavulanic acid +/- Azithromycin or doxycycline
 - (If the patient is getting treatment with chloroquine or hydroxychloroquine, doxycycline should be preferred to azithromycin to avoid QTc prolongation.)
 - If proven or suspected influenza, add oseltamivir.
 - In patients **with** risk factors for *Pseudomonas* or MRSA (i.e., hospital-acquired infection, recent courses of antibiotics): Cefepime or Piperacillin/tazo +/- Teicoplanin or Vancomycin.
 - Consider adding Meropenem or Imipenem-cilastatin if high concern for multidrug resistant organism infection.
 - d. Give oral antibiotics when possible to reduce volume load, unless concerns for poor oral absorption.
 - e. **Antibiotics should be discontinued or deescalated if cultures are reported as negative or if bacterial infection ruled out clinically.**
- Antihypertensive medications: Patients already on anti-hypertensive medications of the groups angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) can continue to use these medications. They should be stopped only

when they develop hypotension. Switching to other groups of antihypertensives is not recommended.

- Management of myocarditis: Patients may develop cardiogenic shock secondary to myocarditis, in which case check ECG and trends of BNP and troponin. Refer these patients to cardiologist for appropriate management.
- Nonsteroidal anti-inflammatory drugs: There is no clear evidence to recommend stopping or avoiding NSAIDs when clinically indicated. However, it is advised to use Paracetamol as the preferred temperature-lowering agent and analgesic, and when NSAIDs are needed, to use the lowest effective dose.
- Nutritional Support:
 - a. Start enteral feeding early.
 - b. Nasogastric or orogastric tube feeding in intubated patients.
 - c. Consider parenteral nutrition if enteral feeding is not tolerated despite prokinetic use or if enteral feeding is contraindicated.
- Psychosocial Support:
 - a. Patients with COVID-19 are at risk of developing fear and worry about their own health and the health of their loved ones, changes in sleep or eating patterns, insomnia, worsening of chronic health problems or preexisting mental health conditions, or increased use of alcohol, tobacco or other drugs.
 - b. Those with higher risk for severe illness such as older adults, along with those with disabilities are at increased risk for increased stress, or even depression.
 - c. Clinicians should have a higher suspicion for development of psychological disturbances in patients with COVID-19.
 - d. Such patients can be helped by connecting them with family and loved ones, by acknowledging their distress, and with psychological or psychiatric evaluation and support if needed.

VI.L. What are the possible ethical issues that need to be considered?

1. End-of-life care and care of the dying patient
 - a. Patients who are terminal because of COVID-19 may be allowed to be visited by only a limited number closest family members at their wish but with appropriate PPE. If appropriate PPE is not available, hospitals may refuse such visits considering the risk of transmission of the virus.
 - b. If the patient's outcome seems grim and the treatment offered may be futile as evidenced by multiple organ failures, refractory shock or refractory hypoxia, this should be conveyed to family members and opted for a DNR status as providing CPR to the patient won't be helpful and will increase the risk of transmission of disease.

2. Resource utilization during crisis

- a. In case of rapid significant increase in the number of cases requiring critical care and mechanical ventilation beyond the effectively available critical care capacity, such increase may give rise to a situation when criteria for access to (and discharge from) intensive care resources and ventilators may need to be set up, based not only on clinical appropriateness and proportionality of care, but also on likelihood of therapeutic success, while also aspiring towards distributive justice. Principles of justice, transparency, non-abandonment of patient, and, non-restriction of autonomy of the patient except for compelling public health concern, should be followed while designing such criteria.
- b. Parameters indicating likelihood of therapeutic success may include:
 - i. the type and severity of the disease
 - ii. the compromise of other organ systems and their reversibility
 - iii. the presence of hypoxic brain Injury
 - iv. types, numbers and severity of underlying comorbidities
 - v. age
- c. Such decisions regarding withholding access to intensive care unit interventions or withdrawing of active life sustaining treatment of patients (including mechanical ventilation) need to be made by a separate team or committee formed by the hospital (Ethics Committee, Triage Committee, or a similar entity) with at least three members (as stipulated in the Nepal Medical Council Guidelines “Professional Ethics During COVID-19 Pandemic”). Treating clinical team members should not be a part of this committee. The Ethics Committee’s decision has to be documented in writing and signed by all members.
- d. Communication about such decisions should be done to the patient’s family or concerned parties by the Ethical Committee members and not by the treating critical care team.

3. Prioritization of resources to healthcare workers:

- a. Critical Covid-19 interventions such as lab tests, personal protective equipment, intensive care unit interventions such as ventilators, therapeutics, and vaccines should preferentially be made available to front-line health care workers and others who care for ill patients and who keep critical infrastructure operating, particularly those who face a high risk of infection.
 - i. Whether healthcare workers who need ventilators will be able to return to work is uncertain, but providing preferential access to appropriate interventions as indicated recognizes the significant risks they have willingly exposed themselves to while taking care of suspected or confirmed COVID-19 patients.

VI.M. What are the criteria for discharge of confirmed COVID-19 patients?

1. Criteria for stepdown from the ICU to isolation ward:

- a. Hemodynamically stable and no vasopressor support required for > 8 hours, **and**

- b. Off ventilator for > 24 hours, **and**
- c. SaO₂ >92% with FiO₂ requirement <35%

2. Criteria for discharge to home:

- a. **Symptomatic patients with COVID-19:** Patients who meet EITHER the **time-based criteria alone** OR the **time-based and test-based criteria** may be discharged to home.
 - i. **Time-based criteria alone:**
 - a) Resolution of fever >72 hours without antipyretics, **and**
 - b) Improvement in respiratory signs and symptoms (cough, shortness of breath and oxygen requirement), **and**
 - c) At least **14 days** have passed since the initial onset of symptoms, **and**
 - d) The patient does not have an underlying severely immunocompromising condition such as human immunodeficiency virus infection with CD4 count <350 cells/mm³, treatment with immunosuppressive medications including high dose steroids (prednisolone >20 mg/day), cancer chemotherapy, leukemia, transplant, etc.

Note: Those discharged based on time-based criteria alone should continue 1 week of isolation at home.

OR

- ii. **Time-based AND test-based criteria (for essential workers):** These criteria are recommended for healthcare workers or other essential workers for whom it would be desirable to shorten hospital stay and avoid additional isolation at home if possible. These patients can be discharged before 14 days if both of the following time-based and test-based criteria are met or at 14 days even if test-based criteria alone is met, whichever is sooner. If RT-PCR test for SARS-CoV-2 is still positive at 14 days, further follow up RT-PCR testing is not recommended.
 - Time-based:**
 - a) Resolution of fever >72 hours without antipyretics, **and**
 - b) Improvement in respiratory signs and symptoms (cough, shortness of breath and oxygen requirement), **and**
 - c) At least **10 days** have passed since the initial onset of symptoms
 - AND**
 - Test-based:**
 - a) Negative results on COVID-19 nucleic acid-based testing from at least 2 respiratory tract specimens collected ≥ 24 hours apart

Note: Those discharged based on time-based plus test-based criteria DO NOT need to maintain 1 week of isolation at home after discharge.

- iii. **Time-based AND test-based criteria (for individuals with immunocompromising conditions):** Those with severely immunocompromising conditions and COVID-19 symptoms must meet *both time-based AND test-based* criteria for essential workers, with the following modifications:
 - a) At least **14 days** have passed since the initial onset of symptoms
 - b) 1 week of isolation needs to be continued at home after discharge

- b. **Patients with confirmed COVID-19 who have NOT had any symptoms:** Patients who have not had symptoms can be discharged to home if they meet EITHER the **time-based criteria alone** OR the **time-based and test-based criteria**.
 - i. **Time-based criteria alone:**
 - a) At least **14 days** have passed since the first positive COVID-19 diagnostic test, **and**
 - b) No symptoms have developed subsequent to the first positive test, **and**
 - c) The patient does NOT have an underlying severely immunocompromising condition such as human immunodeficiency virus infection with CD4 count <350 cells/mm³, treatment with immunosuppressive medications including high dose steroids (prednisolone >20 mg), cancer chemotherapy, leukemia, transplant, etc.

Note: Those discharged based on time-based criteria alone MUST continue 1 week of isolation at home.

OR

- ii. **Time-based AND test-based criteria (for essential workers):** These criteria are recommended for healthcare workers or other essential workers for whom it would be desirable to shorten hospital stay and avoid additional isolation at home if possible. These patients can be discharged before 14 days if both of the following time-based and test-based criterial are met or at 14 days even if test-based criteria alone is met, whichever is sooner. If RT-PCR test for SARS-CoV-2 is still positive at 14 days, further follow up RT-PCR testing is not recommended.
 - Time-based:**
 - a) Resolution of fever >72 hours without antipyretics, **and**
 - b) No symptoms have developed subsequent to the first positive test, **and**
 - c) At least **10 days** have passed since the initial onset of symptoms

AND

Test-based:

- a) Negative results on COVID-19 nucleic acid-based testing from at least 2 respiratory tract specimens collected \geq 24 hours apart

Note: Those discharged based on time-based plus test-based criteria DO NOT need to maintain 1 week of isolation at home after discharge.

- iii. **Time-based AND test-based criteria (for individuals with immunocompromising conditions):** Those with severely immunocompromising conditions and COVID-19 symptoms must meet *both time-based AND test-based* criteria for essential workers prior to discharge, with the following modifications:
 - a) At least **14 days** have passed since the first positive COVID-19 diagnostic test
 - b) 1 week of isolation needs to be continued at home after discharge

3. Home Isolation:

- a. Patients must continue 1 week of isolation at home
 - i. if they are discharged based on time-based criteria alone, **OR**
 - ii. if they have severely immunocompromising conditions
- b. Infected healthcare workers will be exempted from additional 1-week home isolation requirement after discharge. [Please see *Interim Guidance for Infection Prevention and Control When COVID-19 Is Suspected: 1st Update* (June 2020) by the Nepal Medical Council for recommendations regarding return to work for healthcare workers.]

VII. SPECIAL POPULATIONS WITH COVID-19

VII.A Pregnant Women and Lactating Mothers

- Based on currently available information, there is no evidence that pregnant women are at higher risk or at risk of severe illness.
- So far, there is little evidence of mother-to-child transmission when infection occurs in the third trimester.
- SARS-CoV-2 has not been identified in breastmilk of infected mothers.
- All recently pregnant women with COVID-19 should be counseled on safe infant feeding and appropriate infection prevention measures to prevent COVID-19 virus transmission.
- Infants born to mothers with suspected, probable, or confirmed COVID-19 should be fed according to standard infant feeding guidelines, while applying necessary precautions for infection prevention and control
- Symptomatic mothers who are breastfeeding or practicing skin-to-skin contact or kangaroo mother care should practice respiratory hygiene, including during feeding (for example, use of a medical mask when near a child if with respiratory symptoms), perform

hand hygiene before and after contact with the child, and routinely clean and disinfect surfaces which the symptomatic mother has been in contact with.

VII.B Pediatric Population

- *Please refer to the appropriate sections above for other management (e.g. Testing and Laboratory work-up, general treatment including antimicrobials, management of respiratory failure and septic shock.)*
- **Can children get COVID-19?**
Children of all ages can get the COVID-19, although only 1 to 5% of diagnosed COVID-19 cases are seen in children. This may be due to the fact that rate of hospitalization is much lower in children.
- **How do they present?**
Most common presenting symptoms are fever or cough. Other manifestations may include myalgia, shortness of breath, headache, sore throat, runny nose, diarrhea, nausea/vomiting, abdominal pain, new loss of taste or smell, and chills. Some children may present with just gastrointestinal symptoms. Infants may present with fever without any source and minimal or no respiratory symptoms.
Children can also show stress associated symptoms. Younger children may develop excessive crying or irritation. Older children may show regression to previously outgrown behaviors such as bedwetting, excessive worry or sadness, irritability, poor ability to concentrate, unexplained headaches or body pain, etc.
- **What are the findings in laboratory tests and imaging?**
The recommended test for confirming diagnosis is RT-PCR, and nasopharyngeal, oropharyngeal or nasal swab samples can be collected for the test.
In newborns, testing should be performed at approximately 24 hours of age for both symptomatic and asymptomatic newborns born to mothers with confirmed or suspected COVID-19, regardless of the mothers' symptoms. If initial test results are negative, or not available, testing should be repeated at 48 hours of age.
Similar to adults, children may demonstrate leukopenia, lymphopenia, elevate procalcitonin and C-reactive protein. Chest radiographs may be unremarkable or show bilateral consolidation.
- **What is the range of severity of illness in children?**
Most children are asymptomatic or have mild or moderate disease and recover within a week or two. There have been reports of pediatric patients requiring invasive ventilation or even extracorporeal membrane oxygenator (ECMO) or but these are very rare and mainly occur in children with chronic co-morbid conditions.
- **What is Pediatric Multisystem Inflammatory Syndrome (PMIS)?**
There are recent reports of a rare but serious condition associated with COVID-19 in children. PMIS is also referred to as multisystem inflammatory syndrome in children (MIS-C), pediatric hyperinflammatory syndrome, and pediatric hyperinflammatory shock. The pathogenesis may be an antibody or immune complex mediated postinfectious inflammatory syndrome.
 - Its presentation may be varied:

1. Refractory vasodilatory shock (toxic shock syndrome) with normal cardiac function
2. Septic and /or cardiogenic shock state with impaired cardiac function (mainly LV-failure)
3. Kawasaki-like illness (not all patients requiring ICU care) with prolonged persistent fever (>101.3 °F), sore throat, headache, abdominal pain and vomiting, rash, conjunctivitis
4. Some combination of the above

World Health Organization’s preliminary case definition of PIMS

1. Children and adolescents 0–19 years of age with fever for ≥ 3 days
2. **AND two** of the following:
 - i. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
 - ii. Hypotension or shock.
 - iii. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
 - iv. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
 - v. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).
3. **AND**
Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.
4. **AND**
No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
5. **AND**
Evidence of COVID-19 (RT-PCR, antigen test or antibody positive), or likely contact with patients with COVID-19.

• **How are children with COVID-19 managed?**

Management is mainly supportive. The management specific to children is discussed here.

1. Ventilator: A lower level of plateau pressure (< 28 cmH₂O) is targeted, and lower target of pH is permitted (7.15–7.30). Tidal volumes should be adapted to disease severity: 3–6 mL/kg PBW in the case of poor respiratory system compliance, and 5–8 mL/kg PBW with better preserved compliance. Early proning for extended duration (24-48 hours) may be needed in children. Use restrictive fluid strategy. Aim for euvolemia. If signs of volume overload are present consider diuresis with furosemide. Strict intake and output with Foley catheter monitoring is recommended.
2. Septic shock and Decreased cardiac output:
 - a. Recognize shock in children with any hypotension (systolic blood pressure [SBP] < 5 th centile or > 2 SD below normal for age) or two or more of the following: altered mental state; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged

- capillary refill (> 2 sec) or feeble pulses; tachypnea; mottled or cold skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.
- b. Give 10–20 mL/kg crystalloid fluid as a bolus in the first 30 minutes and reassess for signs of fluid after each bolus.
 - c. Administer vasopressors if
 - i. Signs of shock including altered mental state; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 seconds) or feeble pulses; oliguria persists after two repeat boluses; or
 - ii. age-appropriate blood pressure targets are not achieved; or
 - iii. signs of fluid overload are apparent but child is on shock
 - d. Epinephrine is considered first-line treatment, while Norepinephrine can be added if shock persists despite optimal dose of epinephrine or if patient is in warm shock with vasodilatation, wide pulse pressure and near normal cardiac function.
3. Specific treatment of PMIS:
Patient may deteriorate rapidly. Close cardiorespiratory monitoring is indicated.
- a. Kawasaki Syndrome:
 - i. Intravenous immunoglobulin 2 g/kg. May need to be repeated.
 - ii. Aspirin 50-80 mg/kg per day for 5 days. Then continue for 48 hours after defervescence then decrease dose to 3-5 mg/kg per day for 8 weeks.
 - b. Toxic shock syndrome
 - i. Intravenous immunoglobulin 2 g/kg

VIII. INFECTION PREVENTION AND CONTROL

Please refer to the separately published *Nepal Medical Council Interim Guidance for Infection Prevention and Control When COVID-19 Is Suspected: 1st Update (June 2020)* for guidance regarding infection prevention and control in hospitals.

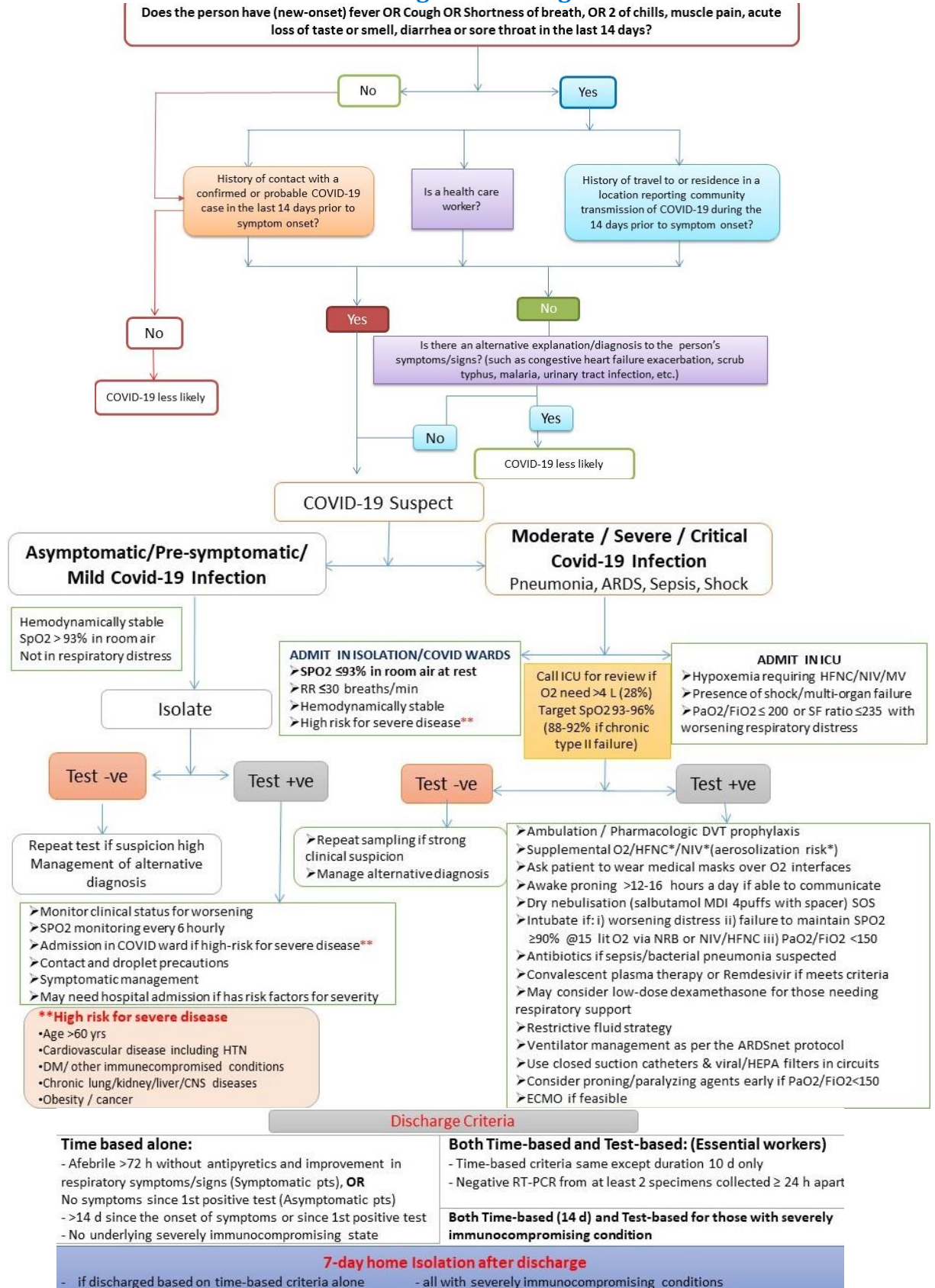
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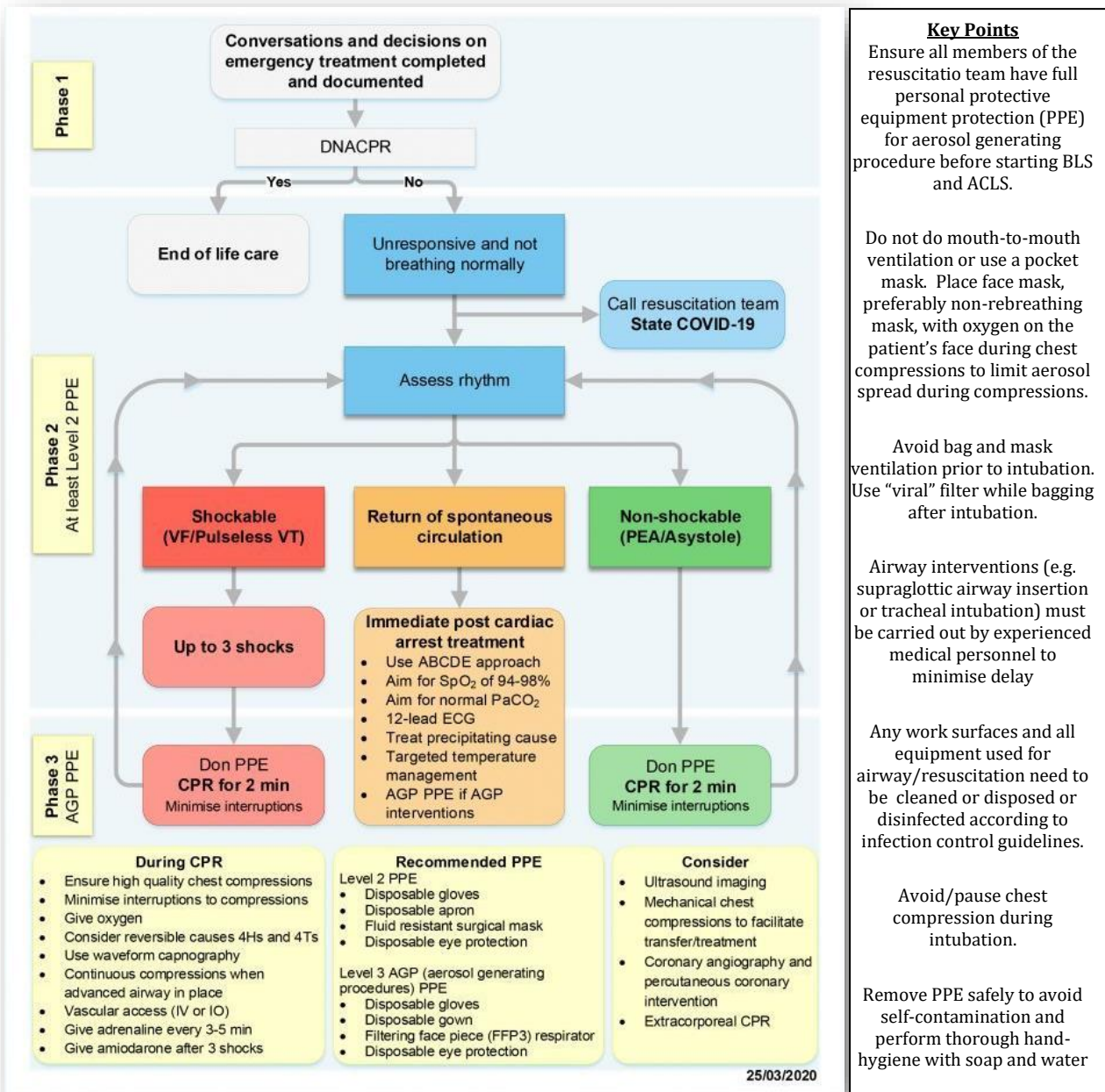
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X. APPENDIX 1: Patient triage and management flow chart



APPENDIX 2: Advanced Cardiovascular Life Support Flowchart in Healthcare Settings
(Source: Resuscitation Council, UK)



Key Points

Ensure all members of the resuscitation team have full personal protective equipment (PPE) for aerosol generating procedure before starting BLS and ACLS.

Do not do mouth-to-mouth ventilation or use a pocket mask. Place face mask, preferably non-rebreathing mask, with oxygen on the patient's face during chest compressions to limit aerosol spread during compressions.

Avoid bag and mask ventilation prior to intubation. Use "viral" filter while bagging after intubation.

Airway interventions (e.g. supraglottic airway insertion or tracheal intubation) must be carried out by experienced medical personnel to minimise delay.

Any work surfaces and all equipment used for airway/resuscitation need to be cleaned or disposed or disinfected according to infection control guidelines.

Avoid/pause chest compression during intubation.

Remove PPE safely to avoid self-contamination and perform thorough hand-hygiene with soap and water

APPENDIX 3: FiO₂ estimation

Method	O₂ flow (l/min)	Estimated FiO₂ (%)
Nasal cannula	1	24
	2	28
	3	32
	4	36
	5	40
	6	44
Face mask (non venturi mask)	5	40
	6-7	50
	7-8	60
Face mask with reservoir	6	60
	7	70
	8	80
	9	90
	10	95
Venturi mask (color code)		
Blue	2	24
White	4	28
Orange	6	31
Yellow	8	35
Red	10	40
Green	15	60

APPENDIX 4: “Dry nebulization” protocol with metered-dose inhaler (MDI) with spacer/valved-holding chamber (VHC) (Adapted from the protocol of National University Hospital, Singapore)

“Dry nebulization” protocol using metered-dose inhaler (MDI) with spacer/ valved-holding chamber (VHC)
<ul style="list-style-type: none"> - Jet nebulization is associated with aerosol generation and can facilitate the transmission of viruses e.g. SARS and possibly 2019-nCoV. - To reduce the risk of disease transmission, we recommend the use of “dry nebulization” in the treatment of acute airflow obstruction. - This is clinically equivalent to nebulization therapy in patients with moderate to severe airflow obstruction.
Instructions
<p>1. Selection of spacer or VHC Choose one with a mouthpiece or facemask depending on your patient’s ability to maintain effective seal (e.g. children, elderly with cognition, acute breathless patients) Prime the new spacer by firing ~ 10 puffs of Salbutamol to reduce the static build-up inside (check product information sheet).</p>
<p>2. Preparation Remove the cap of MDI Shake the inhaler 5-10 times Insert into back of spacer or VHC.</p>
<p>3. Ensure an effective seal Face mask: Place mask over the mouth and nose and ensure minimal gaps Mouthpiece: Put mouthpiece in mouth between teeth and close lips around it.</p>
<p>4. Slow breathing Instruct the patient to breathe in and out <u>slowly</u>. Tell patient to slow down breathing if the spacer/VHC whistles.</p>
<p>5. Administer 1 puff at a time (to reduce clumping of particles) Press the canister <u>once</u> at the beginning of a slow inhalation. Instruct patient to take in 5 slow breaths (“Breathe in and out slowly, 5 times”)</p>
<p>6. Breath-hold for 5 to 10 seconds (<i>optional</i>) Instruct patient to hold breath for 5 to 10 seconds, if he/ she is able to cooperate. This allows the medication time to deposit in the airways. Resume normal breathing</p>

<p>7. Repeat steps 2-6 when more than 1 puff is prescribed.</p> <p>Initial treatment: repeat order every 10-20 min for 1st hour Subsequent treatment: Reduce frequency to every 4-8 hourly-prn Reduce/ stop ipratropium after initial 24 hours*</p>	
<p>8. Escalate in event of poor response:</p>	
<p>Severe features⁴</p> <ol style="list-style-type: none"> 1. Talks in words only, agitated <ul style="list-style-type: none"> - Respiratory rate > 30/ min - Pulse rate > 120/min - SpO2 < 90% (room air) 	<p>Life-threatening</p> <ul style="list-style-type: none"> - Drowsy, confused - Silent chest on auscultation
<p>Medication prescription for “dry nebulization”</p>	
Salbutamol (100mcg)	4 puffs
Ipratropium (20mcg)*	4 puff (if available, if not available then use salbutamol only)
<p>Every 10-20 minute for 1st hour Every 4-8 hours-prn, subsequently</p>	
<p><i>*Ipratropium is administered in combination with short-acting beta-agonist (SABA), if there is poor response to initial SABA nebulization, during acute moderate to severe exacerbations. Though the 2007 NAEPP guidelines suggest that Ipratropium can be dosed up to maximum of 8 puffs every 20 minutes for the first 3 hours in an emergency setting. This is an off-label recommendation. Both GINA 2019 and SIGN 2019 do not explicitly state the recommended dose in an acute setting. As the recommended maximal total daily dose of Ipratropium is 204 mcg, we recommend stopping/ reducing the dose after the initial 1-3 hours.</i></p>	
<p>For patients with preexisting airway disease like asthma/COPD, regular long acting inhalers can be continued using MDI with spacer.</p> <p>If patient is unable to use or has poor response to dry nebulization, switching to conventional nebulization may be needed. Airborne precaution must be applied and patient should preferably be in isolation room.</p> <p>Use mesh nebulizer rather than jet nebulizer for mechanically ventilated patients where available.</p> <p>Since disconnecting the ventilator circuit and nebulization generates aerosols, Healthcare workers must use airborne precaution and use appropriate PPE while caring for such patients with COVID19</p>	

APPENDIX 5: Instructions for “Awake Proning” (Source: Self-positioning guide, Elmhurst Hospital Center, New York City, USA)

Instructions for patients with cough or trouble breathing:

Instrucciones para pacientes con tos o dificultad para respirar:

Please try to not spend a lot of time lying flat on your back! Laying on your stomach and in different positions will help your body to get air into all areas of your lung.

¡Por favor, trate de no estar mucho tiempo acostado sobre su espalda (boca arriba)! Acostarse sobre su estómago (boca abajo), y en diferentes posiciones, le ayudará a su cuerpo a que le llegue aire a todas las áreas de sus pulmones.

Your healthcare team recommends trying to change your position every 30 minutes to 2 hours and even sitting up is better than laying on your back. **If you are able to, please try this:**

El grupo de sus cuidadores de salud le recomienda tratar de cambiar de posición entre cada 30 minutos y 2 horas, y aún permanecer sentado es mejor que estar acostado de espalda. **Si puede, por favor, intente esto:**

1. 30 minutes – 2 hours: lying on your belly
30 minutos – 2 horas: acostado sobre su estómago (boca abajo)
2. 30 minutes – 2 hours: lying on your right side
30 minutos – 2 horas: acostado sobre su lado derecho
3. 30 minutes – 2 hours: sitting up
30 minutos – 2 horas: sentado
4. 30 minutes – 2 hours: lying on your left side; then back to position #1.
30 minutos – 2 horas: acostado sobre su lado izquierdo; y luego vuelva a la posición # 1

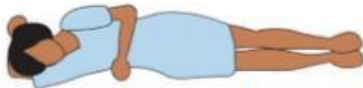
PHOTOS BELOW TO DEMONSTRATE THIS:

LAS FOTOS DEBAJO DEMUESTRAN ESTO:

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



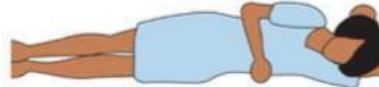
2. 30 minutes – 2 hours: laying on your right side
2. 30 minutos – 2 horas: acostado sobre su lado derecho



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 minutos – 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)!

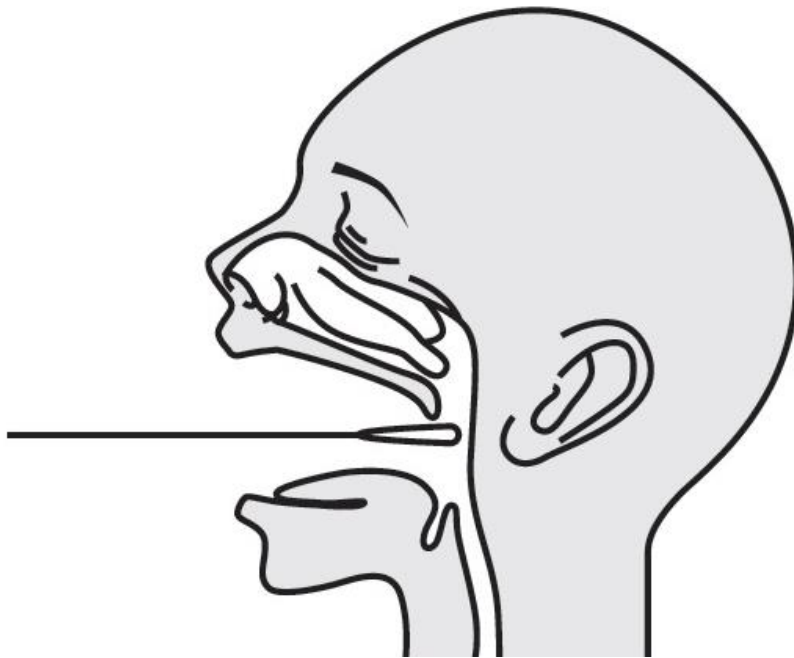
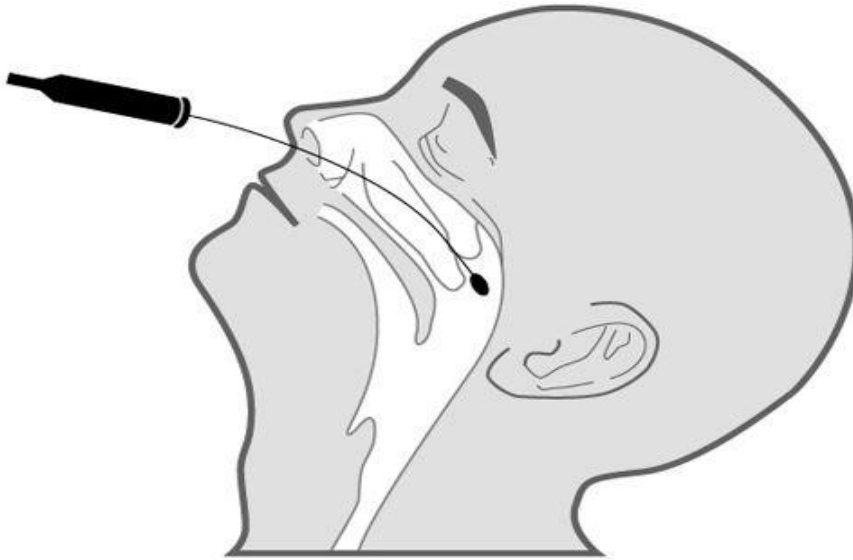


APPENDIX 6: Critical care management including ventilator adjustment (Adapted from Brigham and Women's Hospital COVID-19 Critical Care Clinical Guidelines)

Ventilator adjustment and daily management
<p>Changing ventilation parameters</p> <ol style="list-style-type: none"> 1. Follow ARDSnet ventilation recommendations where possible: <ul style="list-style-type: none"> Tidal volumes should be 4-6 cc/kg using IBW to minimize volumes (and thus ventilator-associated injury). 2. Minute ventilation (respiratory rate x tidal volume) typically drives pH and PCO₂: <ul style="list-style-type: none"> Titrate ventilator parameters to pH, not PCO₂. - To achieve low tidal volumes, tolerate hypercapnia (functionally no limitation unless clinical sequelae) and acidemia (pH > 7.2). - Because tidal volumes are low, the respiratory rate often has to be high to accommodate; typical RR is 20-35 breaths/minute. 3. pH goal is normally 7.25-7.45: <ul style="list-style-type: none"> - If pH > 7.45, decrease respiratory rate - If pH 7.15-7.30, then increase respiratory rate until pH > 7.30, or PaCO₂ < 25 (maximum RR= 35 breaths/minute) • If pH < 7.15, then increase respiratory rate to 35 breaths/minute. If pH still < 7.15, then perform the following: <ol style="list-style-type: none"> a. Tidal volume may be increased by 1 mL/kg until pH > 7.15 (until plateau pressure reaches 30 cm H₂O or tidal volume reaches 8 ml/kg) b. Deep sedation advancing to RASS -5 if needed c. If no improvement, initiate continuous paralysis d. If still no improvement, initiate prone ventilation (may improve V/Q matching and better ventilation)
<p>Changing oxygenation parameters</p> <ol style="list-style-type: none"> 1. Minimize oxygen toxicity: PEEP and FiO₂ drive oxygenation <ul style="list-style-type: none"> - The goal is to deliver a partial pressure of oxygen to perfuse tissues (PaO₂ > 75, SpO₂ >92%) while limiting lung injury from high distending pressures (Ppl < 30) and hyperoxia (FiO₂ < 75, SpO₂ < 96%) - Lower limit goals for PaO₂ / SpO₂ are widely debated; PaO₂ > 55 and SpO₂ >88% are also commonly used. 2. Optimize PEEP: <ul style="list-style-type: none"> - Initial PEEP should be set as explained in the PEEP table below. 3. Adjust FiO₂: <ul style="list-style-type: none"> - Adjust FiO₂ after optimizing PEEP. - Goal FiO₂ < 75%; if FiO₂ > 75%; patient requires ventilator optimization. - It is reasonable to put a desaturating patient temporarily on 100% FiO₂, but remember to wean oxygen as rapidly as possible 4. Check plateau pressure: <ul style="list-style-type: none"> - Check plateau pressure with every change in tidal volume, PEEP, or clinical deterioration (worsening oxygenation) but not as part of routine practice - If plateau pressure is > 30 cm H₂O, then decrease tidal volume by 1 ml/kg (minimum 4 mL/kg). - If plateau pressure is < 25 H₂O and tidal volume < 6 mL/kg, then increase tidal volume by 1 mL/kg until plateau pressure is > 25 cm H₂O or tidal volume = 6 mL/kg. - If plateau pressure is < 30 cm H₂O and patient is breath stacking or dyssynchronous, then increase tidal volume in mL/kg increments to 7 mL/kg or 8 mL/kg so long as plateau pressure is < 30 cm H₂O.

Refractory hypoxemia pathway														
<p>If patient is hypoxic (PaO₂ <55) on Vt = 6 ml/kg, ideal PEEP and FiO₂ >75%, perform the following in this order:</p> <ol style="list-style-type: none"> Optimize volume status by diuresis or RRT if possible. <p>If no improvement, then:</p> <ol style="list-style-type: none"> Deep sedation, advancing to RASS -5 if needed. <p>If no improvement, then:</p> <ol style="list-style-type: none"> Initiate continuous paralysis using available paralyzing agents, titrated to patient-ventilator synchrony). <p>If no improvement then:</p> <ol style="list-style-type: none"> Initiate prone ventilation (see below); high consideration for use early in severe ARDS (<36 hours from ARDS onset, start discussion of proning when P:F< 150, prone within 12 hours of FiO₂ > 75%) <p>If no improvement then:</p> <ol style="list-style-type: none"> Consider ECMO if available 														
Titrate FiO₂ and PEEP for oxygenation for BMI<35 as per the ARDSnet LOW PEEP table														
FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24
Titrate FiO₂ and PEEP for oxygenation for BMI>35 as per the ARDSnet HIGH PEEP table														
FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

APPENDIX 7: Nasopharyngeal and oropharyngeal swab specimen collection



Source for images: www.stanfordlab.com and another online source that could not be verified on the internet

XI. CONTRIBUTORS

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