3 Infection prevention and control for patients with SARI

3 Infection prevention and control for patients with SARI

Summary

Administrative and engineering measures and personal protective equipment (PPE) work in harmony to prevent the spread of infection and keep health care workers and patients safe.

When caring for **all** patients in the hospital, implement standard precautions, which include **hand hygiene!**

When caring for patients with ARI also use droplet precautions.

When caring for patients with SARI that may have avian influenza, MERS-CoV, COVID-19 or novel viral infection, also add contact precautions.

When carrying out certain high-risk procedures such as intubation, use airborne precautions.

Tools

References and resources

CDC. Interim guidance on infection control measures for 2009 H1N1 Influenza in healthcare settings, including protection of healthcare personnel. Atlanta (GA): Centers for Disease Control and Prevention; July 2010 (https://www.cdc.gov/h1n1flu/guidelines_infection_control.htm, accessed 4 July 2019).

Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. PloS One. 2012;7(4):e35797.

WHO. Advice on the use of masks in the community setting in Influenza A (H1N1) outbreaks. WHO interim guidance, May 2009. Geneva: World Health Organization; 2009.

WHO. Coronavirus disease (COVID-19) technical guidance: infection prevention and control / WASH [website]. Geneva: World Health Organization; 2020 (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control, accessed 16 March 2020).

WHO. How to handwash? [poster]. Geneva: World Health Organization; 2009 (https://www.who.int/gpsc/5may/How_To_HandWash_Poster.pdf?ua=1, accessed 4 July 2019).

WHO. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. WHO guidelines. Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/112656/1/9789241507134_eng.pdf?ua=120, accessed 3 July 2019).

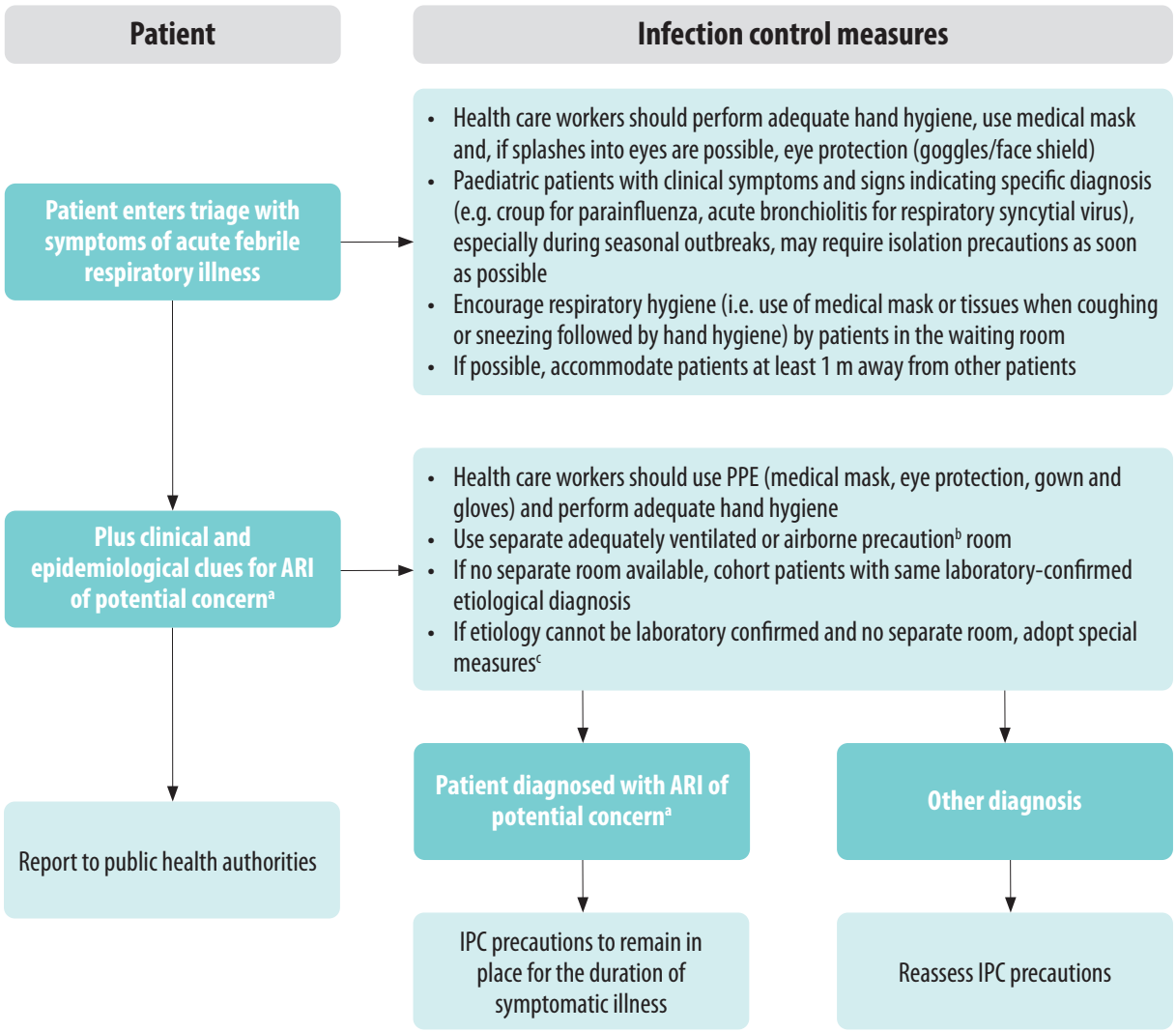
3.1 How to implement infection control measures for COVID-19

Instructions for patients	Give suspect patient a medical mask and direct patient to separate area; an isolation room if available. Keep at least 1 m distance between suspected patients and other patients. Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow and perform hand hygiene after contact with respiratory secretions.
Apply droplet precautions	Droplet precautions prevent large droplet transmission of respiratory viruses. Use a medical mask if working within 1 m 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. When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use eye protection (face mask or goggles), because sprays of secretions may occur. Limit patient movement within the institution and ensure that patients wear medical masks when outside their rooms.
Apply contact precautions	Contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces). Use PPE (medical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving and practise hand hygiene following PPE removal. If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs, pulse oximeters and thermometers). If equipment needs to be shared among patients, clean and disinfect between each patient use. Ensure that health care workers refrain from touching their eyes, nose and mouth with potentially contaminated gloved or ungloved hands. Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). Avoid medically unnecessary movement of patients or transport. Perform hand hygiene.
Apply airborne precautions when performing an aerosol-generating procedure	Ensure that health care workers performing aerosol-generating procedures (e.g. open suctioning of respiratory tract, intubation, bronchoscopy, cardiopulmonary resuscitation) use the appropriate PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection). A scheduled fit test should not be confused with a user's seal check before each use. Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with a minimum of 12 air changes per hour or at least 160 L/second/patient in facilities with natural ventilation. Avoid the presence of unnecessary individuals in the room. Care for the patient in the same type of room after mechanical ventilation begins.

3.2 How to implement infection control measures for SARI

These algorithms are adapted from the WHO guidelines, *Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care* (WHO, 2014).

Decision-tree for infection prevention and control measures for patients known or suspected to have an acute respiratory infection



[a] ARIs of potential concern include SARS, COVID-19, new influenza virus causing human infection (e.g. human cases of avian influenza) and novel organism-causing ARIs that can cause outbreaks with high morbidity and mortality. Clinical and epidemiological clues include severe disease in a previously healthy host, exposure to household member or close contact with severe ARI, cluster of cases, travel, exposure to ill animals or laboratory.
[b] Airborne precaution rooms include both mechanically and naturally ventilated rooms with ≥ 12 air changes per hour and controlled direction of airflow.
[c] The term "special measures" means allowing patients with epidemiological and clinical information suggestive of a similar diagnosis to share a room, but with a spatial separation of at least 1 m.

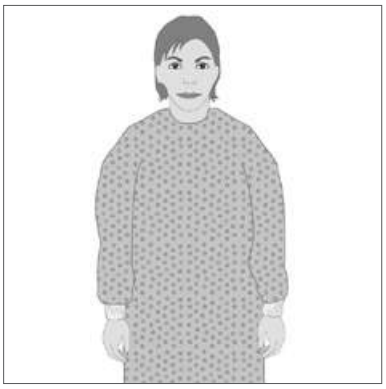
3.3 Personal protective equipment (PPE)

Remember, PPE use should be guided by risk assessment concerning anticipated contact with blood and other bodily fluids, including respiratory droplets and secretions, during patient care and presence of non-intact skin. For example, if there is a risk of splash to the body and face then use hand hygiene, gloves, gown, medical mask and eyewear. How to put and remove PPE appropriately is shown below.

Putting on and removing PPE

A. Putting on PPE (when all PPE items are needed)

1 Identify hazards and manage risk.
- Gather the necessary PPE.
- Plan where to put on and take off PPE.
- Do you have a buddy? Mirror?
- Do you know how you will deal with waste?



2 Put on a gown.

3 Put on particulate respirator or medical mask; perform user seal check if using a respirator.

4 Put on eye protection, e.g. face shield/ goggles (consider anti-fog drops or fog-resistent goggles). Caps are optional; if worn, put on after eye protection.

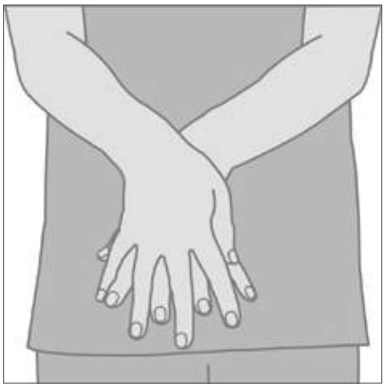
5 Put on gloves (over cuff).

B. Taking off PPE

1 Avoid contamination of self, others and the environment. Remove the most heavily contaminated items first.

Remove gloves and gown:

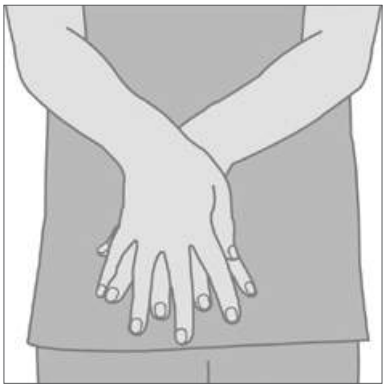
- Peel off gown and gloves and roll inside out.
- Dispose gloves and gown safely.



2 Perform hand hygiene.

3 Remove cap (if worn). Remove goggles from behind. Put goggles in a separate container for reprocessing.

4 Remove respirator from behind.



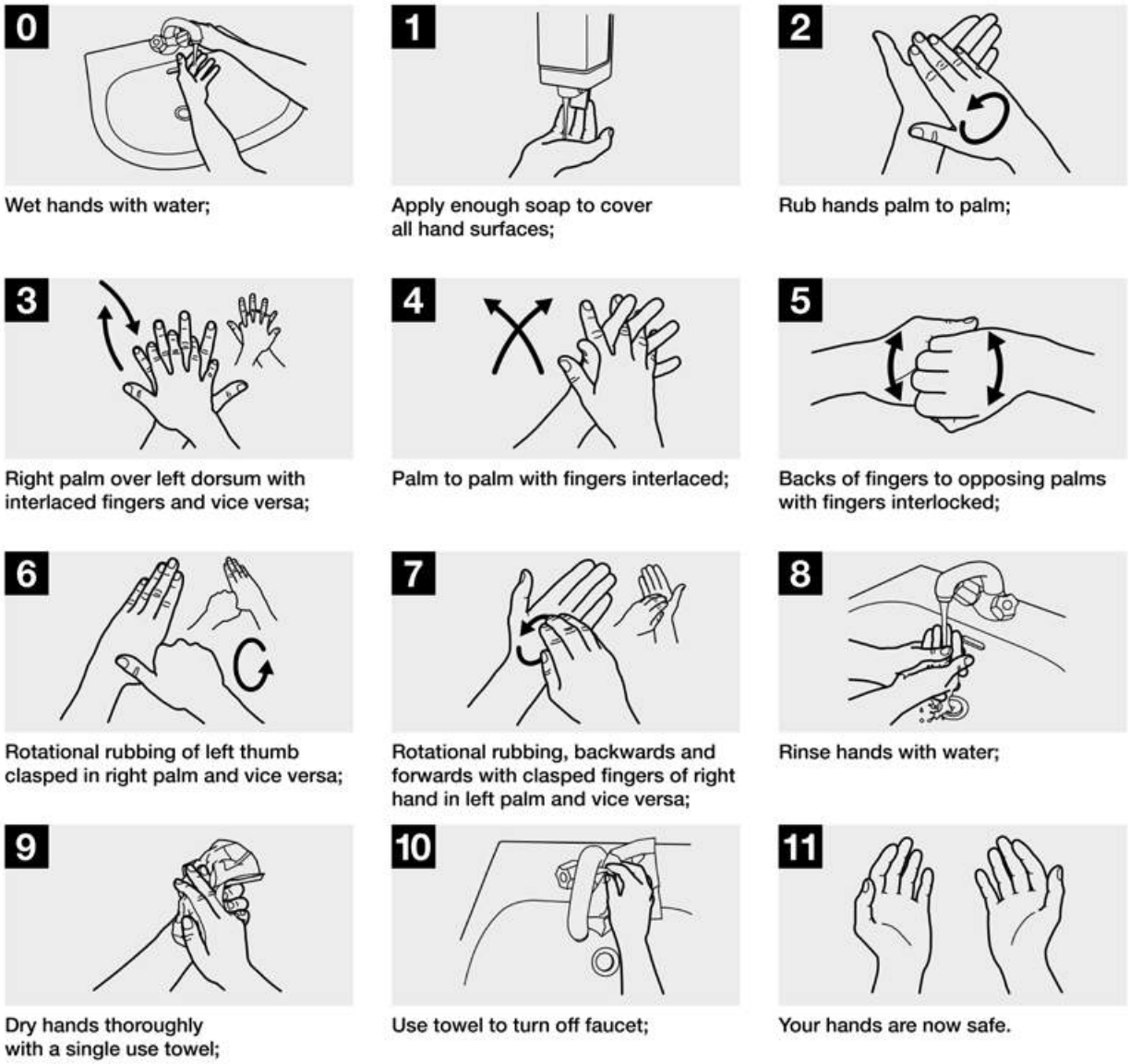
5 Perform hand hygiene.

3.4 Hand hygiene

Hand hygiene must be performed before and after any contact with patients and after contact with contaminated items or surfaces. Use an alcohol-based product if hands are not visibly soiled. Wash hands with soap and water when they are visibly soiled or contaminated with proteinaceous material. Below is an example of hand washing with soap and water. The same rubbing technique can be used with alcohol-based product. This entire procedure can take should take 40–60 seconds (20–30 seconds for alcohol-based hygiene).

WASH HANDS WHEN VISIBLY SOILED! OTHERWISE, USE HANDRUB

Duration of the entire procedure: 40–60 seconds



3.5 Checklist for aerosol-generating procedures

☑ Consider using this checklist when performing aerosol-generating procedures, such as intubation, cardiopulmonary resuscitation, bronchoscopy, aspiration, or open suctioning of respiratory tract secretions.

Note: There is limited research available regarding the risk of non-invasive ventilation and high-flow oxygen therapy, but experts suggest using airborne precautions in these procedures also.

☐ Perform hand hygiene before and after patient contact **and** after PPE removal.

☐ Use a facial particulate respirator (e.g. European Union FFP2 or United States of America National Institute for Occupational Safety and Health-certified N95). Perform a seal check.

☐ Use eye protection (e.g. goggles or a face shield).

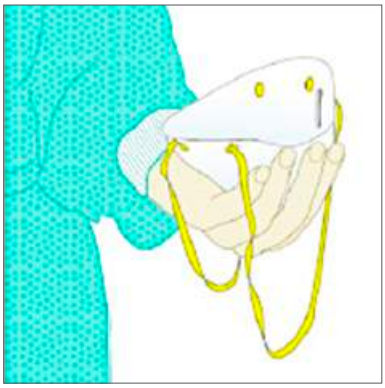
☐ Use a clean, non-sterile, long-sleeved gown.

☐ Use gloves (some of these procedures require sterile gloves).

☐ Make sure adequately ventilated room (e.g. ≥ 12 air changes per hour plus control of airflow direction).

☐ Avoid unnecessary individuals in the room.

Sequence of steps in a particulate respirator seal check



1 Cup the respirator in your hand with the nosepiece at your fingertips allowing the headbands to hang freely below your hand.

2 Position the respirator under your chin with the nosepiece up.

3 Pull the top strap over your head resting it high at the back of your head. Pull the bottom strap over your head and position it around the neck below the ears.

4 Place fingertips of both hands at the top of the metal nosepiece. Mould the nosepiece (USING TWO FINGERS OF EACH HAND) to the shape of your nose. Pinching the nosepiece using one hand may result in less effective respirator performance.

5 Cover the front of the respirator with both hands, being careful not to disturb the position of the respirator.

5A Positive seal check
Exhale sharply. A positive pressure inside the respirator = no leakage. If leakage, adjust position and/or tension straps. Reset the seal.

Repeat the steps until respirator is sealed properly.

5B Negative seal check
Inhale deeply. If no leakage, negative pressure will make respirator cling to your face.

Leakage will result in loss of negative pressure in the respirator due to air entering through gaps in the seal.

4 Monitoring the patient

4 Monitoring the patient

Summary

Patients with severe or critical illness are frequently monitored because of their dynamic clinical condition and need for timely (and titrated) interventions.

The National Early Warning Score (NEWS) is a standardized tool that can be used in hospital and pre-hospital settings to trigger early and appropriate clinical response to deteriorating patients. The Paediatric Early Warning Score (PEWS) is a standardized tool used to identify hospitalized children at risk of clinical decompensation.

In the ICU, haemodynamic and respiratory physiological parameters are monitored frequently (sometimes continuously); along with frequent physical exams and laboratory tests, as needed. Don't forget to take a history.

Pulse oximetry is essential at all health facilities to assess patients at first point of contact, to conduct triage and inform referral.

When patients fail to respond to treatments or deteriorate, use a systematic approach to interpret data and modify the treatment plan, then continue monitoring.

Tools

References and resources

Abbott TE, Vaid N, Ip D, Cron N, Wells M, Torrance HD et al. A single-centre observational cohort study of admission National Early Warning Score (NEWS). Resuscitation. 2015;92:89–93.

Brown SR, Martinez-Garcia D, Agulnik A. Scoping review of pediatric early Warning Systems (PEWS) in resource-limited and humanitarian settings. Front pediatr. 2019;6:410. doi 10.3389/fped.2018.00410.

Burch VC, Tarr G, Morroni C. Modified early warning score predicts the need for hospital admission and inhospital mortality. Emerg Med J. 2008;25(10):674–678.

Frankel HL, Kirkpatrick AW, Elbarbary M, Blaivas M, Desai H, Evans D et al. Guidelines for the appropriate use of bedside general and cardiac ultrasonography in the evaluation of critically ill patients. Part I: general ultrasonography. Crit Care Med. 2015;43(11):2479–502.

Ingham J, Macnaughton PD. Measurement of pO_2, pCO_2, pulse oximetry and capnography. Anaesthesia and Intensive Care Medicine. 2002;6(12):413–415.

Magder S. Understanding central venous pressure: not a preload index? Curr Opin Crit Care. 2015;21(5):369–75.

Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest. 2008;134(1):172–8.

Marino PL. The ICU book (third edition). Philadelphia (PA): Lippincott Williams and Wilkins; 2007.

National Heart, Lung, and Blood Institute ARDS Clinical Trails Network, Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D et al. Comparison of two fluid-management strategies in acute respiratory distress syndrome. N Engl J Med. 2006;354(24):2564–75.

Parshuram CS, Duncan HP, Joffe AR, Farrell CA, Lacroix JR, Middaugh KL et al. Multicentre validation of the bedside paediatric early warning score: a severity of illness score to detect evolving critical illness in hospitalised children. Crit Care. 2011;15(4):R184.

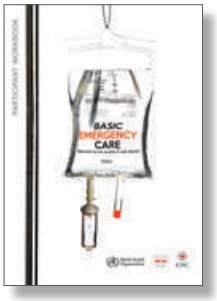
RCP. National Early Warning Score (NEWS) 2 [website]. London: Royal College of Physicians (https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news, accessed 1 July 2019).

Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368–77.

Silcock DJ, Corfield AR, Gowens PA, Rooney KD. Validation of the National Early Warning Score in the prehospital setting. Resuscitation. 2015;89:31–5.

Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. QJM. 2001;94(10):521–6.

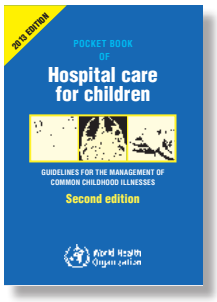
Key resources for supporting management of severe acute respiratory infections in children



Basic emergency care (BEC): approach to the acutely ill and injured (2018)

Developed by WHO and ICRC, in collaboration with the International Federation for Emergency Medicine, *Basic emergency care (BEC): approach to the acutely ill and injured* is an open-access training course for front-line health care providers who manage acute illness and injury with limited resources. Produced in response to requests from multiple countries and international partners, the BEC package includes a Participant Workbook and electronic slide decks for each module. Integrating the guidance from WHO *Emergency triage, assessment and treatment (ETAT)* for children and the *Integrated management of adult/adolescent illness (IMAI)*, BEC teaches a systematic approach to the initial assessment and management of time-sensitive conditions where early intervention saves lives.

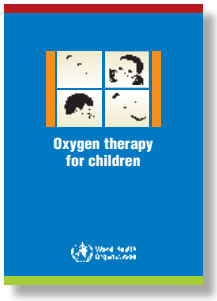
https://www.who.int/publications-detail/basic-emergency-care-approach-to-the-acutely-ill-and-injured



Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources (second edition) (2013)

This is for use by doctors, nurses and other health workers caring for children at first level referral hospitals with basic laboratory facilities and essential medicines. These guidelines focus on the management of the major causes of childhood mortality in most developing countries including pneumonia, and also cover common procedures, patient monitoring and supportive care on the wards.

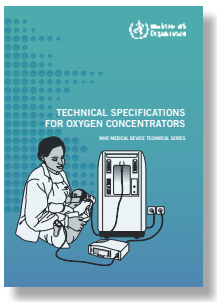
https://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/



Oxygen therapy for children (2016)

This is a bedside manual for health workers to guide the provision of oxygen therapy for children. The manual focuses on the availability and clinical use of oxygen therapy in children in health facilities to guide health workers, biomedical engineers and administrators. It addresses detection of hypoxaemia, use of pulse oximetry, clinical use of oxygen, delivery systems and monitoring of patients on oxygen therapy. The manual also addresses the practical use of pulse oximetry, and oxygen concentrators and cylinders.

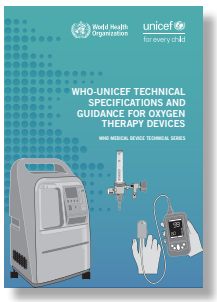
http://www.who.int/maternal_child_adolescent/documents/child-oxygen-therapy/en/



Technical specifications for oxygen concentrators (2015)

This provides an overview of oxygen concentrators and technical specifications to aid in selection, procurement and quality assurance. It highlights the minimum performance requirements and technical characteristics for oxygen concentrators and related equipment that are suitable for the use in health facilities.

https://www.who.int/medical_devices/publications/tech_specs_oxygen-concentrators/en/



WHO-UNICEF technical specifications and guidance for oxygen therapy devices (2019)

The purpose of this document is to increase access to quality products to ensure the supply of oxygen, especially in low- and middle-income countries and low-resource settings within countries from all income groupings. This project is one of many related to improving oxygen supply that other stakeholders are working on. These efforts aim to support ministries of health to ensure oxygen supply is available, as well as raise awareness of the importance of appropriate selection, procurement, maintenance and use of medical devices, both capital equipment and single-use devices.

https://www.who.int/medical_devices/publications/tech_specs_oxygen_therapy_devices/en/

4.1 AVPU scale: a simple tool for assessing level of consciousness

This scale is a simple way to assess a patient's mental status. Each letter corresponds to the patient's level of consciousness.

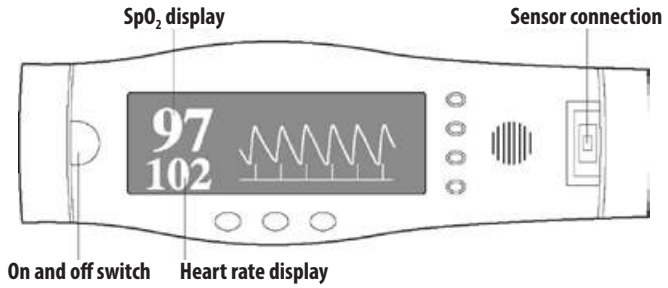
Score	Description
A	Alert
V	Responds to verbal stimuli
P	Responds to painful stimuli
U	Unresponsive or coma

4.2 Pulse oximetry monitoring

A pulse oximeter measures oxygen saturation of haemoglobin in the blood by comparing the absorbance of light of different wavelengths across a translucent part of the body. Pulse oximetry is the best method available for detecting and monitoring hypoxaemia. Even the best combinations of clinical signs commonly lead to misdiagnosis of hypoxaemia in some patients with normal oxygen saturation or fail to detect some hypoxaemic patients. Pulse oximetry should be performed on all patients with SARI.

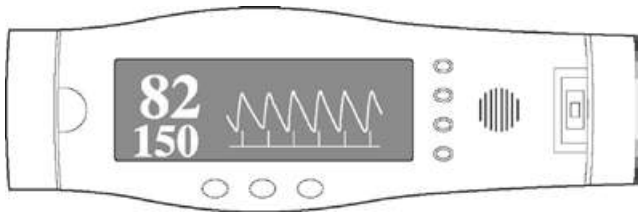
Examples of pulse oximeter displays showing normal and abnormal readings are given below.

Pulse oximeter displaying normal reading



This image shows a pulse oximeter with a normal reading (pulse rate = 102 BPM; SpO_2 = 97%) and a plethysmographic (pulse) wave indicating a good arterial trace and a valid reading.

Pulse oximeter displaying abnormal reading



In this image (pulse rate = 150 BPM; SpO_2 = 82%), the pulse oximeter has a good plethysmographic wave, indicating a valid arterial trace. Therefore, the SpO_2 reading, which is abnormally low (82%), is accurate and indicates that the patient is hypoxaemic. Oxygen should be given. Note the increased heart rate, which is common in seriously ill patients.

Source: Oxygen therapy for children (WHO, 2016).

4.3 Blood gas analysis monitoring

Blood gas analysis can be used to measure the PaO_2 and carbon dioxide in arterial (or venous or capillary) blood. It also indicates the blood pH, which is often abnormal in seriously ill patients with SARI. Metabolic acidosis (low blood pH) is commonly seen when there is major disturbance of the circulation or oxygen delivery, as in severe hypoxaemia due to SARI, ARDS, sepsis and septic shock. Thus, blood gas analysis provides information on oxygenation, ventilation and circulation, and electrolyte concentrations (particularly sodium and potassium) which are measured in the same blood sample and analyser.

Electrolyte abnormalities are common in seriously ill patients with SARI. With an arterial cannula for repeated blood sampling, arterial blood gas analysis is a means for monitoring changes in response to therapy. Venous and capillary blood are easier to monitor than arterial blood but are of no use for determining oxygenation. The carbon dioxide level in arterial, capillary or venous blood helps in assessing alveolar ventilation and monitoring trends in the efficiency of ventilation. The pH is a direct indicator of overall acid–base status in arterial, capillary and venous blood. The probable cause of pH disturbances can be inferred only from the partial pressure of carbon dioxide and the blood bicarbonate concentration (or the base excess or deficit).

Source: Oxygen therapy for children (WHO, 2016).

4.4 National Early Warning Score (NEWS) for adults

The NEWS score was developed by the Royal College of Physicians (United Kingdom of Great Britain and Northern Ireland) to improve the assessment of acute-illness severity of patients in hospital and pre-hospital settings. Please refer to all materials, including posters and training materials, on their website (https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2).

Chart 1: NEWS scoring system

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

Source: Royal College of Physicians (2017).

Chart 2: NEWS thresholds and triggers

NEW score	Clinical risk	Response
Aggregate score 0–4	Low	Ward-based response
Red score Score of 3 in any individual parameter	Low–medium	Urgent ward-based response*
Aggregate score 5–6	Medium	Key threshold for urgent response*
Aggregate score 7 or more	High	Urgent or emergency response**

* Response by a clinician or team with competence in the assessment and treatment of acutely ill patients and in recognising when the escalation of care to a critical care team is appropriate.

**The response team must also include staff with critical care skills, including airway management.

Source: Royal College of Physicians (2017).

Chart 3: Clinical response to NEWS trigger thresholds

NEW score	Frequency of monitoring	Clinical response
0	Minimum 12 hourly	• Continue routine NEWS monitoring
Total 1–4	Minimum 4–6 hourly	• Inform registered nurse, who must assess the patient • Registered nurse decides whether increased frequency of monitoring and/or escalation of care is required
3 in single parameter	Minimum 1 hourly	• Registered nurse to inform medical team caring for the patient, who will review and decide whether escalation of care is necessary
Total 5 or more Urgent response threshold	Minimum 1 hourly	• Registered nurse to immediately inform the medical team caring for the patient • Registered nurse to request urgent assessment by a clinician or team with core competencies in the care of acutely ill patients • Provide clinical care in an environment with monitoring facilities
Total 7 or more Emergency response threshold	Continuous monitoring of vital signs	• Registered nurse to immediately inform the medical team caring for the patient – this should be at least at specialist registrar level • Emergency assessment by a team with critical care competencies, including practitioner(s) with advanced airway management skills • Consider transfer of care to a level 2 or 3 clinical care facility, ie higher-dependency unit or ICU • Clinical care in an environment with monitoring facilities

Source: Royal College of Physicians (2017).

4.5 Paediatric Early Warning Score (PEWS)

This score was published in *Critical Care* in 2011 (see Parshuram et al, 2011), has been used in Canada and the United Kingdom of Great Britain and Northern Ireland and has been shown to be clinically effective in low-resource settings (see Brown et al, 2019).

As in the adult scoring system, it is used to alert staff on general paediatric wards that a child is becoming critically unwell. The scoring system may need calibration or adjustment if used in a different environment to that for which it was developed. A score of 8 or more has a sensitivity of 83% for an impending emergency, including a possible cardiopulmonary arrest, and indicates that the child is critically ill and should be evaluated immediately by a physician and that a higher level of care should be considered.

The seven items in the lefthand column should be scored and added together.

		Item sub-score			
Item	**Age group**	**0**	**1**	**2**	**4**
HR (bpm)	0 to < 3 months	> 110 and < 150	≥ 150 or ≤ 110	≥ 180 or ≤ 90	≥ 190 or ≤ 80
	3 to < 12 months	> 100 and < 150	≥ 150 or ≤ 100	≥ 170 or ≤ 80	≥ 180 or ≤ 70
	1–4 years	> 90 and < 120	≥ 120 or ≤ 90	≥ 150 or ≤ 70	≥ 170 or ≤ 60
	> 4–12 years	> 70 and < 110	≥ 110 or ≤ 70	≥ 130 or ≤ 60	≥ 150 or ≤ 50
	> 12 years	> 60 and < 100	≥ 100 or ≤ 60	≥ 120 or ≤ 50	≥ 140 or ≤ 40
SBP (mmHg)	0 to < 3 months	> 60 and < 80	≥ 80 or ≤ 60	≥ 100 or ≤ 50	≥ 130 or ≤ 45
	3 to < 12 months	> 80 and < 100	≥ 100 or ≤ 80	≥ 120 or ≤ 70	≥ 150 or ≤ 60
	1–4 years	> 90 and < 110	≥ 110 or ≤ 90	≥ 125 or ≤ 75	≥ 160 or ≤ 65
	> 4–12 years	> 90 and < 120	≥ 120 or ≤ 90	≥ 140 or ≤ 80	≥ 170 or ≤ 70
	> 12 years	> 100 and < 130	≥ 130 or ≤ 100	≥ 150 or ≤ 85	≥ 190 or ≤ 75
CR time		< 3 seconds			≥ 3 seconds
RR (breaths/min)	0 to < 3 months	> 29 and < 61	≥ 61 or ≤ 29	≥ 81 or ≤ 19	≥ 91 or ≤ 15
	3 to < 12 months	> 24 or < 51	≥ 51 or ≤ 24	≥ 71 or ≤ 19	≥ 81 or ≤ 15
	1–4 years	> 19 or < 41	≥ 41 or ≤ 19	≥ 61 or ≤ 15	≥ 71 or ≤ 12
	> 4–12 years	> 19 or < 31	≥ 31 or ≤ 19	≥ 41 or ≤ 14	≥ 51 or ≤ 10
	> 12 years	> 11 or < 17	≥ 17 or ≤ 11	≥ 23 or ≤ 10	≥ 30 or ≤ 9
Respiratory effort		Normal	Mild increase	Moderate increase	Severe increase/ any apnoea
SpO_2 (%)		> 94	91 to 94	≤ 90	
Oxygen therapy		Room air		Any to < 4 L/min or < 50%	≥ 4 L/min or ≥ 50%

Source: Parshuram et al (2011).

Notes: CR time – capillary refill time; HR – heart rate; RR – respiratory rate; SBP – systolic blood pressure; SpO_2 – peripheral oxygen saturation.

5 Respiratory specimen collection and processing

5 Respiratory specimen collection and processing

Summary

In patients with SARI, the differential diagnosis should include community-acquired pathogens, including influenza virus infection if influenza activity is known or suspected in the community, or novel virus infection, such as COVID-19, if epidemiological risk factors are present. Differential diagnosis should also be informed by local epidemiology, including viral infections such as malaria, dengue or tuberculosis.

In malaria-endemic areas, patients with fever should be tested for the presence of malaria or other co-infections and treated as appropriate. In endemic settings, arbovirus infection (dengue/chikungunya) should also be considered in the differential diagnosis of undifferentiated febrile illness, particularly when thrombocytopenia is present. Co-infection with COVID-19 virus may also occur and a positive diagnostic test for dengue does not exclude the testing for COVID-19.

If patient meets criteria for SARI treatment, collect blood and sputum cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. However, **do not delay** empiric antimicrobial treatment with antibiotics or antivirals if influenza virus infection is suspected.

Collect specimens from the upper respiratory tract (URT: nasopharyngeal and oropharyngeal) AND, where clinical suspicion remains and URT specimens are negative, collect specimens from the lower respiratory tract when readily available (LRT: expectorated sputum, endotracheal aspirate or bronchoalveolar lavage in ventilated patient) for COVID-19 virus testing by RT-PCR and bacterial stains/cultures.

In hospitalized patients with confirmed COVID-19, repeat URT and LRT samples can be collected to demonstrate viral clearance. The frequency of specimen collection will depend on local epidemic characteristics and resources. For hospital discharge, in a clinically recovered patient, two negative tests, at least 24 hours apart, are recommended.

Tools

References and resources

ANZIC Influenza Investigators, Webb SA, Pettilä V, Seppelt I, Belloma R, Bailey M et al. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. N Engl J Med. 2009;361(20):1925–1934.

Chanez P, Holz O, Ind PW, Djukanovic R, Maestrelli P, Sterk PJ. Sputum induction. Report of Working Group 1. Eur Res J. 2002;20(suppl 37):3s–8s.

Domínguez-Cherit G, Lapinsky SE, Macias AE, Pinto R, Espinosa-Perez L, de la Torre A et al. Critically ill patients with 2009 influenza A(H1N1) in Mexico. JAMA. 2009;302(17):1880–1887.

Gill J, Sheng ZM, Ely SF, Guinee DG, Beasley MB, Suh J et al. Pulmonary pathologic findings of fatal 2009 pandemic influenza A/H1N1 viral infections. Arch Pathol Lab Med. 2010;134(2):235–243.

Heymann DL (editor). Control of communicable diseases manual (20th edition). Washington (DC): APHA Press; 2014.

Kumar A, Zarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J et al. Critically ill patients with 2009 influenza A(H1N1) in Canada. JAMA. 2009;302 (17):1872–1879.

Lister P. Swine-origin influenza virus H1N1, seasonal influenza virus, and critical illness in children. Lancet. 2009;374:605–07.

Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A(H1N1) virus in humans. N Engl J Med. 2009;360:2605–2615.

WHO. Clinical management of human infection with pandemic (H1N1) 2009: revised guidance. Geneva: World Health Organization; 2009.

WHO. Clinical management of severe acute respiratory infection when Middle East respiratory syndrome coronavirus (MERS-CoV) infection is suspected: interim guidance. Updated January 2019 (https://www.who.int/csr/disease/coronavirus_infections/case-management-ipc/en/, accessed 12 August 2019).

WHO. Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans [website]. Geneva: World Health Organization; 2020 (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance, accessed 16 March 2020).

WHO. Fact sheets for avian influenza, seasonal influenza and Middle East respiratory syndrome coronavirus (MERS-CoV) are updated regularly and available on the following WHO websites; 2019: http://www.who.int/mediacentre/factsheets/avian_influenza/en/; http://www.who.int/mediacentre/factsheets/fs211/en/; http://www.who.int/mediacentre/factsheets/mers-cov/en/ (accessed 27 June 2019).

WHO. Information for laboratory diagnosis of pandemic (H1N1) 2009 virus in humans - revised. Geneva: World Health Organization; 2009 (https://www.who.int/csr/resources/publications/swineflu/WHO_Diagnostic_RecommendationsH1N1_20090521.pdf, accessed 27 June 2019).

WHO. Instructions for storage and transport of suspected or confirmed human and animal specimens and virus isolates of pandemic (H1N1). Geneva: World Health Organization; 2009 (https://www.who.int/influenza/gisrs_laboratory/logistic_activities/transport_storage_specimens_isolates/en/, accessed 27 June 2019).

WHO. Recommendations on the use of rapid testing for influenza diagnosis. Geneva: World Health Organization; 2005.

WHO. Regional Office for Europe guidance for sentinel influenza surveillance in humans. Copenhagen: WHO Regional Office for Europe; 2011 (https://apps.who.int/iris/handle/10665/107265, accessed 27 June 2019).

WHO. Safe transport of pandemic influenza A (H1N1) 2009 virus cultures, isolates and patient specimens as Biological Substance, Category B. Geneva: World Health Organization; March 2010.

WHO. Transmission dynamics and impact of pandemic influenza A (H1N1) 2009 virus. WER. 2009;84(46):477–484.

5.1 Differential diagnosis of SARI

It is important to develop a differential diagnosis rapidly for all patients presenting with SARI. This will allow you to guide the initial IPC, diagnostic and treatment measures.

The rate of co-infection (COVID-19 infection complicated by another infection) is unknown. Therefore, a positive diagnostic test for another infection does not exclude the need for COVID-19 testing.

Viral pathogens

Common viral pathogens
Respiratory syncytial virus (RSV), parainfluenza virus, rhinoviruses, adenovirus, enterovirus (EVD68), human metapneumovirus, bocavirus, influenza virus.
Less common, unless at risk or increased risk due to an epidemic
Varicella zoster, measles, human coronavirus including COVID-19, MERS and SARS, hantavirus.
If immunosuppressed (i.e. PL-HIV)
Cytomegalovirus, herpes simplex viruses in addition to above.

Bacterial pathogens

Most common bacterial pathogens
Streptococcus pneumoniae, Hemophilus influenzae, Moraxella catarrhalis, Legionella pneumophila, non-pneumophila Legionella, Chlamydia pneumonia, Mycoplasma pneumoniae, Klebsiella pneumonia, Staphylococcus aureus.
Less common, unless at risk or in high-prevalence country
Mycobacterium tuberculosis, Burkholderia pseudomallei, Rickettsial infections, Coxiella burnetti (Q fever), Leptospira spp, Chlamydia psittaci, Bortedella pertussis, Salmonella sp.
Resistant pathogens
Risk factors for multidrug-resistant pathogens
Intravenous antimicrobial therapy within < 90 days.
Resistant pathogens include
• Methicillin-resistant *S. aureus* (MRSA). • Non-fermenters such as *Pseudomonas aeruginosa, Acinetobacter baumannii.* • Extended spectrum beta-lactamase (ESBL) producers such as *E. coli, Klebsiella, Enterobacter*.

Other endemic infections

Potential endemic infections
Malaria, dengue, chikungunya, tuberculosis, HIV.

5.2 Specimen collection kit for upper respiratory tract specimens

It is best to compile a specimen collection kit before starting to take specimens. Here is an inventory of all items that should be in the specimen collection kit for upper respiratory tract specimens.

Required items

- PPE (gloves, medical mask, gown)
- ice packs/cooler box
- field collection forms
- an alcohol-resistant pen or marker for labelling samples
- sterile Dacron or rayon swabs
- 1–2 mL viral transport medium
- specimen collection containers.

© WHO/Tim Healing

Technique

1. Disinfect bottles.
2. Swab with rigid (plastic) shaft for throat and nasal specimens.
3. Use tongue depressors for throat swabs.
4. Use sterile saline (0.9% NS) for nasopharyngeal aspiration.
5. Use sputum or mucus trap for nasopharyngeal aspiration (also require negative pressure).

Swabs

The type of swab used is very important. Only **sterile Dacron or rayon swabs** with **aluminum or plastic shafts** should be used. This is because calcium alginate or cotton swabs, or swabs with wooden sticks, may contain substances that inactivate some viruses and inhibit PCR testing.

5.3 Nasopharyngeal swab technique

Required materials

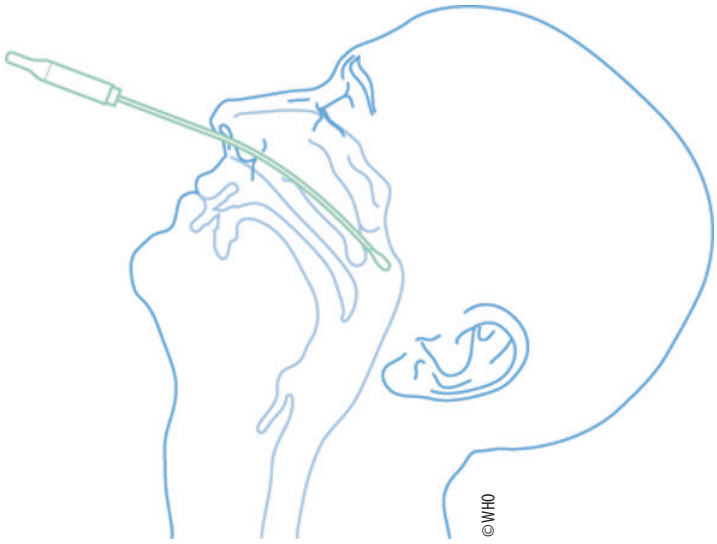
- swab with **flexible** (aluminium) shaft.

Technique

1. Apply standard, contact and droplet precautions.
2. Insert swab into one nostril and back into the nasopharynx.
3. Leave swab in place for a few seconds.
4. Then slowly remove swab while rotating it over surface of posterior nasopharynx.
5. Withdraw swab from collection site; insert into transport tube or container with viral transport medium.
6. Repeat procedure with another swab for the second nostril to deliver optimal combined sample.
7. Label specimen container.
8. After collection, immediately transport specimen to the laboratory for viral PCR testing and viral antigen detection. If transport to the laboratory is delayed, place specimen on ice or in refrigeration.

In case of nasopharyngeal swab in **infants** and **young children**:

- Use a swab of appropriate size: measure the distance from the nose to the ear (philtrum to the tragus).
- Insert the swab half to full amount of that distance, stopping if you encounter resistance.
- Insert the swab horizontally, below the inferior turbinate, not diagonally up the nose.



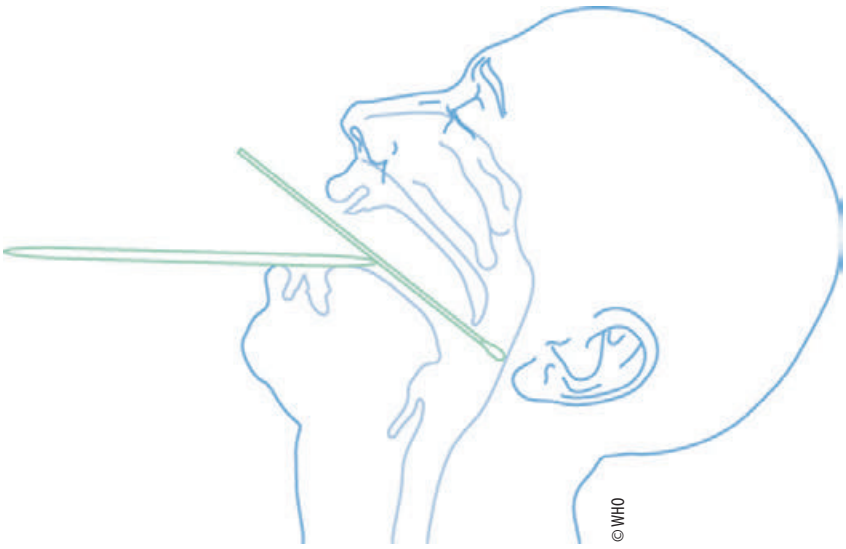
5.4 Posterior pharyngeal swab or throat swab technique

Required materials

- swab with rigid (plastic) shaft
- tongue depressor.

Technique

1. Apply standard, contact and droplet precautions.
2. Ask the subject to open his or her mouth and say "ah" to elevate the uvula.
3. Depress the tongue to hold out of way with tongue depressor.
4. Swab the posterior pharynx and avoid tonsils and do not touch tongue with swab.
5. Insert into transport tube or container with viral transport medium. Break applicator tip to ensure closure of vial.
6. Label specimen container.
7. Immediately transport specimen to the laboratory for viral PCR testing and viral antigen detection. If transport to the laboratory is delayed, place specimen on ice or in refrigeration.



5.5 Tracheal aspirate technique

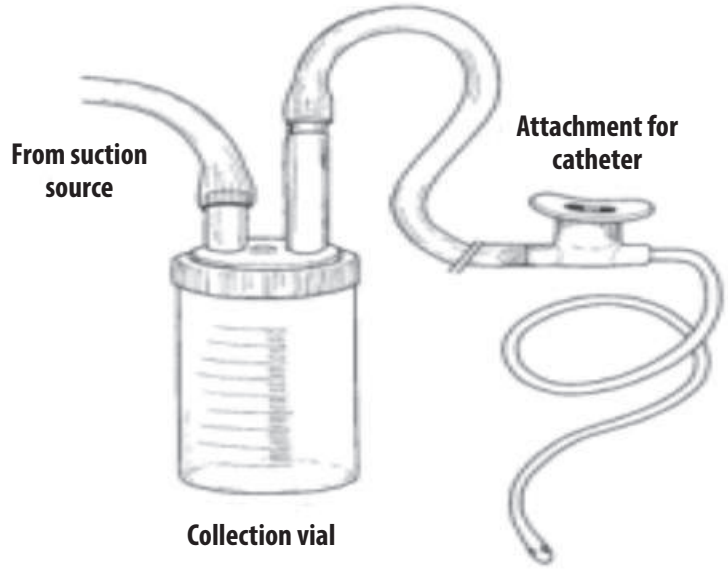
Intended for patients intubated and receiving invasive mechanical ventilation (IMV).

Required materials

- suction outlet (portable or wall)
- sterile suction catheter
- specimen mucus trap (i.e. Lucken's tube)
- sterile saline (0.9% NS)
- IPC for airborne precautions (N-95 particulate mask)
- a sterile suction catheter (not a closed, inline system)
- suction tubing
- airway emergency equipment.

Technique

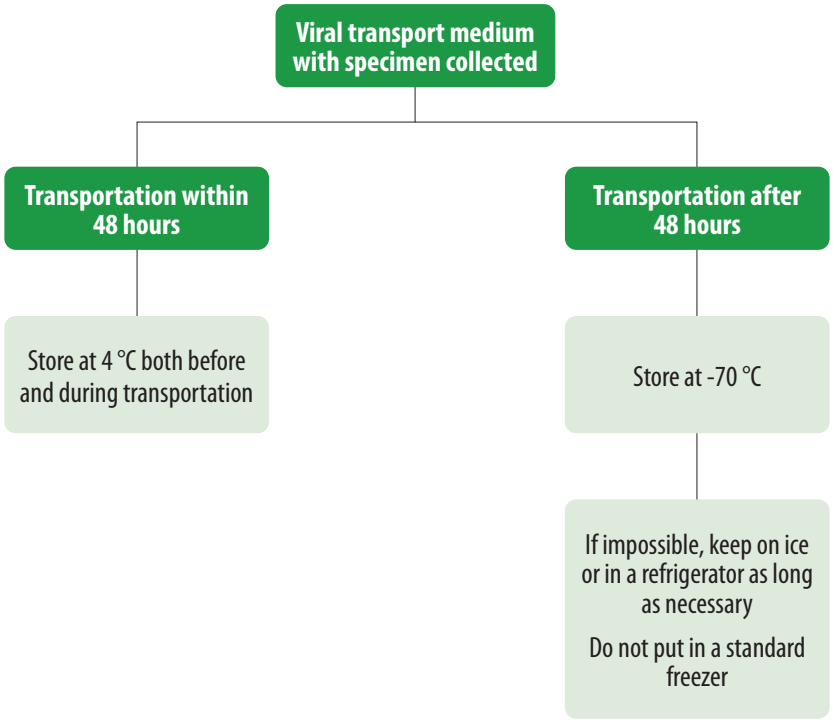
1. Apply standard, contact, droplet and airborne precautions.
2. Prepare patient: pre-oxygenate with 100% fraction of inspired oxygen (FiO_2). Give adequate sedation.
3. Attach mucous trap to catheter and suction outlet. Turn on suction to make sure functioning. Then turn it off.
4. When you are ready, disconnect ventilator tubing from endotracheal tube.
5. Without applying suction, insert sterile suction catheter apparatus into endotracheal tube, about 2–3 cm beyond tip.
6. Apply suction and collect sample into the mucous trap. Hold trap upright to prevent secretions from going into the pump. Slowly withdraw catheter. Replace ventilator tubing.
7. If inadequate sample, instill 3–5 mL of sterile saline, give two sigh breaths and apply suction.
8. After collection, immediately transport specimen to laboratory for viral testing and bacteriology.
9. Store in refrigerator (2–8 °C) for maximum 24 hours.
10. If delay, store in freezer < -20 °C.



5.6 Guideline for specimen storage

Viral transport medium is used immediately after the collection of samples for viral isolation and testing. It prevents the specimen from drying out and prevents bacterial and fungal growth.

Although you should send specimens in viral transport medium to the laboratory as soon as possible, it is important to properly store them before you send them to a laboratory if there is a delay.



Do not freeze samples in the standard freezer. It is very important to avoid freeze-thaw cycles because this will destroy the virus. It is better to keep a sample on ice even for a week, than to allow the sample to freeze and thaw multiple times.

Viral transport medium information

Possible suppliers
Local laboratory and commercial supplier.

Description
It is usually supplied in the form of 1–3 mL of viral transport medium in sterile container.

Stock management
It is important that clinicians liaise with the laboratory to make sure that there is sufficient stock of viral transport medium available at facility, and that the viral transport medium is stored in an area which is accessible to clinicians when needed.

Conservation
If viral transport medium must be stored for long periods this should be done in a freezer at -20 ºC. For short periods of time viral transport medium may be stored in a fridge at 4–6 ºC.

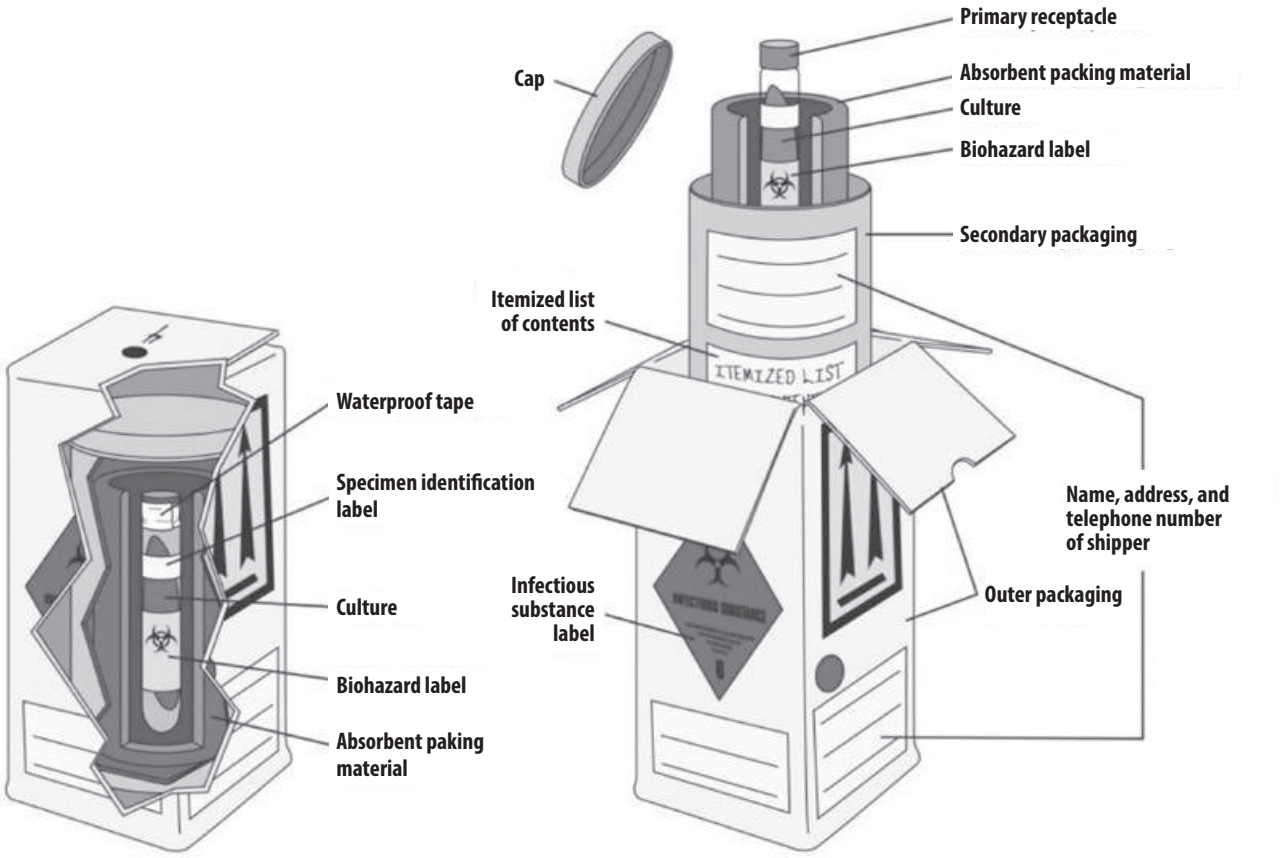
5.7 Material for specimen transportation

When you are ready to pack specimens, no more than 500 mL should be in the specimen container. For transportation from the field to the laboratory, you must use three packaging layers. This is done to protect specimens from damage during transportation.

Required materials

- primary waterproof container (e.g. Falcon tube)
- absorbent material:
  - bubble wrap
  - secondary recipient
  - cooler box
  - ice packs
  - sample identification form.

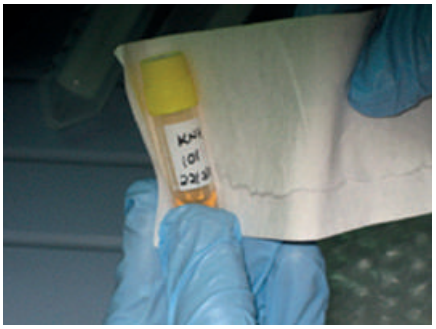
Packing and labelling of infectious substances not refrigerated



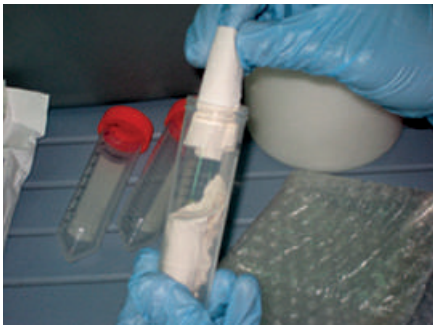
5.8 Guideline for specimen transportation

Viral transport medium is used immediately after the collection of samples for viral isolation and testing. It prevents the specimen from drying out and prevents bacterial and fungal growth.

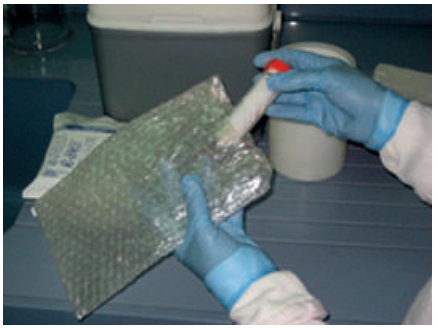
Although you should send specimens in viral transport medium to the laboratory as soon as possible, it is important to properly store them before you send them to a laboratory if there is a delay.



1 Envelop the cryo-tube with blotting paper.



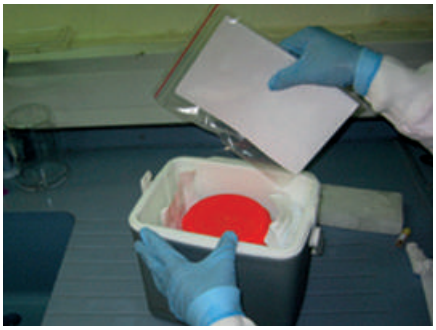
2 Place the enveloped cryo-tube in the primary waterproof container and close in order to be watertight.



3 Place the primary waterproof container in bubble wrap or a shock-absorbing material.

4 Place all components in a waterproof secondary recipient container and close in order to be watertight.

5 Place ice packs in the cooler box. Put the filled secondary container in the cooler box. The recipient container should be in a vertically position.



6 Insert the sample identification form in a zip bag and place the zip bag in the cooler box, next to the secondary recipient container.

7 Close the cooler box in order to be watertight. Write expeditor and addressee on the external part of the cooler box. Put infectious substance label if necessary.

Source: Adapted from influenza sentinel surveillance training, Institute Pasteur of Madagascar, CDC and WHO.

5.9 Guide for blood culture collection

Blood cultures should be obtained before starting antimicrobial therapy in all patients with sepsis in the hospital. The Surviving Sepsis Campaign guidelines caution that this should not delay antimicrobial treatment by more than 45 minutes. This technique is adapted from the United States Centers for Disease Control and Prevention (CDC) website (http://www.cdc.gov/getsmart/healthcare/implementation/clinicianguide.html).

Required materials

- PPE (gloves and mask)
- alcohol swabs
- chlorhexidine swabs (associated with less contamination than standard povidone-iodine)
- blood culture bottles (two bottles per set, one anaerobe and one aerobe)
- two sterile needles (adult: 22 gauge; paediatric: 25 gauge)
- two syringes (adult 20 mL; paediatric 5 mL)
- tourniquet
- sterile gauze pad
- adhesive tape
- patient labels
- plastic zip lock bag for transport.

Technique

1. Check patient ID, explain procedure.
2. Hand washing.
3. Disinfect bottle tops with 70% isopropyl alcohol (alcohol pad) in a circular motion, allow to dry.
4. Clean the puncture site with chlorhexidine swab. Using aseptic technique, remove applicator from package. Holding applicator downward, squeeze wings and release solution. Scrub back and forth over the site for 30 seconds on dry skin. Allow to dry.
5. Puncture the vein with clean needle. Use sterile gloves if you plan to palpate vein after cleaning site.
6. For adults, collect 10–20 mL and 3–5 mL for a child for each blood culture set.
7. Remove needle from vein, divide blood into two blood culture bottles, by placing same needle perpendicularly into the bottle. Do not overfill bottles. If not enough for both bottles, preferably fill the aerobic bottle.
8. Gently rotate bottle to mix blood and broth.
9. Two blood cultures (by separate stick) per septic episode is sufficient.
10. Place label and put into plastic bag and send to the laboratory.

Contaminated blood culture

If skin is not adequately cleansed before obtaining culture, bacteria from the skin may be injected into the bottle, producing contamination and a false positive blood culture. This may lead to misdiagnosis and prolonged antimicrobial use.

6 Oxygen therapy

6 Oxygen therapy

Summary

Give supplemental oxygen therapy immediately to patients with SARI and respiratory distress, hypoxaemia or shock and target SpO_2 > 94%.

In adults, start at 5 L/min and in children at 1–2 L/min using nasal cannula. Monitor SpO_2 immediately because clinical signs of hypoxaemia are unreliable.

Pulse oximeters should be available in all areas where emergency oxygen is delivered. Blood gas analyser should be available in the ICU to also measure ventilatory parameters (pH, $PaCo_2$).

Titrate oxygen to target SpO_2 ≥ 90% (or > 92–95% in pregnant females) using the appropriate dose (flow rate) and delivery device.

Newer high-flow oxygen systems can be used in select cases of non-hypercapnic, hypoxaemia respiratory failure.

Tools

References and resources

Duke T, Graham SM, Cherian MN, Ginsburg AS, English M, Howie S et al. Oxygen is an essential medicine: a call for international action. Int J Tuberc Lung Dis. 2010;149(11):1362–1368.

Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med. 2015;372(23):2185–96.

Jensen LA, Onyskiw JE, Prasad NG. Meta-analysis of arterial oxygen saturation monitoring by pulse oxymetry in adults. Heart Lung. 1998;27(6):387–408.

Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. Scand J Trauma Resusc Emerg Med. 2016;24:93.

O'Driscoll BR, Howard LS, Davison GA. BTS Guideline for emergency oxygen use in adult patients. Thorax. 2008;63(suppl 6):vi1–68.

Potter VA. Pulse oximetry in general practice: how would a pulse oximeter influence patient management? Eur J Gen Pract. 2007;13(4):216–20.

Rojas-Reyes MX, Granados Rugeles C, Charry-Anzola LP. Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. Cochrane Database Syst Rev. 2014;(12):CD005975.

WHO. IMAI district clinician manual: hospital care for adults and adolescents. Guidelines for the management of common illnesses with limited resources. Volume 1. Geneva: World Health Organization; 2011 (https://www.who.int/influenza/patient_care/IMAI_DCM/en/, accessed 26 June 2019).

WHO. Oxygen therapy for children. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/204584/1/9789241549554_eng.pdf, accessed 1 July 2019).

WHO. Patient safety pulse oximetry project [website]. Geneva: World Health Organization; 2019 (http://www.who.int/patientsafety/safesurgery/pulse_oximetry/en/, accessed 1 July 2019).

WHO. Pocket book of hospital care for children. Guidelines for the management of common illnesses with limited resources (second edition). Geneva: World Health Organization; 2013 (https://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/, accessed 26 June 2019).

6.1 Algorithm to deliver increasing oxygen in adults

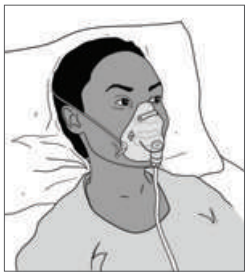
This is reproduced from the WHO *IMAI district clinician manual: hospital care for adolescents and adults: guidelines for the management of illnesses with limited resources* (Volume 1) (WHO, 2011).

How to deliver increasing oxygen

Place prongs inside the nostril. Hook tubing behind ears. Flow rates higher than 5 L will dry mucous membranes.

➜ **Start oxygen at 5 L/min**
➜ Use nasal prongs
➜ Assess response

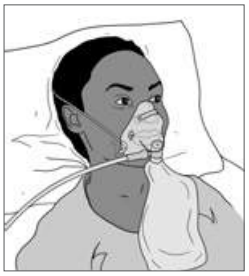
If increasing respiratory distress or SpO_2 < 90%[a]



Secure mask firmly on face over nose and mouth. Pull strap over head.

➜ Use face mask
➜ **Increase oxygen to 6–10 L/min**
➜ Assess response

If increasing respiratory distress or SpO_2 < 90%[a]



Make sure bag is full to deliver highest oxygen concentration. An empty bag is dangerous.

➜ Use face mask with reservoir
➜ **Increase oxygen to 10–15 L/min**
➜ Make sure bag inflates
➜ Call for help from district clinician
➜ Assess response

If increasing respiratory distress or SpO_2 < 90%[a], transfer to a hospital with available invasive mechanical ventilator possible

➜ Call for help from district clinician for possible tracheal intubation
➜ **Start manual ventilation (bagging) with high-oxygen flow**

Estimating FiO_2 when delivering oxygen

Adults

- 2–4 L/min ~ FiO_2 0.28–0.36
- 5 L/min ~ FiO_2 0.40
- 6–10 L/min ~ FiO_2 0.44–0.60
- 10–15 L/min ~ FiO_2 0.60–0.95

Note:

[a] Patients presenting with emergency signs should receive oxygen therapy if SpO_2 is < 94%.
Emergency signs:

- Obstructed or absent breathing
- Severe respiratory distress
- Central cyanosis
- Signs of shock, defined as cold extremities with capillary refill time > 3 sec and weak and fast pulse
- Coma (or seriously reduced level of consciousness)
- Seizures
- Signs of severe dehydration: lethargy or unconscious, sunken eyes, very slow return after pinching the skin.

6.2 Algorithm to deliver increasing oxygen in children

Nasal prongs are the preferred method of delivering oxygen to infants and children < 5 years of age with hypoxaemia who require oxygen therapy.

Practical considerations

The distal prong should fit well into the nostril (premature infants: 1 mm; infants weighing up to 10 kg: 2 mm). The prongs should be secured with a piece of tape on the cheeks near the nose as shown above. Care should be taken to keep the nostrils clear of mucus to avoid blockage.

Starting flow and titration parameters

When the child has only respiratory distress, oxygen supplementation is recommended at SpO_2 < 90%. Children presenting with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, signs of shock, coma or seriously reduced level of consciousness, seizures, signs of severe dehydration) with or without respiratory distress should receive oxygen therapy if their SpO_2 is < 94%. These children should receive oxygen initially by nasal prongs at a standard flow rate (0.5–1 L/min for neonates; 1–2 L/min for infants; and 2–4 L/min for older children) or through an appropriately sized face mask (> 4 L/min) to reach an SpO_2 of ≥ 94%.

If severe hypoxaemia persists despite maximal flow rates:

- start CPAP (if available);
- start secondary source of oxygen with face mask with reservoir bag.

Oxygen delivery methods in children and infants

Method	Maximum O_2 flow (L/min)[a]	Actual inspired O_2 fraction (%) from 1 L/min by a 5-kg infant	PEEP	Humidification	Risk for hypercapnia	Risk for airway obstruction	Equipment required	Nursing demand
Nasal prongs	Neonates: 0.5–1							
	Infants: 2							
	Preschool: 4							
	School: 6	45	Minimal	Not required	No	Minimal	Nasal prongs	+
Nasal catheter	Neonates: 0.5							
	Infants: 1	50	+	Not required	No	+	8-F catheter	++
Nasopharyngeal catheter	Neonates: 0.5							
	Infants: 1	55	++	Required	No	++	8-F catheter, humidifier	+++
Head box, face mask, incubator tent *Not recommended as oxygen is used inefficiently*	Head box: 2–3 L/kg per min		Nil	Not required	Yes	No	Head box, face mask	+++

Source: Oxygen therapy for children (WHO, 2016).

Notes:
[a] Higher flow rates without effective humidification may cause drying of nasal mucosa, with associated bleeding and airway obstruction.
F – French; PEEP – positive end-expiratory pressure.

6.3 Checklist to troubleshoot warning signs during oxygen delivery

☑ If **respiratory distress and hypoxaemia fail to improve** despite increasing oxygen, use a systematic approach to manage your patient. Consider using this checklist.

Repeat the quick check BEC ABCDE approach (Tool 2.3).

Equipment

- Is the measurement correct?
  - ☐ Repeat measurement (e.g. place pulse oximeter correctly; use another pulse oximeter, get an arterial blood gas if appropriate).
- Is there technical difficulty in delivering treatments?
  - ☐ Check that the oxygen source is working:
    - ☐ Is the gas oxygen?
    - ☐ Is the cylinder full?
    - ☐ Is the concentrator on?
  - ☐ Check equipment (e.g. tubing and masks) are appropriate and functioning:
    - ☐ Are the flows correct for type of mask being used?
    - ☐ If using a face mask with reservoir bag, is reservoir bag full?
    - ☐ Is the tubing kinked?
- Is there an alternate diagnosis?
  - ☐ Does the patient have acute respiratory distress syndrome (ARDS)?
  - ☐ Does the patient have acute heart failure?
- Is the patient getting appropriate therapy for the correct diagnosis?
  - ☐ Ensure underlying etiology is being appropriately managed (e.g. antimicrobials given for pneumonia).
- Is our treatment causing harm?
  - ☐ Consider complications and modify management accordingly (e.g. too much fluid leading to pulmonary oedema? Allergic reaction to medication?).
- Does the patient have hypoxemia that is refractory to high-flow oxygen (e.g. significant shunt from ARDS)?
  - ☐ Consider initiation of mechanical ventilator support for management of respiratory failure.

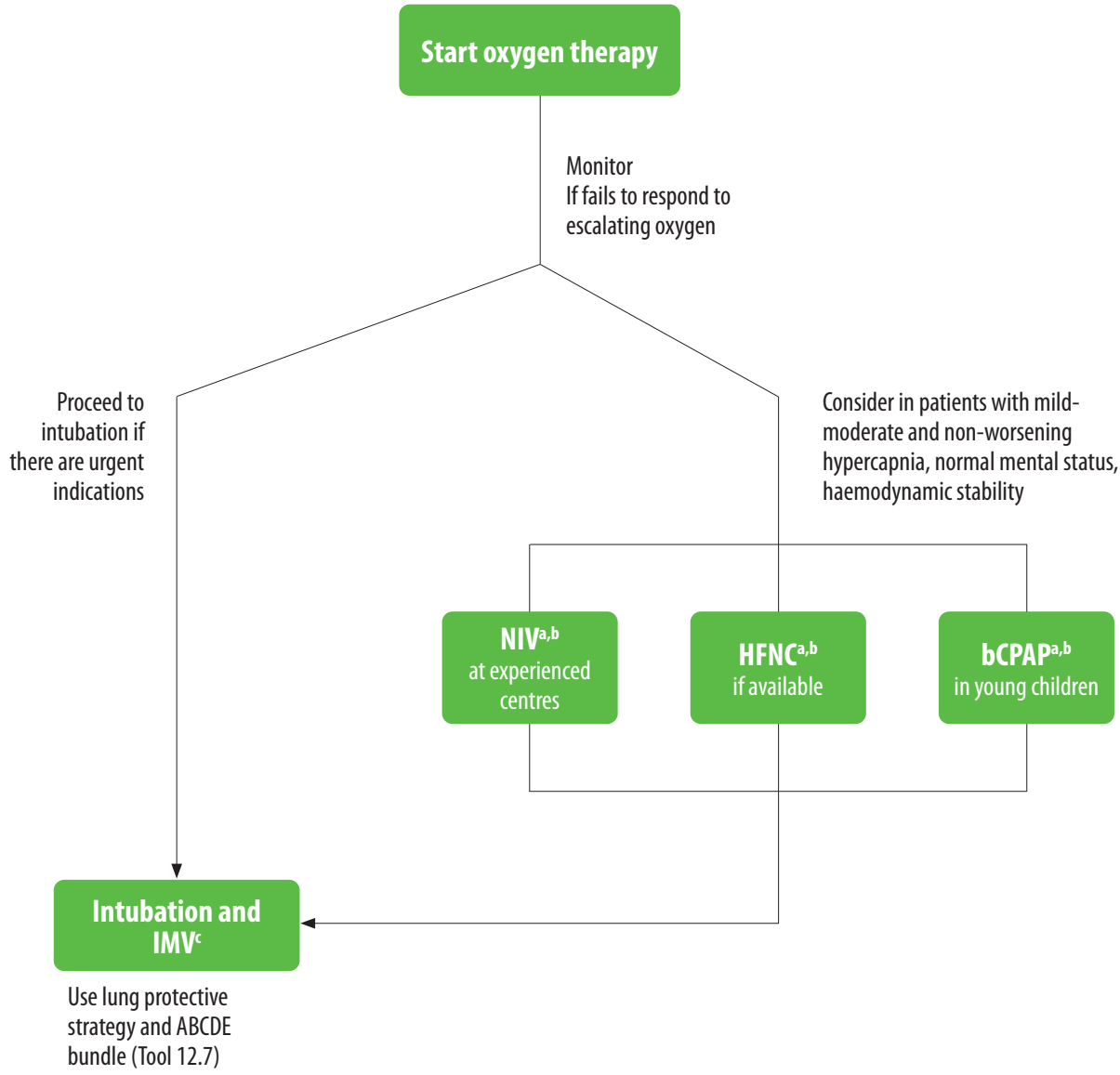
☑ If the **patient's mental status deteriorates** despite SpO_2 > 90%, consider the following:

☐ Manage airway, assist ventilation if needed – do not wait for arterial blood gas results if the patient requires assisted ventilation on clinical grounds.

☐ Check arterial blood gas, if available, to evaluate ventilation. Patients with acute respiratory acidosis from carbon dioxide (CO_2) retention will not be detected with SpO_2 alone.

☐ Consider alternate causes of altered mental status and treat appropriately (e.g. acute central nervous system [CNS] event, electrolyte abnormalities, low glucose).

6.4 Algorithm to escalate supportive respiratory therapy



Notes:
[a] Health care worker must apply airborne precautions.
[b] Patients receiving NIV, HFNC or bCPAP should be in a monitored setting and cared for by experienced personnel capable of performing endotracheal intubation in case the patient acutely deteriorates or does not improve after a short trial (about 1 hour). Do not delay intubation if there is an indication.
[c] Intubation and IMV only in experienced centres; and the most experienced clinicians should intubate given the risk of decompensation and aerosolization during the procedure.

bCPAP – bubble continuous positive airway pressure; HCW – health care worker; HFNC – high-flow nasal cannula; IMV – invasive mechanical ventilation; NIV – non-invasive ventilation; SARI – severe acute respiratory illness.

7 Antimicrobial therapy

7 Antimicrobial therapy

Summary

Give empiric antimicrobials to treat all likely pathogens causing SARI and sepsis as soon as possible, within 1 hour of initial assessment for patients with sepsis.

For COVID-19 with severe pneumonia, treat with IV antibiotics. For COVID-19 uncomplicated pneumonia, treat with oral antibiotics.

If suspect other etiologies, such as influenza, empiric therapy with a neuraminidase inhibitor should be considered. In malaria-endemic areas, patients with fever should be tested for the presence of malaria or other co-infections and treated as appropriate.

When seasonal influenza A or B viruses are known or suspected to be circulating among persons in the community, or there is suspected avian influenza A virus infection, treat SARI patients with empiric antiviral **and** antimicrobials for all likely pathogens as soon as possible (within 1 hour).

Oseltamivir is a neuraminidase inhibitor antiviral drug and is active against all currently circulating influenza viruses that infect humans. It can be delivered enterically to a ventilated patient via nasogastric (NG) or orogastric (OG) tube.

If the clinical course remains severe or progressive, despite ≥ 5 days of treatment, continue on with treatment but also consider alternate diagnosis and oseltamivir resistance.

Tools

References and resources

Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011;53(7):e25–76 (http://cid.oxfordjournals.org/content/early/2011/08/30/cid.cir531.full, accessed 1 July 2019).

Chan-Tack KM, Kim C, Moruf A, Birnkrant DB. Clinical experience with intravenous zanamivir under an Emergency IND program in the United States (2011–2014). Antivir Ther. 2015;20(5):561–4.

Chu CM, Cheng VC, Hung IF, Wong MM, Chan KH, Chan KS et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax. 2004;59(3):252–6.

de Jong MD, Ison MG, Monto AS, Metev H, Clark C, O'Neil B et al. Evaluation of intravenous peramivir for treatment of influenza in hospitalized patients. Clin Infect Dis. 2014;59(12):e172–85.

Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. Lancet. 2015;385(9979):1729–37.

Eccles S, Pincus C, Higgins B, Woodhead M; Guideline Development Group. Diagnosis and management of community and hospital acquired pneumonia in adults: summary of NICE guidance. BMJ. 2014;349:g6722.

EMEA. CHMP assessment report on novel influenza (H1N1) outbreak Tamiflu (oseltamivir) Relenza (zanamivir). London: European Medicines Agency; 2009 (EMEA/H/A-5.3/1172, 7 May 2009; https://www.ema.europa.eu/en/documents/other/chmp-assessment-report-novel-influenza-h1n1-outbreak-tamiflu-oseltamivir-relenza-zanamivir_en.pdf, accessed 1 July 2019).

Hernandez JE, Adiga R, Armstrong R, Bazan J, Bonilla H, Bradley J et al. Clinical experience in adults and children treated with intravenous peramivir for 2009 influenza A (H1N1) under an Emergency IND program in the United States. Clin Infect Dis. 2011;52(6):695–706.

Hung IF, To KK, Lee CK, Lee KL, Yan WW, Chan K et al. Hyperimmune IV immunoglobulin treatment: a multicenter double-blind randomized controlled trial for patients with severe 2009 influenza A(H1N1) infection. Chest. 144(2):464–73.

Kim WY, Young Suh G, Huh JW, Kim SH, Kim MJ, Kim YS et al. Triple-combination antiviral drug for pandemic H1N1 influenza virus infection in critically ill patients on mechanical ventilation. Antimicrob Agents Chemother. 2011;55(12):5703–9.

Kiselev OI, Maleev VV, Deeva EG, Leneva IA, Selkova EP, Osipova EA et al. [Clinical efficacy of arbidol (umifenovir) in the therapy of influenza in adults: preliminary results of the multicenter double-blind randomized placebo-controlled study ARBITR.] Ter Arkh. 2015;87(1):88–96.

Laidler MR, Thomas A, Baumbach J, Kirley PD, Meek J, Aragon D et al. Statin treatment and mortality: propensity score-matched analyses of 2007–2008 and 2009–2010 laboratory-confirmed influenza hospitalizations. Open Forum Infect Dis. 2015;2(1):ofv028.

Lee N, Chan PK, Wong CK, Wong KT, Choi KW, Joynt GM et al. Viral clearance and inflammatory response patterns in adults hospitalized for pandemic 2009 influenza A(H1N1) virus pneumonia. Antivir Ther. 2011;16(2):237–47.

Lee N, Leo YS, Cao B, Chan PK, Kyaw WM, Uyeki TM et al. Neuraminidase inhibitors, superinfection and corticosteroids affect survival of influenza patients. Eur Respir J. 2015;45(6):164–52.

Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax. 2009;64(suppl 3):iii1–55 (https://thorax.bmj.com/content/64/Suppl_3/iii1, accessed 1 July 2019).

Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44(suppl 2):S27–72 (http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Infections_by_Organ_System/Lower/Upper_Respiratory/Community-Acquired_Pneumonia_%28CAP%29/, accessed 1 July 2019).

Miller, PE, Rambachan A, Hubbard RJ, Li J, Meyer AE, Stephens P et al. Supply of neuraminidase inhibitors related to reduced influenza A (H1N1) mortality during the 2009-2010 H1N1 pandemic: an ecological study. PLoS One. 2012;7(9):e43491.

Muthuri SG, Venkatesan S, Myles PR, Leonardi-Bee J, Al Khuwaitir TS, Al Mamun A et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. Lancet Respir Med. 2014;2(5):395–404.

NICE. Pneumonia in adults: diagnosis and management. Clinical guideline. London: National Institute for Health and Care Excellence; 2014 (https://www.nice.org.uk/guidance/cg191/resources/pneumonia-in-adults-diagnosis-and-management-35109868127173, accessed 1 July 2019).

Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam JS, Lim WS. Effect of corticosteroid therapy on influenza-related mortality: a systematic review and meta-analysis. J Infect Dis. 2015;212(2):183–94.

South East Asia Infectious Disease Clinical Research Network. Effect of double dose oseltamivir on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial. BMJ. 2013;346:f3039.

Wang MZ, Cai BQ, Li LY, Lin JT, Su N, Yu HX et al. [Efficacy and safety of arbidol in treatment of naturally acquired influenza]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2004;26(3):289–93.

WHO. Clinical management of human infection with pandemic (H1N1) 2009: revised guidance. Geneva: World Health Organization; 2009.

WHO. Coronavirus disease (COVID-19) R&D [website]. Geneva: World Health Organization; 2020 (https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/, accessed 20 March 2020).

WHO. Guidelines for pharmacologic management of pandemic influenza A (H1N1) 2009 and other influenza viruses. Revised February 2010. Geneva: World Health Organization; 2010.

WHO. IMAI district clinician manual: hospital care for adolescents and adults. Volume 2. Geneva: World Health Organization; 2011 (https://apps.who.int/iris/bitstream/handle/10665/77751/9789241548290_Vol2_eng.pdf?sequence=3, accessed 18 March 2020).

WHO. Pocket book of hospital care for children (second edition). Geneva: World Health Organization; 2013.

Zhang Y, Sun W, Svendsen ER, Tang S, MacIntyre RC, Yang P et al. Do corticosteroids reduce the mortality of influenza A (H1N1) infection? A meta-analysis. Crit Care. 2015;19:46.

7.1 Anti-COVID-19 therapeutics

There is no current evidence to recommend any specific anti-COVID-19 treatment for patients with confirmed COVID-19.

There are many ongoing clinical trials testing various potential antivirals; these are registered on https://clinicaltrials.gov/ or on the Chinese Clinical Trial Registry (http://www.chictr.org.cn/abouten.aspx).

Investigational anti-COVID-19 therapeutics should be used only in approved, randomized controlled trials.

COVID-19 research needs

Research need	Additional information
Standardized clinical data to improve understanding of the natural history of disease	• Contact COVID_ClinPlaftorm@who.int for log-in credentials • Clinical characterization research protocols available at: https://isaric.tghn.org/protocols/severe-acute-respiratory-infection-data-tools/
If RCT not possible, use the Monitored Emergency Use of Unregistered Interventions Framework	https://www.who.int/ethics/publications/infectious-disease-outbreaks/en/
Prioritization of therapeutics	WHO R&D Blueprint website: https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/

7.2 Pneumonia severity and empiric antimicrobial therapy

Pneumonia severity and treatment recommendations

Classification	Sign or symptom	Treatment
Mild illness	Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion or headache. Rarely, patients may also present with diarrhoea, nausea and vomiting. The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as dyspnea, fever, GI symptoms or fatigue, may overlap with COVID-19 symptoms.	• Isolation in hospital, community facility or home care • Soothe the throat and relieve cough with safe remedy • Give antipyretics for fever • Monitor and return immediately if signs of decompensation
Pneumonia	**Adult** with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen. **Child** with non-severe pneumonia who has a cough or difficulty breathing + fast breathing: fast breathing (in breaths/min): < 2 months ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40, and no signs of severe pneumonia.	• Isolation in hospital, community facility or home care depending on risk factors • Give appropriate antibiotic • Monitor and return immediately if signs of decompensation
Severe pneumonia	**Adolescent or adult:** fever or suspected respiratory infection, plus one of: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 ≤ 90% on room air. **Child** with cough or difficulty in breathing, plus at least one of the following: central cyanosis or SpO_2 < 90%; severe respiratory distress (e.g. grunting, very severe chest indrawing); signs of pneumonia with a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. Other signs of pneumonia may be present: chest indrawing, fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40. While the diagnosis is made on clinical grounds; chest imaging may identify or exclude some pulmonary complications.	• Isolation and treatment in a hospital, consider intensive care • Manage airway as appropriate • Give oxygen if saturation < 90% and haemodynamically stable; give oxygen if saturation < 94% and patient has emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) • Give antipyretics for fever • Give recommended antibiotic • Monitor for signs of decompensation

Sources:
Pocket book of hospital care for children (WHO, 2013); Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected (WHO, 2020; https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected); *Paediatric emergency triage, assessment and treatment: care of critically ill children* (WHO 2016; https://apps.who.int/iris/bitstream/handle/10665/204463/9789241510219_eng.pdf;jsessionid=165EAA36C70BD5B3ACE05675A9BE9925?sequence=1).

Empiric antibiotics for adults with SARI and severe pneumonia

For severe pneumonia in adults, give empirical broad-spectrum IV antimicrobials within the first hour. This is crucially important. Refer to national or institutional recommendations. Common choices include:

- ceftriaxone 1–2 g once daily PLUS a macrolide (preferred); OR
- ampicillin 2 g IV 4 times a day PLUS a macrolide.

Macrolides include erythromycin 500 mg 4 times a day, azithromycin 500 mg once a day, clarithromycin 500 mg twice a day. Alternatives to a macrolide include doxycycline 100 mg twice a day (avoid in pregnancy) or an oral respiratory quinolone (e.g. levofloxacin).

Empiric antibiotics for children with SARI and severe pneumonia

Give intravenous ampicillin (or benzylpenicillin) and gentamicin.

- ampicillin 50 mg/kg or benzylpenicillin 50 000 U/kg IM or IV every 6 hours for at least 5 days
- gentamicin 7.5 mg/kg IM or IV once a day for at least 5 days.

If the child does not show signs of improvement within 48 hours and staphylococcal pneumonia is suspected, switch to gentamicin 7.5 mg/kg IM or IV once a day and cloxacillin 50 mg/kg IM or IV every 6 hours. Use ceftriaxone (80 mg/kg IM or IV once daily) in cases of failure of first-line treatment.

7.3 Oseltamivir notice

WHO recommendations

- Oseltamivir can be used when influenza is suspected or known to be circulating. If testing for influenza is not possible, empiric treatment is indicated.
- Oseltamivir is not proven to be effective for COVID-19.

Treatment dosing

	Dosing[a]
Adults	
Mild illness	75 mg orally, twice daily for 5 days
With severe illness or severe immunocompromising conditions	75 mg orally, twice daily for 5 days Consider higher dose[b] –150 mg orally, twice daily
Children ≥ 1 year old	
< 15 kg	30 mg orally twice daily for 5 days
15 to < 23 kg	45 mg orally twice daily for 5 days
23 to < 40 kg	60 mg orally twice daily for 5 days
≥ 40 kg	75 mg orally twice daily for 5 days
Children < 1 year old	
14 days to 1 year	3 mg/kg orally twice daily for 5 days

Notes:
[a] The route of administration can be either via NG or OG tube if the patient cannot take medication orally (see safety profile). Where the clinical course remains severe or progressive, despite ≥ 5 days of antiviral treatment, treatment should be continued without a break until virus infection is resolved or there is satisfactory clinical improvement.
[b] The rationale for higher dosing is that there is decreased enteral absorption along with high and prolonged viral replication during severe illness. In children, consider double the daily dose.

Safety considerations and side-effects

Safety profile: Oseltamivir has not been associated with increased adverse effects in adult outpatients. However, oseltamivir has not been evaluated in severely ill patients, pregnancy, or paediatric populations. Oseltamivir should be used with caution:

- In patients with **kidney disease**: reduce dose to 75 mg daily if creatinine clearance is 10–30 mL/min.
- In patients with **liver disease** the safety and efficacy has not been evaluated, so dose reduction is not recommended at this time.
- For **pregnant** or **nursing mothers**, oseltamivir is recommended as therapy in pandemic influenza (H1N1) 2009 virus as there is a high risk of severe illness in pregnant women and there is no evidence of adverse effects or birth defects.

Side-effects: Side-effects are generally minor and involve the gastrointestinal tract, although rare neuropsychiatric complications have also been described:

- Nausea (mitigated by taking with food), vomiting.
- Rare neuropsychiatric adverse events – association seen primarily in one country, causality has not been established.

Oral formulations

Formulations	Description
Capsules	30 mg, 45 mg, 75 mg each Brand names: Antiflu®, Tamiflu®, etc. Store at room temperature (15–30 °C)
Liquid suspension	White powder mixed with 23 mL of drinking water Fruit flavoured Refrigeration required Use within 10 days Oral dispenser included (must confirm dosage and volume when administering)
Oral suspension	If commercial suspension unavailable a suspension may be prepared from oseltamivir capsules

Preparation of oral oseltamivir suspension

If a commercial oseltamivir powder for oral suspension is unavailable, a suspension may be compounded in a pharmacy:

- The inhouse suspension should be made at 15 mg/mL for persons > 1 year; and 10 mg/mL for those ≤ 1 year.
- The suspension can be made from oseltamivir phosphate capsules using sterile water at the bedside.