

INTERIM GUIDANCE DOCUMENT

Clinical management of severe acute respiratory infections when novel coronavirus is suspected: What to do and what not to do

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Introduction

The emergence of novel coronavirus in 2020 (see http://www.who.int/csr/disease/coronavirus_infections/en/index.html for the latest updates) has presented challenges for clinical management.

Pneumonia has been the most common clinical presentation; five patients developed Acute Respiratory Distress Syndrome (ARDS). Renal failure, pericarditis and disseminated intravascular coagulation (DIC) have also occurred.

Our knowledge of the clinical features of coronavirus infection is limited and no virus-specific prevention or treatment (e.g. vaccine or antiviral drugs) is available. Thus, this interim guidance document aims to help clinicians with supportive management of patients who have acute respiratory failure and septic shock as a consequence of severe infection. Because other complications have been seen (renal failure, pericarditis, DIC, as above) clinicians should monitor for the development of these and other complications of severe infection and treat them according to local management guidelines.

As all confirmed cases reported to date have occurred in adults, this document focuses on the care of adolescents and adults. Paediatric considerations will be added later.

This document will be updated as more information becomes available and after the revised *Surviving Sepsis Campaign Guidelines* are published later this year (1).

This document is for clinicians taking care of critically ill patients with severe acute respiratory infection (SARI). It will be helpful if you work in an Intensive Care Unit (ICU) that has limited resources – i.e. limited access to mechanical ventilation, invasive hemodynamic monitoring and arterial blood gas analyzers – or if you have limited access to specialty training. It is not meant to replace clinical training or specialist consultation but rather to strengthen your current clinical management of SARI and link you to the most up-to-date guidance.

This document is organized into four sections, which correspond to clinical management steps. **Section 1** focuses on the early recognition and management of patients with SARI and includes early initiation of supportive and infection prevention and control measures, and therapeutics. **Section 2** focuses on management of patients who deteriorate and develop severe respiratory distress and ARDS. **Section 3** focuses on the management of patients who deteriorate and develop septic shock. **Section 4** focuses on ongoing care of the critically ill patient and best practices to prevent complications.

Three symbols are used:

-  Do: the intervention is known to be beneficial.
-  Don't: the intervention is known to be harmful.
-  Be careful when considering this intervention.

The recommendations in this document are derived mainly from evidence-based guidelines that WHO has published, including the WHO *Integrated Management of Adolescent and Adult Illness (IMAI) District Clinician Manual* (2). Where WHO guidance is not available, we have used widely accepted global consensus statements, such as guidelines of the *Surviving Sepsis Campaign*, and the results of recently published randomized controlled trials. The recommendations have also been reviewed by a WHO global network of clinicians (see [Acknowledgements](#) for names and affiliations).

Links are given here to additional sources and evidence. If you have further questions, contact us by e-mail to outbreak@who.int with 'Novel coronavirus clinical question' in the subject line.

This interim guidance document will expire in 12 months from the date of publication.

SECTION 1

Early recognition and management

✔ Recognize severe manifestations of acute respiratory infections

Table 1. Definitions of clinical syndromes

<p>“Patient under investigation” for novel coronavirus infection</p>	<p>A person with an acute respiratory infection, which may include history of fever or measured fever ($\geq 38\text{ }^{\circ}\text{C}$, $100.4\text{ }^{\circ}\text{F}$) and cough; AND suspicion of pulmonary parenchymal disease (e.g. pneumonia or ARDS), based on clinical or radiological evidence of consolidation: AND residence in or history of travel to the Arabian Peninsula or neighboring countries within 10 days before onset of illness: AND not already explained by any other infection or aetiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines. It is not necessary to wait for test results for other pathogens before testing for novel coronavirus.</p> <p>See updates of the case definition at: http://www.who.int/csr/disease/coronavirus_infections/en/index.html</p>
<p>Severe pneumonia</p>	<p>Adolescent or adult patient with fever or suspected infection, cough, respiratory rate > 30 breaths/min, severe respiratory distress, oxygen saturation (SpO_2) $< 90\%$ on room air.</p>
<p>Acute Respiratory Distress Syndrome</p> 	<p>Onset: acute, i.e. within 1 week of known clinical insult or new or worsening respiratory symptoms</p> <p>Chest imaging (e.g. X-ray or CT scan): bilateral opacities, not fully explained by effusions, lobar/lung collapse or nodules</p> <p>Origin of pulmonary edema: respiratory failure not fully explained by cardiac failure or fluid overload</p> <p>Degree of hypoxemia: $200\text{ mm Hg} < \text{PaO}_2/\text{FiO}_2 \leq 300\text{ mm Hg}$ with PEEP or CPAP $\geq 5\text{ cm H}_2\text{O}$ (mild ARDS); $100\text{ mm Hg} < \text{PaO}_2/\text{FiO}_2 \leq 200\text{ mm Hg}$ with PEEP $\geq 5\text{ cm H}_2\text{O}$ (moderate ARDS); $\text{PaO}_2/\text{FiO}_2 \leq 100\text{ mm Hg}$ with PEEP $\geq 5\text{ cm H}_2\text{O}$ (severe ARDS). When PaO_2 is not available, an $\text{SpO}_2/\text{FiO}_2$ ratio ≤ 315 suggests ARDS.</p>
<p>Sepsis</p>	<p>Documented or suspected infection, with two or more of the following conditions: temperature $> 38\text{ }^{\circ}\text{C}$ ($100.4\text{ }^{\circ}\text{F}$) or $< 36\text{ }^{\circ}\text{C}$ ($96.8\text{ }^{\circ}\text{F}$), HR $> 90/\text{min}$, RR $> 20/\text{min}$ or $\text{PaCO}_2 < 32\text{ mm Hg}$, white blood cells $> 12\text{ }000$ or $< 4000/\text{mm}^3$ or $> 10\%$ immature (band) forms.</p>
<p>Severe sepsis</p>	<p>Sepsis associated with organ dysfunction, hypoperfusion (lactic acidosis) or hypotension. Organ dysfunction may include: oliguria, acute kidney injury, hypoxemia, transaminitis, coagulopathy, thrombocytopenia, altered mental status, ileus or hyperbilirubemia.</p>
<p>Septic shock</p>	<p>Sepsis-induced hypotension (SBP $< 90\text{ mm Hg}$) despite adequate fluid resuscitation and signs of hypoperfusion.</p>

SpO_2 , oxygen saturation; PaO_2 , partial pressure of oxygen; FiO_2 , fraction of inspired oxygen; CPAP, continuous positive airway pressure; PEEP, positive end-expiratory pressure; HR, heart rate; RR, respiratory rate; PaCO_2 , partial pressure of carbon dioxide; SBP, systolic blood pressure. Table adapted from (3).

✔ Initiate infection prevention and control measures

Droplet precautions should be added to standard precautions for any patient known or suspected to have an acute respiratory infection, including patients with suspected or confirmed infection with novel coronavirus. These infection prevention and control measures should be started when the patient enters triage with symptoms of acute febrile respiratory illness. Organize the space and process to permit spatial separation (at least 1 meter) between each patient with acute respiratory infections and other individuals not wearing PPE. Ensure that triage and waiting areas are adequately ventilated. Encourage the use of respiratory hygiene (i.e. covering the mouth and nose during coughing or sneezing with a medical mask, cloth mask, tissue, sleeve or flexed elbow), followed by hand hygiene.

Airborne precautions should be used for aerosol-generating procedures, which have been consistently associated with an increased risk of pathogen transmission (4). The most consistent association of increased risk of transmission to healthcare workers (based on studies done during the SARS outbreaks of 2002–2003) was found for tracheal intubation. Increased risk of SARS transmission was also reported when performing non-invasive ventilation, tracheotomy and manual ventilation before intubation; however, these findings were identified from a limited number of very low-quality studies.

Table 2. Infection control measures: how to implement

Standard precautions	Apply routinely in all health-care settings for all patients. Standard precautions include: hand hygiene and use of personal protective equipment (PPE) to avoid direct contact with patients' blood, body fluids, secretions (including respiratory secretions) and non-intact skin. When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use eye protection, because sprays of secretions may occur. Standard precautions include: prevention of needle-stick or sharps injury; safe waste management; cleaning and disinfection of equipment; and cleaning of the environment.
Droplet precautions	Use a medical mask if working within 1 meter of the patient. Place patients in single rooms, or group together those with the same etiological diagnosis. If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation of at least 1 meter. Limit patient movement and ensure that patients wear medical masks when outside their rooms.
Airborne precautions	Ensure that healthcare workers performing aerosol-generating procedures use PPE, including gloves, long-sleeved gowns, eye protection and particulate respirators (N95 or equivalent). Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures.

✔ Give supplemental oxygen therapy to patients with SARI

Give oxygen therapy to patients with signs of severe respiratory distress, hypoxaemia (i.e. $SpO_2 < 90\%$) or shock. Initiate oxygen therapy at 5 L/min and titrate to $SpO_2 \geq 90\%$ in non-pregnant adults and $SpO_2 \geq 92-95\%$ in pregnant patients. Pulse oximeters (5), functioning oxygen systems and appropriate oxygen-delivering interfaces should be available in all areas where patients with SARI are cared for.

✘ DO NOT restrict oxygen because of concerns about a patient's respiratory drive.

✔ Collect respiratory and other specimens for laboratory testing

Collect routine clinical specimens (e.g. blood and sputum bacterial cultures) for community-acquired pneumonia, ideally before antimicrobial use. Also collect respiratory specimens from the upper respiratory tract (i.e. nasal, nasopharyngeal and/or throat swab) and lower respiratory tract (i.e. sputum, endotracheal aspirate, bronchoalveolar lavage) for known respiratory viruses (such as influenza A and B, influenza A virus subtypes H1, H3, and H5 in countries with H5N1 viruses circulating among poultry;

RSV, parainfluenza viruses, rhinoviruses, adenoviruses, human metapneumoviruses, and non-SARS coronaviruses).

Testing should be done by reverse-transcriptase polymerase chain reaction (RT-PCR) if possible. Serial collection of respiratory specimens from multiple sites on multiple days (every 2–3 days) will inform viral shedding; and blood to assess viremia; conjunctival swabs if conjunctivitis is clinically present; urine, stool, and cerebrospinal fluid if lumbar puncture is performed. Contact WHO for information about laboratories that can test for the presence of novel coronavirus.

While there are few data to determine the most appropriate specimens for novel coronavirus testing, early experience indicates that lower respiratory specimens are more likely to be positive than upper respiratory specimens (6).

 **Give empiric antimicrobials to treat suspected pathogens, including community-acquired pathogens**

Although the patient may be suspected to have novel coronavirus infection, administer appropriate empiric antimicrobials as soon as possible for community-acquired pathogens based on local epidemiology and guidance until the diagnosis is confirmed. Empiric therapy can then be adjusted on the basis of laboratory testing results.

 **Use conservative fluid management in patients with SARI when there is no evidence of shock**

Patients with SARI should be treated cautiously with intravenous fluids, because aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation (7).

 **Do not give high-dose systemic corticosteroids or other adjunctive therapies for viral pneumonitis outside the context of clinical trials**

Prolonged use of systemic high-dose corticosteroids can result in serious adverse events in patients with SARI, including opportunistic infection, avascular necrosis, new health-care-associated bacterial infection and possibly prolonged viral replication. Therefore, corticosteroids should be avoided unless they are indicated for another reason (8).

 **Closely monitor patients with SARI for signs of clinical deterioration, such as severe respiratory distress/respiratory failure or tissue hypoperfusion/shock, and apply supportive care interventions**

SECTION 2

Management of severe respiratory distress, hypoxemia and ARDS

✔ **Recognize severe cases, when severe respiratory distress may not be sufficiently treated by oxygen alone, even when administered at high flow rates**

Even when high oxygen flows (10 to 15 L/min) are delivered through a face mask with reservoir bag, and the concentration of oxygen (FiO_2) is high (between 0.60 and 0.95); patients may continue to have increased work of breathing or hypoxemia because of high intrapulmonary shunt fractions and require mechanical ventilation. There are higher flow oxygen systems now that deliver up to 50–60 L/min flow rates using newer nasal cannula interfaces. Small studies have shown improvement in respiratory distress and oxygenation compared with traditional face masks, but these newer masks are not widely available and more clinical trials are needed to understand their efficacy (9).

✔ **Wherever available, and when staff members are trained, mechanical ventilation should be instituted early in patients with increased work of breathing or hypoxemia that persists despite high-flow oxygen therapy**

In resource-limited settings, the type of mechanical ventilation will be determined by availability and experience with non-invasive ventilation (NIV) (administration of ventilatory support through a mask) or invasive mechanical ventilation administered through an endotracheal tube or tracheostoma.

✔ **Consider NIV if local expertise is available, when immunosuppression is also present, or in cases of mild ARDS without impaired consciousness or cardiovascular failure**

NIV is the delivery of bi-level positive airway pressure through a tight-fitting mask. It reduces the need for endotracheal intubation in patients with severe exacerbations of chronic obstructive pulmonary disease and cardiogenic pulmonary edema. There is, however, insufficient evidence to promote its use in patients with severe pneumonia or ARDS, unless immunosuppression is also present (10). Patients with mild ARDS may be considered for a trial of NIV if there is local experience (11).

⚠ If NIV is tried, monitor the patient closely in an ICU; if NIV is unsuccessful, do not delay endotracheal intubation.

✔ **If equipment is available and staff are trained, proceed with endotracheal intubation to deliver invasive mechanical ventilation**

Patients with ARDS, especially those who are obese or pregnant, may desaturate quickly during intubation. Pre-oxygenate patients with 100% FiO_2 for 5 minutes, via a bag-valve mask or NIV and then proceed with rapid-sequence intubation.

✔ **Use a lung-protective ventilation strategy (LPV) for patients with ARDS**

Implementing a low-volume, low-pressure ventilation strategy/protocol (12), which targets a tidal volume of 6 ml/kg (predicted body weight), a plateau airway pressure (P_{plat}) of ≤ 30 cm H_2O and SpO_2 88–93% or PaO_2 55–80 mm Hg (7.3–10.6 kPa) has been shown to reduce mortality in a heterogeneous population of ARDS patients (13).

- ✔ To reach LPV targets, allow permissive hypercapnia.
 - ✔ To reach target SpO₂, use adequate PEEP for the degree of hypoxemia.
 - ✔ Double-triggering, a common form of asynchrony, can be treated by increasing inspiratory flow, prolonging inspiratory time, suctioning trachea, eliminating water from ventilator tubing, and eliminating circuit leaks.
 - ✔ Deep-sedation targets should be considered if unable to control tidal volume.
 - ⚠ Avoid disconnecting the patient from the ventilator. Disconnection results in loss of PEEP and lung collapse. Use in-line catheters for airway suctioning, clamp tube when disconnection is required and minimize transport.
- ✔ **In patients with severe ARDS, consider adjunctive therapeutics early, especially if failing to reach LPV targets**
- Administration of neuromuscular blockade for initial 48 hours has been associated with improved survival and increased time off the ventilator without causing significant weakness (14).
 - Placing the patient in the prone position improves oxygenation and survival but care must be taken to turn the patient safely (15,16).
 - Delivering a recruitment maneuver and high PEEP improves oxygenation and reduces need for other rescue therapies (17).
- ✔ **Use a conservative fluid management strategy for ARDS patients who are not in shock to shorten the duration of mechanical ventilation (18)**

SECTION 3

Management of septic shock

- ✔ **Recognize sepsis-induced shock when patient develops hypotension (SBP < 90 mm Hg) that persists after initial fluid challenge or signs of tissue hypoperfusion (blood lactate concentration > 4 mmol/L) and initiate resuscitation by protocol**

Resuscitation protocols are available at the Surviving Sepsis Campaign website. In resource-limited settings, acute interventions may need to be modified based on availability of and experience with invasive hemodynamic monitoring devices (i.e. central venous catheter, arterial catheter) and medications.

- ✔ **Give early and rapid infusion of crystalloid intravenous fluids for septic shock**

Give crystalloid fluids, i.e. normal saline or lactated Ringer's solution as fluid loading/bolus (i.e. one L over 30 minutes or faster) and determine need for further fluid boluses based on response (e.g. whether perfusion targets are improving or not).

- ⚠ Overly aggressive fluid resuscitation may lead to respiratory impairment. If there is no response to fluid loading and signs of volume overload appear (i.e. crackles on auscultation, pulmonary edema on chest X-ray) then reduce or discontinue fluid administration. This is particularly important in resource-limited settings where mechanical ventilation is not available.
- ✘ Do not give hypotonic or starch-based solutions for resuscitation. Starches have been associated with an increased incidence of renal dysfunction and failure (19,20)
- ✘ Do not use fluid balance as a guide to administer or withhold further volume loading.

- ✔ **Use vasopressors when shock persists despite liberal fluid resuscitation**

Vasopressors (i.e. norepinephrine, epinephrine and dopamine) are most safely given through a central venous catheter, at a strictly controlled rate, while monitoring blood pressures frequently, and at the minimum dose necessary to maintain perfusion (i.e. SBP > 90 mm Hg) to prevent side effects.

- ⚠ In resource-limited settings, if central venous catheters are not available, vasopressors can be given carefully through a peripheral IV placed in a large vein but closely monitor for signs of extravasation and necrosis. If this occurs, stop infusion.

- ✔ **Consider administration of intravenous hydrocortisone (up to 200 mg/day) or prednisolone (up to 75 mg/day) to patients with persistent shock who require escalating doses of vasopressors**

SECTION 4

Prevention of complications

Implement the following interventions to prevent complications associated with critical illness.

Anticipated Outcome	Interventions
Reduce days of invasive mechanical ventilation (IMV)	<ul style="list-style-type: none"> ✔ Weaning protocols that include daily assessment for readiness to breathe spontaneously ✔ Sedation protocols to titrate administration of sedation to a specific target, with or without daily interruption of continuous sedative infusions
Reduce incidence of ventilator-associated pneumonia	<ul style="list-style-type: none"> ✔ Oral intubation is preferable to nasal intubation ✔ Perform regular antiseptic oral care ✔ Keep patient in semi-recumbent position ✔ Use a closed suctioning system; periodically drain and discard condensate in tubing ✔ Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged but not routinely ✔ Change heat moisture exchanger when it malfunctions, when soiled or every 5–7 days ✔ Reduce days of IMV
Reduce incidence of venous thromboembolism	<ul style="list-style-type: none"> ✔ Use pharmacological prophylaxis (for example, heparin 5000 units subcutaneously twice daily) in patients without contraindications. For those with contraindications, use mechanical prophylactic device such as intermittent pneumatic compression devices.
Reduce incidence of catheter-related bloodstream infection	<ul style="list-style-type: none"> ✔ Use a simple checklist during insertion as reminder of each step needed for sterile insertion and daily reminder to remove catheter if no longer needed (21)
Reduce incidence of pressure ulcers	<ul style="list-style-type: none"> ✔ Turn patient every two hours
Reduce incidence of stress ulcers and gastric bleeding	<ul style="list-style-type: none"> ✔ Give early enteral nutrition (within 24–48 hours of admission), administer histamine-2 receptor blockers or proton-pump inhibitors
Reduce incidence of ICU-related weakness	<ul style="list-style-type: none"> ✔ Early mobility

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