8 Sepsis and septic shock

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Summary

Deliver early targeted resuscitation to treat patients with sepsis-induced shock using crystalloids, vasopressors and, in some cases, inotropes and blood transfusion.

Resuscitation targets for adults and children include improved blood pressure and other markers of tissue perfusion (mental status, urine output, skin, lactate, and in children specifically, improved heart rate). In children, tachycardia is an early sign of sepsis-induced shock and low blood pressure is a late finding.

Resuscitation with crystalloid fluid remains the most common intervention for septic shock and should be given as a challenge to improve targets of perfusion; and promptly stopped when no longer responsive, to avoid harms of excess fluid.

Resuscitation strategies for children with septic shock should be modified if the child has severe malaria with anaemia or severe malnutrition; or is being cared for in settings without ICU capacity.

Refer to the shock quick cards from the WHO/ICRC *Basic emergency care (BEC): approach to the acutely ill and injured* (https://www.who.int/publications-detail/basic-emergency-care-approach-to-the-acutely-ill-and-injured) (Tool 2.3) for initial approach and management of patients with septic shock.

Tools

8.1 Sepsis definitions
8.2 Targeted resuscitation in adults in an ICU setting
8.3 Initial resuscitation, fluid and vasoactive-inotrope management algorithm for children with septic shock
8.4 Guide to to the use of vasopressors in septic shock for adults and children
8.5 Passive leg raise

References and resources

Annane D, Bellissant E, Cavaillon JM. Septic shock. Lancet. 2005;365(9453):63–78.

Annane D, Vignon P, Renault A, Bollaert PE, Charpentier C, Martin C et al. Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial. Lancet. 2007;370(9588):276–684.

Annane D, Bellisant E, Bollaert PE, Briegel J, Keh D, Kupfer Y. Corticosteroids for treating sepsis. Cochrane Database Syst Rev. 2015;12: CD002243.

The ARISE Investigators and the ANZICS Clinical Trials Group. Goal-directed resuscitation for patients with early septic shock. N Engl J Med. 2014;371:1496–1506.

ASA. CPR and ECC guidelines. Part 12: Pediatric advanced life support. Dallas (TX): American Heart Association; 2018 (https://eccguidelines.heart.org/index.php/circulation/cpr-ecc-guidelines-2/part-12-pediatric-advanced-life-support/, accessed 1 July 2019).

Brierley J, Carcillo JA, Choong K, Cornell T, Decaen A, Deymann A et al. Clinical practice parameters for haemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care. 2009;37(2)666–88.

Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C et al. Consensus on circulatory shock and hemodynamic monitoring. Task Force of the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40(12):1795–815.

de Caen AR, Berg MD, Chameides L, Gooden CK, Hickey RW, Scott HF et al. Part 12: Pediatric advanced life support: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132(suppl 2):S526–S542.

de Oliveira CF, De Oliveira DS, Gottschald AF, Moura JD, Costa GA, Ventura AC et al. ACCM/PALS haemodynamic support guidelines for paediatric shock: an outcomes comparison with and without monitoring central venous oxygen saturation. Intensive Care Med. 2008;34(6):1065–1075.

Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al. Surviving Sepsis Campaign: guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580–637.

Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. Am J Respir Crit Care Med. 2016;193(3):259–72.

Grissom CK, Hirshberg EL, Dickerson JB, Brown SM, Lanspa MJ, Liu KD et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. Crit Care Med. 2015;43(2):288–95.

Holst LB, Haase N, Wetterslev J, Werneman J, Guttormsen AB, Karlsson S et al. Lower versus higher hemoglobin threshold for transfusion in septic shock. N Engl J Med. 2014;371(15):1381–1391.

Jones AE, Brown MD, Trzeciak S, Sahpiro NI, Garrett JS, Heffner AC et al. The effect of a quantitative resuscitation strategy on mortality in patients with sepsis: a meta-analysis. Crit Care Med. 2008;36(10):2734–2739.

Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA et al. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA. 2010;303(8):739–46.

Kaukonen KM, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic inflammatory response syndrome criteria in defining severe sepsis. N Engl J Med. 2015;372(17):1629–38.

Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. Crit Care Med. 2018;46(6)997–1000.

Magder S. Invasive intravascular hemodynamic monitoring: technical issues. Crit Care Clin. 2007;23(3):401–14.

Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO et al. Mortality after fluid bolus in African children with severe infection. N Engl J Med. 2011;364:2483–95.

Marik J, Monnet X, Teboul JL. Hemodynamic parameters to guide fluid therapy. Ann Intensive Care. 2011;1:1.

Monnet X, Teboul JL. Passive leg raising: five rules, not a drop of fluid! Crit Care. 2015;19(1)18.

Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med. 2012;367:1901–11.

Perner A, Haase N, Guttormsen AB, Tenhunen J, Klemenzson G, Aneman A et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med. 2012;367:124–34.

ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. N Engl J Med. 2014;370:1683–93.

Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43(3):304–377.

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.

Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219);P200-211 (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32989-7/fulltext, accessed 18 March 2020).

Russell JA. Management of sepsis. N Engl J Med. 2006;355(16):1699–1713.

Seymour CW, Rosengart MR. Septic shock: advances in diagnosis and treatment. JAMA. 2015;314(7):708–17.

Siddiqui S, Razzak J. Early versus late pre-intensive care unit admission broad spectrum antibiotics for severe sepsis in adults. Cochrane Database Syst Rev. 2010;10:CD007081.

Singer M, Deutschman CS, Seymour CW. The Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-810 (https://jamanetwork.com/journals/jama/fullarticle/2492881, accessed 19 March 2020).

Vasu TS, Cavallazzi R, Hirani A, Kaplan G, Leiby B, Marik PE. Norepinephrine or dopamine for septic shock: systematic review of randomized clinical trials. J Intensive Care Med. 2012;27(3):172–178.

Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med. 2014;2(5):380–6.

Weiss SL, Fitzgerald JC, Pappachan J, Wheeler D, Jaramillo-Bustamante JC, Salloo A et al. Global epidemiology of pediatric severe sepsis: the sepsis prevalence, outcomes, and therapies study. Am J Respir Crit Care Med. 2015;191(10):1147–57.

Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP et al. Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med. 2020;21(2):e52-e106 (https://journals.lww.com/pccmjournal/fulltext/2020/02000/surviving_sepsis_campaign_international_guidelines.20.aspx, accessed 18 March 2020).

Wills BA, Nguyen MD, Ha TL, Dong TH, Tran TN, Le TT et al. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. N Engl J Med. 2005;353:877–89.

WHO. Pocket book of hospital care for children (2nd edition). Geneva: World Health Organization; 2013.

WHO/ICRC. Basic emergency care (BEC): approach to the acutely ill and injured. Geneva: World Health Organization and International Committee of the Red Cross; 2018 (https://www.who.int/publications-detail/basic-emergency-care-approach-to-the-acutely-ill-and-injured, accessed 4 April 2020).

8.1 Sepsis definitions

Sepsis

Adults: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection.[a] Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.

Children: suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome (SIRS) criteria, of which one must be abnormal temperature or white blood cell count. SIRS criteria include: abnormal temperature < 36 °C or > 38.5 °C, heart rate > 2 SD above normal for age or bradycardia if < 1 year of age, respiratory rate > 2 SD above normal for age, and abnormal white blood cell count or > 10% immature neutrophils.

Septic shock

Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L.

Children: any hypotension (SBP < 5th centile or > 2 SD below normal for age) or two or three of the following: altered mental state; tachycardia or bradycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulse; tachypnoea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.

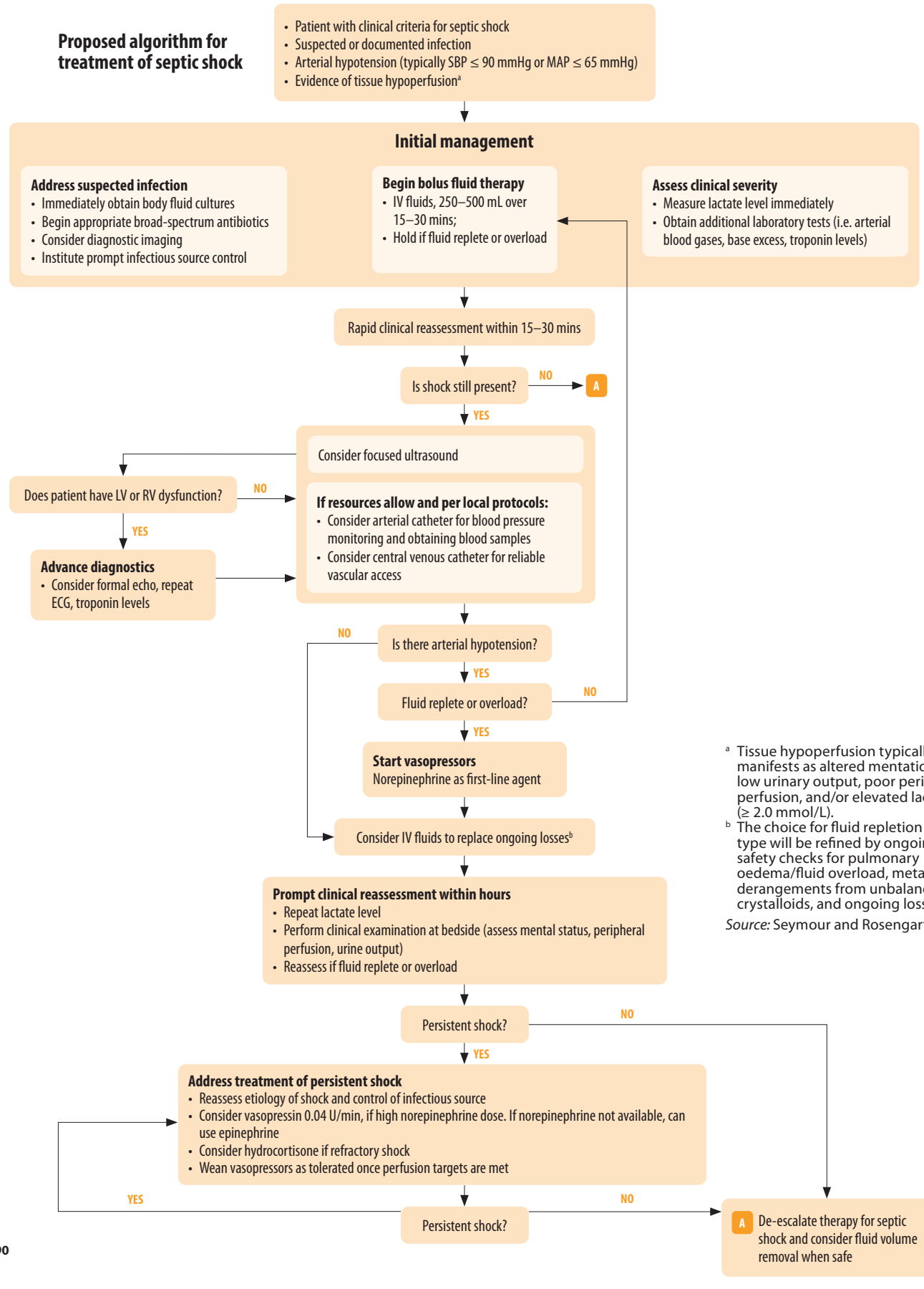
Sources: Rhodes et al (2020); Weiss et al (2020).

[a] The SOFA score ranges from 0 to 24 and includes points related to six organ systems: respiratory (hypoxemia defined by low PaO_2/FiO_2); coagulation (low platelets); liver (high bilirubin); cardiovascular (hypotension); central nervous system (low level of consciousness defined by Glasgow Coma Scale); and renal (low urine output or high creatinine). Sepsis is defined by an increase in the sepsis-related SOFA score of ≥ 2 points. Assume the baseline score is 0 if data are not available.

Notes: bpm beats/minute; FiO_2 fraction of inspired oxygen; MAP mean arterial pressure; PaO_2 partial pressure of oxygen; SBP systolic blood pressure; SOFA sequential organ failure assessment.

8.2 Targeted resuscitation in adults in an ICU setting

This algorithm is adapted from Seymour and Rosengart (2015) (see References and resources). It can be adapted to your settings.



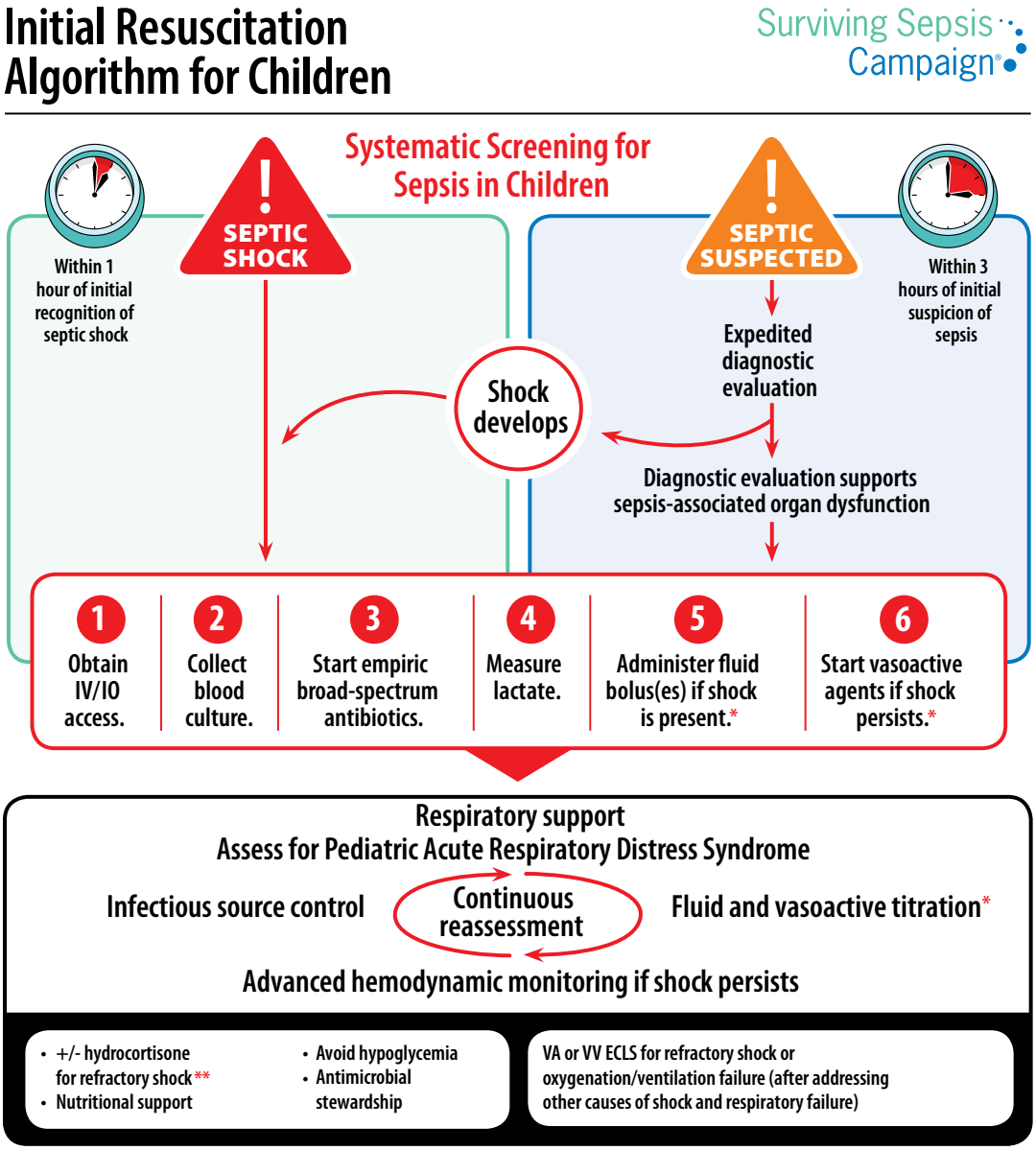
[a] Tissue hypoperfusion typically manifests as altered mentation, low urinary output, poor peripheral perfusion, and/or elevated lactate (≥ 2.0 mmol/L).

[b] The choice for fluid repletion and type will be refined by ongoing safety checks for pulmonary oedema/fluid overload, metabolic derangements from unbalanced crystalloids, and ongoing losses.

Source: Seymour and Rosengart (2015).

8.3 Initial resuscitation, fluid and vasoactive–inotrope management algorithm for children with septic shock

This algorithm, from the Surviving Sepsis Campaign, is based on recently published paediatric sepsis and septic shock guidelines and has been adapted for use in health care systems with and without intensive care (see References and resources).



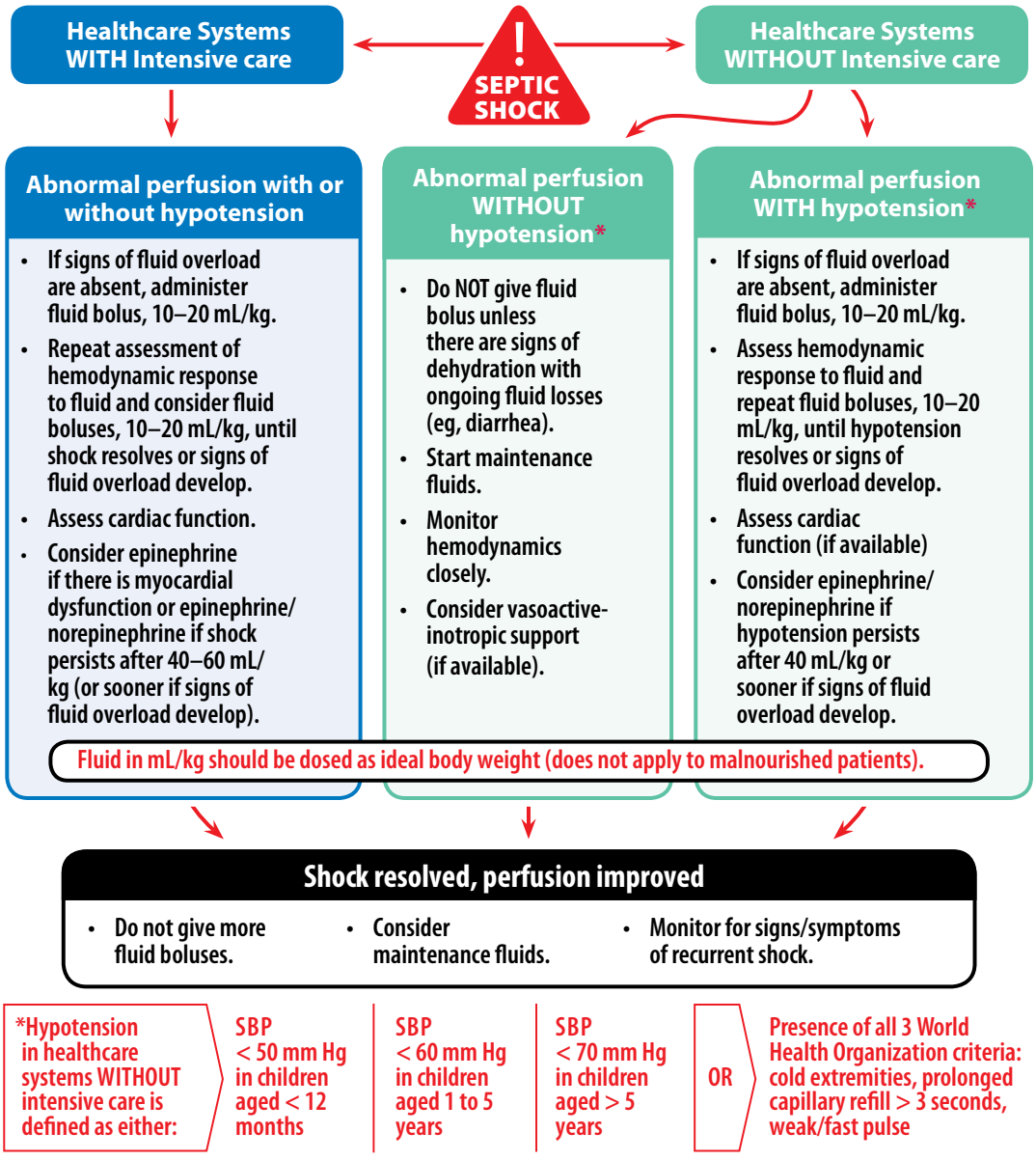
*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

**Hydrocortisone may produce benefit or harm.

www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients

Fluid and Vasoactive-Inotrope Management Algorithm For Children

Surviving Sepsis Campaign



www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients

Sources: Rhodes et al (2020); Weiss et al (2020).

8.4 Guide to the use of vasopressors in septic shock for adults and children

In adults, the Surviving Sepsis Campaign guidelines recommend vasopressors to be started if MAP < 65 mmHg. Norepinephrine is recommended as the first-line agent; however, epinephrine can be used as an alternative. Administer vasopressors at a strictly controlled rate, titrate to maintain MAP 65 mmHg, reduce as the MAP improves and discontinue promptly when no longer needed. Dopamine is not recommended because of the risk of tachyarrythmias and concern of poorer outcome. Administer dobutamine, an inotrope, when there are persistent signs of hypoperfusion and clinical evidence of myocardial dysfunction (i.e. echo, $ScvO_2$ < 70%) after adequate MAP and fluid status achieved.

In children, the Surviving Sepsis Campaign guidelines recommend vasopressors if clinical signs of shock persist after fluid resuscitation and should not be delayed. The recommended first-line agent is epinephrine in children with septic shock. If shock persists, add a second agent, and vasopressin can be added in children requiring high-dose vasopressors. These agents should be administered at a strictly controlled rate and titrated to achieve targets of adequate tissue perfusion.

Route of administration	Norepinephrine	Dobutamine	Epinephrine	Vasopressin
Central vein preferred	Initial: 0.1–0.2 µg/kg/min Range: increase by 0.1 µg/kg/min increments; consider refractory if > 1 µg/kg/min	Initial: 2–5 µg/kg/min Range: increase by 2.5 µg/kg/min increments; maximum 20 µg/kg/min	Initial: 0.1–0.2 µg/kg/min Range: increase by 0.1 µg/kg/min increments; consider refractory if > 1 µg/kg/min	Initial: 0.01–0.08 units/min Fixed dose No titration necessary
Peripheral vein if necessary	Same dosing	Same dosing	Same dosing	Same dosing

Dose initiation and titration should be individualized. The MAP goal can be individualized based on other clinical history (i.e. consider higher MAP target > 80 mmHg in patients with chronic hypertension). Also target other markers of perfusion, such as capillary refill, absence of skin mottling, strong peripheral pulses, warm and dry extremities, urine output and normal mental status.

Note: Children can move between various shock states and vasopressors should be adjusted accordingly.

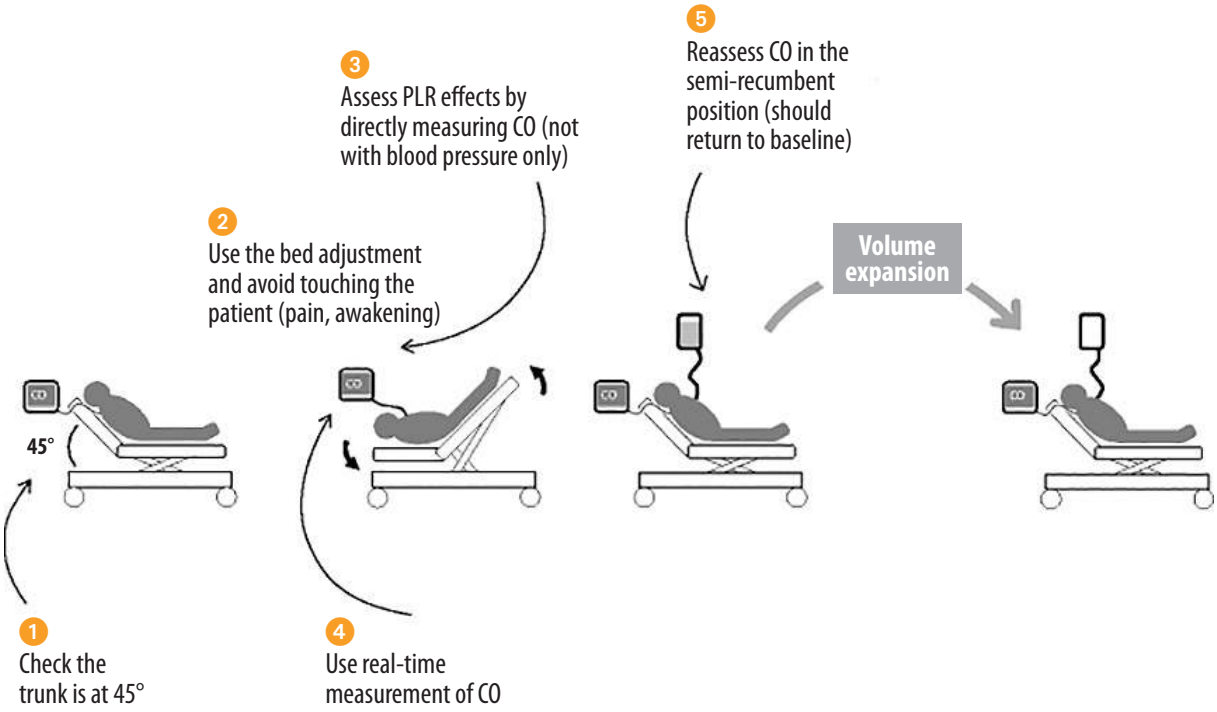
Side-effects of vasopressors include tachyarrhythmias, ischaemia to organs and cool or cyanotic extremities. Peripheral administration may be complicated by soft tissue necrosis if the vasopressor is extravasated.

Side-effects of inotropes, such as dobutamine, include tachyarrythmias and hypotension due to peripheral vasodilation. Thus, in septic shock, inotropes should be used in combination with vasopressors to maintain MAP at goal in adults, and children with low systemic vascular resistance.

8.5 Passive leg raise

In acute circulatory failure, passive leg raising (PLR) is a test that predicts whether cardiac output (CO) will increase with volume expansion. By transferring a volume of around 300 mL of venous blood from the lower body towards the right heart, PLR mimics a fluid challenge. However, no fluid is infused and the haemodynamic effects are rapidly reversible.

Best method for passive leg raising – the five rules to be followed



Source: Monnet and Teboul (2015).

9 Acute respiratory distress syndrome (ARDS)

9 Acute respiratory distress syndrome (ARDS)

Summary

Intubation and invasive mechanical ventilation are indicated in most patients with ARDS and hypoxaemic respiratory failure. Lung protective ventilation (LPV) reduces mortality in patients with ARDS. LPV means:

- delivering low tidal volumes (TV) (target 6 mL/kg ideal body weight or less);
- achieving low plateau airway pressure (Pplat) (target Pplat ≤ 30 cm H_2O); and
- use of moderate positive end-expiratory pressure (PEEP) to recruit lung.

In adults and paediatric patients with moderate-severe ARDS (P/F < 150) use prone position. Extracorporeal membrane oxygenation (ECMO) has been used for COVID-19 patients and should only be done at expert centres under strict protocols in patients that are not responding to lung protective ventilation and prone position strategy. More information about outcomes is needed.

High-flow nasal cannula (HFNC) may be safe in patients with mild-moderate and non-worsening hypercapnia (mild ARDS), normal mental status, haemodynamic stability, and no need for emergent intubation. Patients receiving HFNC 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.

Use airborne precautions when conducting aerosol-generating procedures.

Tools

References and resources

Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372(8):747–55.

ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E et al. Acute respiratory distress syndrome: the Berlin definition. JAMA. 2012;307(23):2526–33.

ARDS Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301–1308.

Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA. 2016;315(8):788–800.

Diaz JV, Brower R, Calfee CS, Matthay MA. Therapeutic strategies for severe acute lung injury. Crit Care Med. 2010;38(8):1644–1650.

Egan J. Acute lung injury in the child. Paediatr Resp Rev. 2010:11;171–176.

Ekhaguere OA, Mairami AB, Kirpalani H. Risk and benefits of bubble continuous positive airway pressure for neonatal and childhood respiratory diseases in low- and middle-income countries. Paediatr Respir Rev. 2019;29:31-6. Epub 2018/06/17. doi: 10.1016/j.prrv.2018.04.004. PubMed PMID: 29907334.

Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med. 2012;38(10):1573–82.

Goligher EC, Kavanagh BP, Rubenfeld GD, Adhikari NK, Pinto R, Fan E et al. Oxygenation response to positive end-expiratory pressure predicts mortality in acute respiratory distress syndrome. A secondary analysis of the LOVS and ExPress trials. Am J Respir Crit Care Med. 2014;190(1):70–6.

Grissom CK, Hirshberg EL, Dickerson JB, Brown SM, Lanspa MJ, Liu KD et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. Crit Care Med. 2015;43(2):288–95.

Guérin C, Reignier J, Richard J-C, Beuret P, Gacouin A, Boulain T et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368:2159–2168.

Hess DR. Using the ventilator to probe physiology: monitoring graphics and lung mechanics during mechanical ventilation (course). Boston (MA): Massachusetts General Hospital; 2005.

Laffey JG, Bellani G, Pham T, Fan E, Madotto F, Bajwa EK et al. Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study. Intensive Care Med. 2016;42(12):1865–1876.

Lee MK, Choi J, Park B, Kim B, Lee SJ, Kim SH et al. High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. Clin Respir J. 2018;12(6):2046-56. Epub 2018/02/03. doi: 10.1111/crj.12772. PubMed PMID: 29392846.

Lichtenstein D, Goldstein I, Mourgeon E, Cluzel P, Grenier P, Rouby JJ. Comparative diagnostic performances of auscultation, chest radiography, and lung ultrasonography in acute respiratory distress syndrome. Anesthesiology. 2004;100:9–15.

Luo Y, Ou R, Ling Y, Qin T. [The therapeutic effect of high flow nasal cannula oxygen therapy for the first imported case of Middle East respiratory syndrome to China]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2015;27(10):841-4. Epub 2016/05/03. PubMed PMID: 27132449.

Malhotra A. Low-tidal-volume ventilation in the acute respiratory distress syndrome. N Engl J Med. 2007;357(11):1113–1120.

Meade M, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2008;299(6):637–645.

Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2008;299(6):646–655.

Messerole E, Peine P, Wittkopp S, Marini JJ, Albert RK. The pragmatics of prone positioning. Am J Respir Crit Care Med. 2002;165(10):1359–1363.

Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis. 1988;138(3):720–3.

National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med. 2006;354:2564–2575.

Papazian L, Aubron C, Brochard L, Chiche JD, Combes A, Dreyfuss D et al. Formal guidelines: management of acute respiratory distress syndrome. Ann Intensive Care. 2019;9(1):69. doi:10.1186/s13613-019-0540-9.

Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med. 2015;16(5):428–439.

Randolph AG. Management of acute lung injury and acute respiratory distress syndrome in children. Crit Care Med 2009; 37:2448–2454.

Riviello ED, Kiviri W, Twagirumugabe T, Mueller A, Banner-Goodspeed VM, Officer L et al. Hospital incidence and outcomes of ARDS using the Kigali modification of the Berlin definition. Am J Respir Crit Care Med. 2016;193(10:52–9.

Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50(2). Epub 2017/09/02. doi: 10.1183/13993003.02426-2016. PubMed PMID: 28860265.

Slutsky AS. Neuromuscular blocking agents in ARDS. N Engl J Med. 2010;363(12):1176–80.definition. Am J Respir Crit Care Med. 2016;193(1):52–9.

Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med. 2014;370(10):980.

Sud S, Fredrich JO, Taccone P, Polli F, Adhikari NK, Latini R et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. Intensive Care Med. 2010;36(4):585–599.

Taccone P, Presenti A, Latini R, Polli F, Vagginelli F, Mietto C et al. Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2009;302(18):1977–1984.

Tobin M. Advances in mechanical ventilation. N Engl J Med. 2001;344(26):1986–1996.

Wheeler AP, Bernard GR. Acute lung injury and the acute respiratory distress syndrome: a clinical review. Lancet. 2007;369(9572):1553–1565.

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Cavalcanti AB, Suzumura ÉA et al. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA. 2017;318(14):1335–1345. doi:10.1001/jama.2017.14171.

9.1 Memory aid: diagnosis and classification of ARDS

Berlin definition of acute respiratory distress syndrome (ARDS)

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities – not fully explained by effusions, lobar/lung collapse or nodules
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (e.g. echocardiography) to exclude hydrostatic oedema if no risk factor present
Oxygenation[b]	
Mild	$200 < PaO_2/FiO_2 \leq 300$ with PEEP or CPAP ≥ 5 cm H_2O[c]
Moderate	$100 < PaO_2/FiO_2 \leq 200$ with PEEP ≥ 5 cm H_2O
Severe	$PaO_2/FiO_2 \leq 100$ with PEEP ≥ 5 cm H_2O

Notes:
[a] Chest radiograph or computed tomography scan;
[b] If altitude is higher than 1000 m, the correction factor should be calculated as follows: [$PaO_2/FiO_2 \times$ (barometric pressure/760)];
[c] This may be delivered non-invasively in the mild ARDS group;
CPAP – continuous positive airway pressure; FiO_2 – fraction of inspired oxygen; PaO_2 – partial pressure arterial oxygen; PEEP – positive end-expiratory pressure.

A recent publication suggests a modified definition for resource-constrained environments, that excludes the need for CPAP or PEEP, arterial blood analysis and chest radiograph.

Note: This definition requires validation before widespread use.

Kigali modifications of Berlin definition

Chest imaging	Bilateral opacities – not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or ultrasound. Ultrasound findings defined as presence of B-lines or consolidations without associated effusions found in at least one area on each side of the chest. The protocol requires six areas of each side of chest (two anterior, two lateral, two posterolateral) to be examined.
Oxygenation	$SpO_2/FiO_2 \leq 315$, no PEEP or CPAP requirement

9.2 Memory aid: diagnosis and classification of pARDS

Paediatric acute respiratory distress syndrome (pARDS) definition

Age	Exclude patients with perinatal related lung disease			
Timing	Within 7 days of known clinical insult			
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload			
Chest imaging	Chest imaging findings of new infiltrates(s) consistent with acute pulmonary parenchymal disease			
Oxygenation	**Non-invasive mechanical ventilation**	**Invasive mechanical ventilation**		
	pARDS (no severity stratification)	**Mild**	**Moderate**	**Severe**
	Full face mask bilevel ventilation of CPAP ≥ 5 cm H_2O PF ratio ≤ 300 SF ratio ≤ 264	4 ≤ OI < 8 5 ≤ OSI < 7.5	8 ≤ OI < 16 7.5 ≤ OSI < 12.3	OI ≥ 16 OSI ≥ 12.3

CPAP – continuous positive airway pressure; OI – Oxygenation Index ([FiO_2 × mean airway pressure × 100]/PaO_2); OSI – oxygen saturation index ([FiO_2 × mean airway pressure × 100]/SpO_2); PF ratio – PaO_2:FiO_2 ratio; SF ratio – SpO_2:FiO_2 ratio.

Source: Khemani RG, Smith LS, Zimmerman JJ, Ericson S, for the Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury Conference. PCCM. 2015;16(5):S23-S40.

9.3 Checklist for rapid sequence intubation procedure

☑ This tool can be used before performing endotracheal intubation. This is adapted with permission from the ICU and Emergency Medical Retrieval Service at the Royal Alexandria Hospital, Paisley, Scotland.

Equipment

- ☐ suction: working Yankauer sucker under right side of pillow
- ☐ ambu-bag, 15 L/min oxygen, PEEP valve (pre-oxygenation and post-intubation)
- ☐ endotracheal tube (ETT): correct size, cuff checked and lubricated +/- stylet
- ☐ two working laryngoscopes with blades
- ☐ 20 mL syringe
- ☐ tube tie
- ☐ gum elastic bougie on trolley top
- ☐ oropharyngeal airway on trolley top
- ☐ confirm laryngeal mask airway and surgical airway kit
- ☐ capnograph set up
- ☐ stethoscope
- ☐ ventilator checks complete
- ☐ alternate oxygen source (cylinder/flowmeter)

Drug

- ☐ IV access patent and accessible
- ☐ induction agents: hypnotic/opiate/neuromuscular blockers
- ☐ maintenance infusions prepared
- ☐ vasopressor and atropine drawn up

Team role

- ☐ doctor 1: airway management and drug administration order
- ☐ nurse 1: assistant and drug administration
- ☐ nurse 2: cricoid pressure (controversial)
- ☐ team role respiratory therapist: airway management and ventilation assistance

Appropriate infection prevention precautions

- ☐ if suspect COVID-19, use airborne precautions

Rapid sequence intubation (RSI)

Definition: RSI is an advanced medical protocol of advanced airway support designed for the expeditious intubation of the trachea of a patient.

Target: Patients suspected of having an increased risk of aspirating stomach contents into the lungs.

Technique: Quicker form of the process normally used to "induce" a state of general anaesthesia. It uses drugs to rapidly allow an ETT to be placed between the vocal cords, by blocking the patient's involuntary reflexes and muscle tone in the oropharynx and larynx. Once the ETT has been passed between the vocal cords, a cuff is inflated around the tube in the trachea and the patient can then be artificially ventilated. Correct ETT position can be verified by direct visualization through the vocal cords; capnography (persistent CO_2 return; may show CO_2 transiently if in oesophagus); high SpO_2, bilateral breath sounds on chest auscultation; and correct position on X-ray.

9.4 Checklist for preparing for intubation and mechanical ventilation in children

☑ This tool can be used before performing endotracheal intubation. Intubation and IMV can be indicated, as in adults, in case of hypoxaemia refractory to supplemental oxygen, depressed level of consciousness (AVPU) and severe shock.

☐ Pre-oxygenate for 5 minutes with 100% FiO_2.
Children and infants have reduced functional residual capacity; they can desaturate quickly on induction.

☐ Decompress the stomach to prevent diaphragmatic splinting:
- ☐ use airway adjuncts to reduce stomach inflation;
- ☐ in bag-mask ventilation place NG tube early and regularly aspirate with large bore syringe to decompress stomach.

☐ Anticipate shock.
Benzodiazepines, thiopental, inhalational agents and propofol cause myocardial depression and vasodilation; this can unmask or worsen shock:
- ☐ anticipate and use ketamine for induction if available (with atropine);
- ☐ anticipate by pre-loading with volume (10–20 mL/kg 0.9% saline) and/or starting/increasing inotropic support.

☐ Consider atropine in all neonates and children to prevent bradycardia caused by vagal stimulation during laryngoscopy.

☐ Use induction agent ± opiate and neuromuscular relaxant in all patients including neonates; it will optimize the view and make intubation easier.

☐ Confirm correct ETT placement. As in adults, an adequate end-tidal CO_2 reading remains the gold standard. But correct placement can be inferred from:
- ☐ improving SpO_2;
- ☐ bilateral equal air on auscultation;
- ☐ chest X-ray position of ETT tip 1–2 cm above the carina, or T3 posteriorly.

Choice of an induction agent

		Intravenous dose	Notes
Opiates	Atropine	20 mcg/kg (min dose 100 mcg); > 12 years 300–600 mcg	
	Fentanyl	2–5 mcg/kg	Can cause ↓ blood pressure
	Morphine	0.1–0.2 mg/kg	Takes long time to be effective ~10 mins
Induction agent	Ketamine	1–2 mg/kg	Can cause ↑ intracranial pressure
	Etomidate	0.3 mg/kg	Can cause adrenal suppression, do not use in sepsis
	Propofol 1% (induction only)	2.5–3.5 mg/kg (> 3 years)	Can cause ↓ blood pressure
Neuromuscular blockers	Suxamethonium	3 mg/kg/dose (neonate); 1–2 mg/kg all other ages	Avoid if K+ high, neuromuscular patients, acute burn or renal failure
	Rocuronium	1 mg/kg	First-line RSI paralytic
	Vecuronium	0.1 mg/kg	
	Atracurium	0.5 mg/kg	
	Pancuronium	0.1 mg/kg	

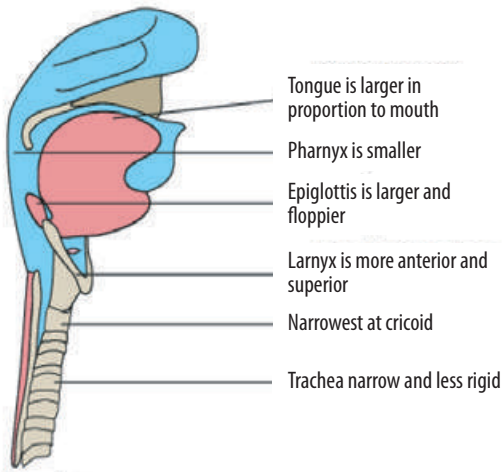
Choice of size of endotracheal tubes

	Term infant	Estimate at 6 months	Children ≥ 1 year (kg)
Diameter (size) of ETT (cuffed preferred)	3–3.5	3.5–4	(Age/4) + 4 (uncuffed); (Age/4) + 3.5 (cuffed)
Length oral ETT at lips (confirm on X-ray)	8–9	10	(Age/2) + 12 cm
Length nasal ETT at nose (confirm on X-ray)	10–11	12	(Age/2) +15 cm
Suction catheter size	2 x ETT = 6	2 x ETT = 8	2 x ETT

Anatomical differences between children and adults

Anatomical differences between children and adults can make ventilation more difficult.

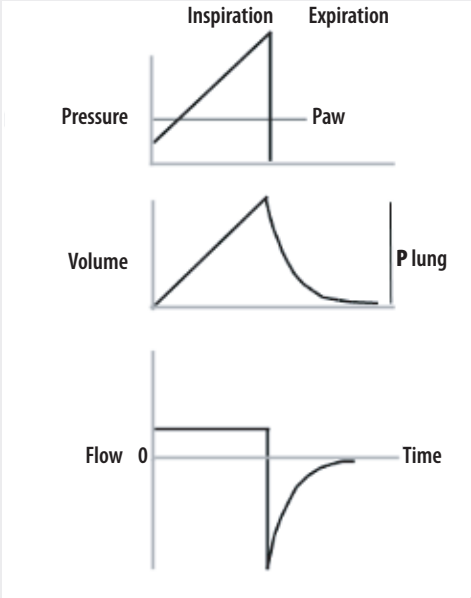
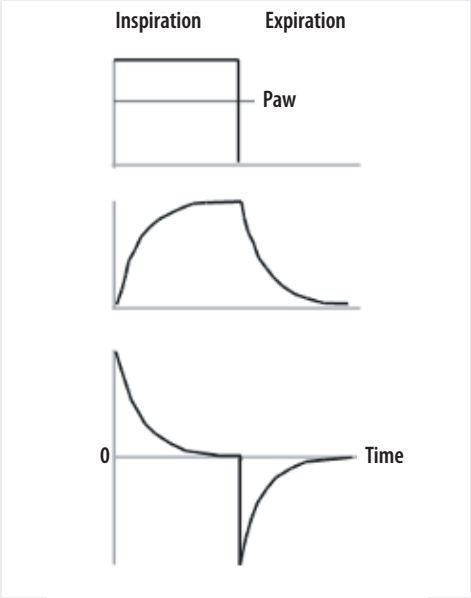
- **Lower chest wall rigidity** of children implies an earlier respiratory failure in infants in any pathology that causes ↓ compliance of lung, e.g. viral pneumonitis.
- **Smaller airway diameter** of children implies an upper airway resistance.
- **Larger abdomen** of children implies a ↓ functional residual capacity → ↑ atelectasis at end expiration and atelectrauma.
- **Larger tongue**, anterior **larynx, narrow cricoid ring, larger occiput** require positioning of the airway (e.g. use of neck rolls) to optimize visualization on laryngoscopy:
  - neonates and infants in neutral position
  - older children in "sniffing morning air" position.



Child's upper airway

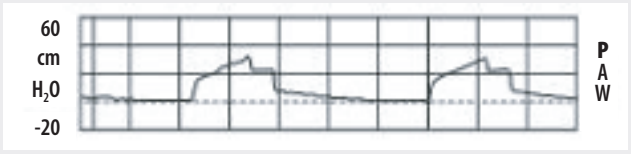
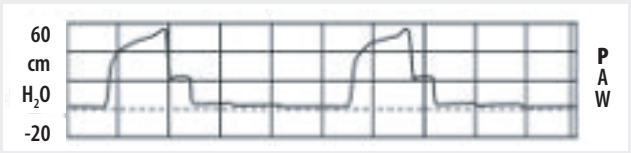
Tips: Anticipate a difficult airway, particularly if stridor or a small posteriorly placed jaw are present. Pre-oxygenate, have a range of ETT and blades and the most experienced operator available.

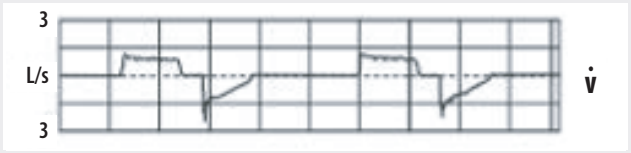
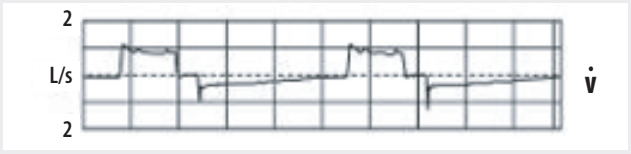
9.5 Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation

Volume control	Pressure control
	
• Volume limited ventilation • Flow is fixed (shown) or descending • Volume is set and the airway pressures are variable • Inspiration cycles to expiration after fixed time or volume delivered • To measure Pplat you need to perform an inspiratory pause, which means briefly stopping gas flow at the end of inspiration • Patient can trigger a breath	• Pressure limited ventilation • Flow is variable • Pressure is set (see square wave form) and the volumes are variable • Inspiration cycles to expiration after fixed time • Pplat is the set inspiratory pressure (Pinsp), equal to driving pressure + PEEP • Patient can trigger a breath

Notes: Paw – airway pressure; PEEP – positive end-expiratory pressure; Pplat – plateau airway pressure.

9.6 Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation

Pressure curves	Characteristics	Interpretation
	Normal pressure curve	Normal
	Increased peak airway pressure Increased Pplat	Reduced compliance
	Increased peak airway pressure Normal Pplat Intrinsic PEEP	Increased resistance

Flow curves	Characteristics	Interpretation
	Normal flow pattern	Normal
	High expiratory peak flow rate expiratory flow is shorter	Reduced compliance
	Prolonged expiratory flow Intrinsic PEEP	Increased resistance

Source: Adapted from *Using the ventilator to probe physiology: monitoring graphics and lung mechanics during mechanical ventilation* (course), Hess DR (2005).

9.7 Guide to distinguishing between the causes of high peak airway pressures: resistance versus compliance

Abnormal airway pressure(s)	High peak with high plateau airway pressure	High peak with normal plateau airway pressure
Main physiologic problem	Reduced respiratory system compliance (Crs)	High resistance (R)
Formula	$C_{rs} = \frac{\text{Tidal volume}}{P_{plat} - PEEP}$	$R = \frac{P_{peak} - P_{plat}}{\text{Flow}}$
Normal	60–100 mL/cm H_2O	5–10 cm H_2O/L/sec for intubated adult
Problems that can be treated quickly	• mainstem bronchus intubation • tension pneumothorax • pleural effusion • abdominal distension • congestive heart failure • atelectasis • hyperinflation	**Patient problems:** • patient biting, coughing, fighting ventilator • secretions • bronchospasm **Ventilator problems:** • tube kinked • circuit filled with water • small endotracheal tube
Other problems that may improve over the time	• ARDS • consolidation • fibrosis • chest wall oedema • thoracic deformity	• Asthma • Chronic obstructive pulmonary disease (COPD)

Factors influencing peak airway pressure

P airway = **P** resistance + **P** compliance

Airflow resistance	Respiratory system compliance	Chest wall compliance
• size of airway • lower airway obstruction • mechanical obstruction	• chest wall • tidal volume • lung elasticity	• chest wall • patient position • external compression of chest from abdomen

9.8 Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patient

☑

☐ **Is the endotracheal tube in the trachea?**
- Large cuff leak or no chest rise with inspiration suggest that ETT is dislodged: assess with direct laryngoscopy and re-intubate.

☐ **Is there a problem with the ventilator circuit or oxygen supply?**
- Take the patient off the ventilator and hand ventilate with 100% oxygen while checking equipment.

☐ **Can you pass a suction catheter through the endotracheal tube?**
- If no, ETT may be kinked: straighten or insert bite block to prevent patient from biting.
- If no, ETT may be blocked with secretions: reintubate with new ETT.
- If yes, suction ETT to remove sputum/mucus plugs.

☐ **Are there breath sounds bilaterally?**
- Unilaterally absent breath sounds: evaluate for mainstem intubation/lobar collapse versus pneumothorax by assessing mediastinal shift and by chest X-ray if patient not in extremis:
  - Suspicion of tension pneumothorax mandates immediate needle decompression followed by chest tube placement, without a chest X-ray.
  - Mainstem intubation may be suspected clinically if ETT further in patient than previously. Withdraw to previous position; can confirm with bronchoscopy if available.
  - Lobar collapse or atelectasis may respond to aggressive suctioning and can be confirmed with chest X-ray.
- Bilateral wheezing: consider bronchospasm; give bronchodilators.
- Bilateral crackles: consider pulmonary oedema; give diuretic or more PEEP depending on full clinical evaluation of volume status.

☐ **Are there other problems causing low compliance?**
- Abdominal distension: drain stomach with NG tube.
- Auto-PEEP: diagnose by examining ventilator waveforms. Treat with bronchodilators, sedation; may require temporary disconnection from positive pressure.

☐ **Is there haemodyamic instability?**
- Restore haemodyamic stability with fluid or vasopressors while determining and treating primary cause.
- If severe hypotension, evaluate for tension pneumothorax or severe auto-PEEP (often in patients with asthma or COPD).
- Other causes include high airway pressures reducing venous return, vasodilation due to sedative and analgesic medications or a new problem (sepsis, bleeding, pulmonary embolism, myocardial infarction).

☐ **Is the patient agitated and asynchronous with the ventilator?**
- May be secondary to any other problem or may be primary problem and causing asynchrony: treat cautiously with sedation.

9.9 ARDS Network protocol to deliver lung protective ventilation

This protocol to deliver lung protective ventilation (LPV) was used in the low tidal volume (TV) trial published in 2000 (ARDS Network et al, 2000) (see References and resources). There are two PEEP/FiO_2 grids; the second one can be used for more severe hypoxaemia.

Principles are the same for children except that children younger than 8 years require a lower maximum PEEP – 15 cm H_2O and the peak Pplat should be < 28 cm H_2O.

Ventilator set up and adjustment

1. Calculate predicted body weight (PBW):
   Males = 50 + 1.1 [height (cm) – 152]
   Females = 45.5 + 1.1 [height (cm) – 152].
2. Select any ventilator mode.
3. Set ventilator settings to achieve initial TV = 8 mL/kg PBW.
4. Reduce TV by 1 mL/kg at intervals ≤ 2 hrs until TV = 6mL/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 breaths/min).
6. Adjust TV and RR to achieve pH and Pplat goals below.

Oxygenation goal: PaO_2 55–80 mmHg or SpO_2 88–95%

Use a minimum PEEP of 5 cm H_2O. Consider incremental PEEP/FiO_2 combinations such as shown below to achieve goal. PEEP levels > 15 should not be used in children < 8 years.

Lower PEEP/higher FiO_2														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher PEEP/lower FiO_2 for more severe hypoxaemia														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	18–24

- **Pplat goal: ≤ 30 cm H_2O**
  Check Pplat using 0.5 second inspiratory pause, at least every 4 hours and after each change in PEEP or TV.
  – If Pplat > 30 cm H_2O or > 28 cm H_2O in children: decrease TV by 1mL/kg steps (minimum = 4 mL/kg).
  – If Pplat < 25 cm H_2O and TV < 6 mL/kg: increase TV by 1 mL/kg until Pplat > 25 cm H_2O or TV = 6 mL/kg.
  – If Pplat < 30 cm H_2O and breath stacking or asynchrony occurs: may increase TV in 1 mL/kg increments to 7–8 mL/kg if Pplat remains ≤ 30 cm H_2O.

- **pH goal: 7.30–7.45**
  Acidosis management: (pH < 7.30).
  – If pH 7.15–7.30: increase RR until pH > 7.30 or $PaCO_2$ < 25 (maximum set RR = 35).
  – If pH < 7.15: increase RR to 35.
  – If pH remains < 7.15, TV may be increased in 1 mL/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded). May give $NaHCO_3$ to act as a transient buffer.

- **Alkalosis management: pH > 7.45**
  – Decrease ventilator rate if possible.

- **Inspiration to expiration ratio goal**
  – Recommend that duration of inspiration be ≤ duration of expiration.

9.10 Checklist for proning a patient with severe ARDS

This checklist is adapted from Messerole et al (2002) and the most recent randomized control trial by Guérin et al (2013) (see References and resources). These studies found an improved mortality in patients treated with LPV plus prone position.

Prone ventilation should be carried out by four to five team members using a protocol rehearsed in advance. It is easier to perform in children. See the following article and video (https://www.nejm.org/doi/full/10.1056/).

Timing and duration of prone position

The most recent clinical trial (Guérin et al, 2013) observed mortality benefit in patients with severe ARDS. Patients were turned prone within 24 hours of recognition and kept prone for at least 12–16 consecutive hours a day.

Contraindications (from Guérin et al, 2013)

- elevated intracranial pressure > 30 mmHg or cerebral perfusion pressure < 60 mmHg
- massive haemoptysis
- recent tracheal surgery or sternotomy
- serious facial trauma or facial surgery
- deep venous thrombosis treated for less than 2 days
- cardiac pacemaker inserted in the last 2 days
- unstable spine, femur or pelvic fractures
- MAP < 65 mmHg
- pregnancy
- single anterior chest tube with air leaks.

Preparation

1. Check for contraindications:
   - facial or pelvic fractures
   - burns or open wounds on the ventral body surface
   - conditions associated with spinal instability (e.g. rheumatoid arthritis, trauma)
   - conditions associated with increased intracranial pressure
   - life-threatening arrhythmias.

2. Consider possible adverse effects of prone positioning on chest tube drainage.

3. Whenever possible, explain the manoeuvre to the patient or their family.

4. Confirm from a recent chest X-ray that the tip of the endotracheal tube is located 2–4 cm above the main carina.

5. Inspect and confirm that the endotracheal tube and all central and large bore peripheral catheters are firmly secured.

6. Consider exactly how the patient's head, neck and shoulder girdle will be supported after they are turned prone. Assemble all needed pillows, foam pads or other supports that might be needed.

7. Stop tube feeding, check for residual, fully evacuate the stomach, and cap or clamp the feeding and gastric tubes.

8. Prepare endotracheal suctioning equipment, and review what the process will be if copious airway secretions abruptly interfere with ventilation.

9. Decide whether the turn will be rightward or leftward.

10. Prepare all IV tubing and other catheters and tubing for connection when the patient is prone:
- assure sufficient tubing length
- relocate all drainage bags on the opposite side of the bed
- move chest tube drains between the legs
- reposition IV tubing toward the patient's head, on the opposite side of the bed.

Turning procedure

1. Place one (or more) people on both sides of the bed (to be responsible for the turning processes) and another at the head of the bed (to assure the central lines and the endotracheal tube do not become dislodged or kinked).

2. Increase the FiO_2 to 1.0 and note the mode of ventilation, the tidal volume, the minute ventilation, and the peak and plateau airway pressures.

3. Pull the patient to the edge of the bed furthest from whichever lateral decubitus position will be used while turning.

4. Place a new draw sheet on the side of the bed that the patient will face when in this lateral decubitus position. Leave most of the sheet hanging.

5. Turn the patient to the lateral decubitus position with the dependent arm tucked slightly under the thorax. As the turning progresses the nondependent arm can be raised in a cocked position over the patient's head. Alternatively, the turn can progress using a log-rolling procedure.

6. Remove ECG leads and patches. Suction the airway, mouth and nasal passages if necessary.

7. Continue turning to the prone position.

8. Reposition in the centre of the bed using the new draw sheet.

9. If the patient is on a standard hospital bed, turn their face toward the ventilator. Assure that the airway is not kinked and has not migrated during the turning process. Suction the airway if necessary.

10. Support the face and shoulders appropriately avoiding any contact of the supporting padding with the orbits or the eyes.

11. Position the arms for patient comfort. If the patient cannot communicate avoid any type of arm extension that might result in a brachial plexus injury.

12. Auscultate the chest to check for right mainstem intubation. Reassess the tidal volume and minute ventilation.

13. Adjust all tubing and reassess connections and functions.

14. Reattach ECG patches and leads to the back.

15. Tilt the patient into reverse Trendelenburg. Slight, intermittent lateral repositioning (20–30°) should also be used, changing sides at least every 2 hours.

16. Document a thorough skin assessment every shift, specifically inspecting weight bearing, ventral surfaces.

The criteria for stopping prone treatment were:

- Oxygenation improvement defined as $PaO_2/FiO_2 \geq 150$ mmHg with PEEP ≤ 10 cm H_2O and $FiO_2 \leq 0.6$; in the prone group, these criteria had to be met in supine at least 4 hours after the end of the last prone session.
- PaO_2/FiO_2 ratio deterioration by more than 20% relative to supine before two consecutive prone sessions; and
- Complications occurring during a prone session and leading to its immediate interruption, such as non-scheduled extubation, mainstem bronchus intubation, endotracheal tube obstruction, haemoptysis, $SpO_2 < 85\%$ or $Pa_2 < 55$ mmHg for more than 5 minutes under FiO2 1.0, cardiac arrest, HR < 30 BPM for more than 1 minute, SBP < 60 mmHg for more than 5 minutes, or any other life-threatening reason for which the clinician decided to stop.

10 Manage pain, sedation and delirium

10 Manage pain, sedation and delirium

Summary

Implement a protocolized management approach to pain, agitation and delirium to improve patient outcomes.

Regularly assess patients using standardized, reproducible scales (i.e. VAS, RASS, CAM-ICU).

First, treat pain (with opioids and non-opioids) to minimize the harmful effects of sedatives.

Then treat anxiety using non-benzodiazepines sedatives (when possible) and target **light** sedation in most patients.

Delirium should be prevented using non-pharmacologic interventions first.

Tools

References and resources

Ambuel B, Hamlett KW, Marx CM, Blumer JL. Assessing distress in pediatric intensive care environments: the COMFORT scale. J Pediatr Psychol. 1992;17(1):95–109.

Balas MC, Vasilevskis EE, Olsen KM, Schmid KK, Shostrom V, Cohen MZ et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. Crit Care Med. 2014;42(5):1024–36.

Bar J, Fraser GL, Puntillo K, Ely EW, Gélinas C, Dasta GF et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 2013;41(1):263–306.

Barnes-Daly MA, Phillips G, Ely EW. Improving hospital survival and reducing brain dysfunction at seven California community hospitals: implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. Crit Care Med. 2017;45(2):171–178.

Bradt J, Dileo C. Music interventions for mechanically ventilated patients. Cochrane Database Syst Rev. 2014;12:CD006902. doi: 10.1002/14651858.CD006902.pub3.

Davidson JE, Harvey MA, Bemis-Dougherty A, Smith JM, Hopkins RO. Implementation of the Pain, Agitation, and Delirium Clinical Practice Guidelines and promoting patient mobility to prevent post-intensive care syndrome. Crit Care Med. 2013;41(9 suppl 1):S136–145.

Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al. Surviving Sepsis Campaign: guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580–637.

Ely EW. The ABCDEF bundle: science and philosophy of how ICU liberation serves patients and families. Crit Care Med. 2017;45(2):321–330.

Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA. 2001;286(21):2703–2710.

Ely EW, Truman B, Shintani A, Thomason JW, Wheeler AP, Gordon S et al. Monitoring sedation status over time in ICU patients: the reliability and validity of the Richmond Agitation-Sedation Scale (RASS). JAMA. 2003;289(22):2983–2991.

Ely EW and Vanderbilt University. The confusion assessment method for the ICU (CAM-ICU) training manual. Nashville,TN: Vanderbilt University Medical Center; 2002.

Gélinas C, Fillion L, Puntillo KA, Viens C, Fortier M. Validation of the critical-care pain observation tool in adult patients. Am J Crit Care. 2006;15(4):420–427.

Girard TD, Jackson JC, Pandharipande PP, Pun BT, Thompson JL, Shintani AK et al. Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. Crit Care Med. 2010;38(7):1513–20.

Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet. 2008;371(9607):126–134.

Ista E, van Dijk M, Tibboel D, de Hoog M. Assessment of sedation levels of paediatric intensive care patients can be improved using the COMFORT "behavior" scale. Pediatr Crit Care Med. 2005;6(1):58–63.

Iwashyna T. Survivorship will be the defining challenge of critical care in the 21st century. Ann Intern Med. 2010;153(3):204–205.

Iwashyna TJ, Ely EW, Smith DM, Langa KM. Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA. 2010;304(16):1787–94.

Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med. 2002;30(1):119–141.

Johansson M, Kokinsky E. The COMFORT behavioural scale and the modified FLACC scale in paediatric intensive care. Nurs Crit Care. 2009;14(3):122–130.

Lonergan E, Britton AM, Luxenberg J, Wyller T. Antipsychotics for delirium. Cochrane Database Syst Rev. 2007;2:CD005594.

Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. Pediatr Nurs. 1997;23(3):293–297.

National Heart, Lung, and Blood Institute (NHLBI) PCTN, Moss M, Huang DT, Brower RG, Ferguson ND, Ginde AA et al. Early neuromuscular blockade in the acute respiratory distress syndrome. N Engl J Med. 2019;380(21):1997-2008. Epub 2019/05/22. doi: 10.1056/NEJMoa1901686. PubMed PMID: 31112383; PMCID: PMC6741345.

Pandharipande PP, Pun BT, Herr DL, Maze M, Girard TD, Miller RR et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. JAMA. 2007;298(22):2644–2653.

Papazian L, Forel J-M, Gacouin A, Penot-Ragon C, Perrin G, Loundou A et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med. 2010;363:1107–16.

Payen JF, Bru O, Bosson JL, Lagrasta A, Novel E, Deschaux I et al. Assessing pain in critically ill sedated patients by using a behavioral pain scale. Crit Care Med. 2001;29(12):2258–2263.

Rijkenberg S, Stilma W, Endeman H, Bosman RJ, Oudemans-van Straaten HM. Pain measurement in mechanically ventilated critically ill patients: Behavioral Pain Scale versus Critical-Care Pain Observation Tool. J Crit Care. 2015;30(1):167–72.

Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care patients. Am J Respir Crit Care Med. 2002;166(10):1338–1344.

Smith HAB, Boyd J, Fuchs C, Melvin K, Berry P, Shintani A et al. Diagnosing delirium in critically ill children: validity and reliability of the Pediatric Confusion Assessment Method for the intensive care unit. Crit Care Med. 2011;39(1):150–157.

Umunna P, Tekwani K, Barounis D, Kettaneh N, Kulstad E. Ketamine for continuous sedation of mechanically ventilated patients. J Emerg Trauma Shock. 2015;8(1):11–15.

Wong DL, Hockenberry MJ. Wong's essentials of pediatric nursing (sixth edition). St Louis, MO: Elsevier (Mosby); 2001.

10.1 Numerical pain assessment scales

Visual analogue scale

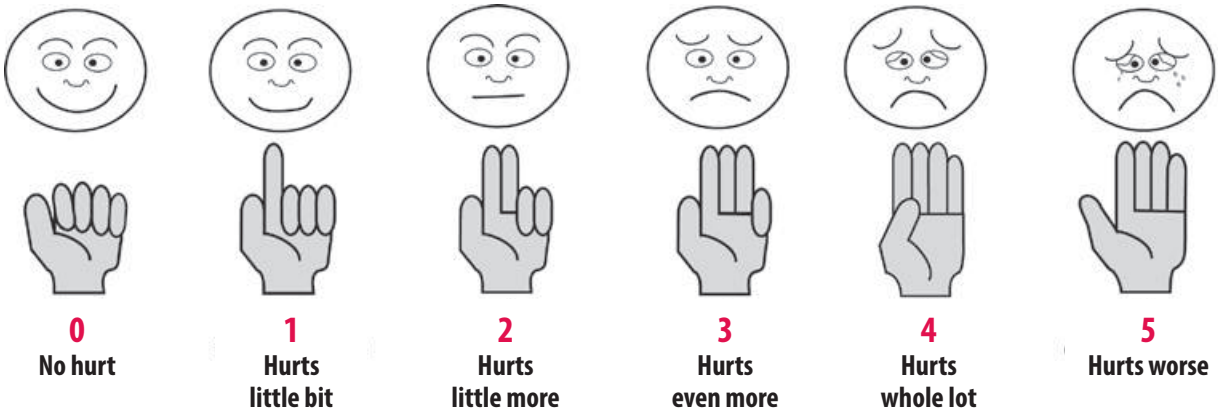
The visual analogue scale (VAS) for pain assessment in adults and adolescents is a validated and widely used method of monitoring the subjective level of pain experienced by patients. It is a 10 cm long scale, which ranges from 0 (no pain) to 10 (the worst pain that one can imagine). It is flexible, in that patients can make verbal or visual responses (i.e. if verbal communication is not possible, the patient can be shown a 10 cm scale and can point to the region which corresponds to their pain).

A major limitation of the VAS is that it requires an awake patient who grasps the concept of a scale. These conditions are frequently not satisfied in ICU patients.

The lower the VAS score, the higher the quality of the analgesia. However, a low VAS score with excessive sedation must be avoided, if possible. The level of sedation must be also closely monitored (see the Richmond Agitation-Sedation Scale tool).

Wong-Baker Faces Scale

The Wong-Baker Faces Scale can be used in younger children – they are asked to point to the face that reflects their pain level.



Source: Wong and Hockenberry (2001).

10.2 Behavioural pain assessment scales

There are two validated behavioural pain assessment scales that can be used to assess pain in adult patients on mechanical ventilation. In the noncommunicative patient these are recommended to use instead of physiological indicators alone.

Behavioural Pain Scale (BPS)

BPS score ranges from 3 (no pain) to 12 (maximum pain).

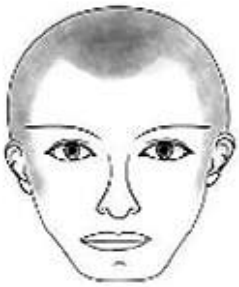
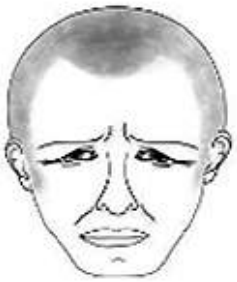
Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limb movements	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with mechanical ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Critical-Care Pain Observation Tool (CPOT)

Indicator	Score		Description
Facial expressions	Relaxed, neutral	0	No muscle tension
	Tense	1	Presence of frowning, brow lowering, orbit tightening and levator contraction or any other change (e.g. opening eyes or tearing during nociceptive procedures)
	Grimacing	2	All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting endotracheal tube)
Body movements	Absence of movements or normal position	0	Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)
	Protection	1	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements
	Restlessness/agitation	2	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed
Compliance with the ventilator (intubated patients) *or* **Vocalization (extubated patient)**	Tolerating ventilator or movement	0	Alarms not activated, easy ventilation
	Coughing but tolerating	1	Coughing, alarms may be activated but stop spontaneously
	Fighting ventilator	2	Asynchrony; blocking ventilation, alarms frequently activated
	Talking in normal tone or no sound	0	Talking in normal tone or no sound
	Sighing, moaning	1	Sighing, moaning
	Crying out, sobbing	2	Crying out, sobbing
Muscle tension Evaluation by passive flexion and extension of upper limbs when patient is at rest or evaluation when patient is being turned	Relaxed	0	No resistance to passive movements
	Tense, rigid	1	Resistance to passive movements
	Very tense or rigid	2	Strong resistance to passive movements or incapacity to complete them
	Total	(_ /8)	

Source: Adapted from Gélinas et al (2006).

Facial expressions

	0	1	2
	Relaxed, neutral (no muscle tension)	**Tense** (frowning, brow lowering, orbit tightening, little levator contraction)	**Grimacing** (contraction of the whole face: frowning, brow lowering, eyes tightly closed, levator contraction – mouth may be opened or the patient may be biting the endotracheal tube)
Intubated patient			
Non-intubated patient			

Source: Adapted from Payen et al (2001).

Note: A score of 1 may be attributed when a change in the patient's facial expression is observed compared with rest (e.g. opening or weeping).

How to use the Critical-Care Pain Observation Tool

1. The patient must be observed at rest for 1 minute to obtain a baseline vaue of the CPOT.
2. Then, the patient should be observed during nociceptive procedures known to be painful (e.g. turning, wound care) to detect any changes in the patient's behaviours to pain.
3. The patient should be evaluated before and at the peak effect of an analgesic agent to assess whether the treatment was effective or not in relieving pain.
4. For the rating of the CPOT, the patient should be attributed the highest score observed for each item during the observation period.
5. The patient should be attributed a score for each behaviour included in the CPOT and muscle tension should be evaluated last, especially when the patient is at rest because the stimulation of touch alone (when performing passive flexion and extension of the arm) may lead to behavioural reactions.

Free teaching CPOT video available from the Society of Critical Care Medicine:
https://www.sccm.org/ICULiberation/Resources/Critical-Care-Pain-Observation-Tool-How-to-Use-it

Observation of patient at rest (baseline)
The nurse looks at the patient's face and body to note any visible reaction for an observation period of 1 minute. She/he gives a score for all items except for muscle tension. At the end of the 1-minute period, the nurse holds the patient's arm in both hands – one at the elbow, and uses the other one to hold the patient's hand. Then she/he performs and passive flexion and extension of the upper limb, and feels any resistance the patient may exhibit. If the movements are performed easily, the patient is found to be relaxed with no resistance (score 0). If the movements can still be performed but with more strength, then it is concluded that the patient is showing resistance to movement (score 1). Finally, if the nurse cannot perform the movement, strong resistance is felt (score 2). This can be observed in patients who are spastic.

Observation of patient during turning
Even during the turning procedure, the nurse can still assess the patient's pain. While she/he is turning the patient on one side, she/he looks at the patient's face to note any reactions such as frowning or grimacing. These reactions may be brief or can last longer. The nurse also looks out for body movements. For instance, she/he looks for protective movements like the patient trying to reach or touching the pain site (e.g. surgical incision, injury site). In the mechanically ventilated patient the nurse pays attention to alarms and if they stop spontaneously or require that she/he intervenes (reassurance, administering medication). According to muscle tension, the nurse can feel if the patient is resisting to the movement or not. A score of 2 is given when the patient is resisting against the movement and attempts to get on his/her back.

10.3 COMFORT–B Scale to assess sedation in children

The sedation and pain levels of children in intensive care should be assessed at least 4 hourly in intensive care. A number of tools are available to assess pain and sedation. Here we describe the use of COMFORT- B scale for sedation and the Face, Legs, Activity, Cry, Consolability (FLACC) scale for pain.

COMFORT–B Scale

The COMFORT-B cannot be used in children who are receiving muscle relaxant drugs or children with severe neurological impairment. The child should be observed for 2 minutes and six behaviours are scored as below (score either respiratory response or crying, depending on the child's intubation status).

Children scoring 11–22 are in the optimal range of sedation; children scoring < 10 may be oversedated (consider weaning); and children > 23 are undersedated.

COMFORT-B Scale

Item	Description	Score
Alertness	1. Deeply asleep	
	2. Lightly asleep	
	3. Drowsy	
	4. Fully awake and alert	
	5. Hyperalert	
Calmness/agitation	1. Calm	
	2. Slightly anxious	
	3. Anxious	
	4. Very anxious	
	5. Panicky	
Respiratory response (ventilated children)	1. No coughing and no spontaneous respiration	
	2. Spontaneous respiration with little or no response to ventilation	
	3. Occasional cough or resistance to ventilator	
	4. Actively breathes against ventilator or coughs regularly	
	5. Fights ventilator, cough or choking	
Cry (non-ventilated children)	1. Quiet breathing, no crying	
	2. Sobbing or gasping	
	3. Moaning	
	4. Crying	
	5. Screaming	

COMFORT-B Scale

Item	Description	Score
Physical movement	1. No movement	
	2. Occasional, slight movements	
	3. Frequent, slight movements	
	4. Vigorous movement limited to extremities	
	5. Vigorous movements including torso and head	
Muscle tone	1. Muscles totally relaxed, no muscle tone	
	2. Reduced muscle tone	
	3. Normal muscle tone	
	4. Increased muscle tone and flexion of fingers and toes	
	5. Extreme muscle rigidity and flexion of fingers and toes	
Facial tension	1. Facial muscle totally relaxed	
	2. Facial muscle tone normal; no facial muscle tension evident	
	3. Tension evident in some facial muscles	
	4. Tension evident throughout facial muscles	
	5. Facial muscles contorted and grimacing	
	Total score	

Source: Adapted from Ambuel et al (1992).

FLACC Behavioural Pain Assessment Scale

The FLACC scale is a measurement used to assess pain for children between 2 months and 7 years or for individuals who are unable to communicate their pain. The scale has five criteria, each of which is assigned a scale of 0, 1 or 2.

FLACC Behavioural Pain Assessment Scale

	Scoring		
Categories	**0**	**1**	**2**
Face	No particular expression or smile	Occasional grimace or frown; withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arches, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

How to use the FLACC

In patients who are awake: observe for 1 to 5 minutes or longer. Observe legs and body uncovered. Reposition patient or observe activity. Observe body for tenseness and tone. Initiate consoling interventions if needed.

In patients who are asleep: observe for 5 minutes or longer. Observe legs and body uncovered. If possible, reposition the patient. Touch the body and observe for tenseness and tone.

Face

- Score 0 if the patient has a relaxed face, makes eye contact, shows interest in surroundings.
- Score 1 if the patient has a worried facial expression, with eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed.
- Score 2 if the patient has deep furrows in the forehead, closed eyes, an open mouth, deep lines around nose and lips.

Legs

- Score 0 if the muscle tone and motion in the limbs are normal.
- Score 1 if the patient has increased tone, rigidity, or tension; if there is intermittent flexion or extension of the limbs.
- Score 2 if the patient has hypertonicity, the legs are pulled tight, there is exaggerated flexion or extension of the limbs, tremors.

Activity

- Score 0 if the patient moves easily and freely, normal activity or restrictions.
- Score 1 if the patient shifts positions, appears hesitant to move, demonstrates guarding, a tense torso, pressure on a body part.
- Score 2 if the patient is in a fixed position, rocking; demonstrates side-to-side head movement or rubbing of body part.

Cry

- Score 0 if the patient has no cry or moan, awake or asleep.
- Score 1 if the patient has occasional moans, awake or asleep.
- Score 2 if the patient has frequent or continuous moans, cries, grunts.

Consolability

- Score 0 if the patient is clam and does not require consoling.
- Score 1 if the patient responds to comfort by touching or talking in 30 seconds to 1 minute.
- Score 0 if the patient requires constant comforting or is inconsolable.

When feasible, behavioural measurement of pain should be used in conjunction with self-report. When self-report is not possible, interpretation of pain behaviours and decisions regarding treatment of pain require careful consideration of the context in which pain behaviours are observed.

Interpreting the **Behavioural Score**
Each category is scored on the 0–2 scale, which results in a total score of 0–10; 0 = Relaxed and comfortable; 1–3 = Mild discomfort; 4–6 = Moderate pain; 7–10 = Severe discomfort or pain or both.

Source: Merkel et al (1997).

10.4 Richmond Agitation–Sedation Scale (RASS)

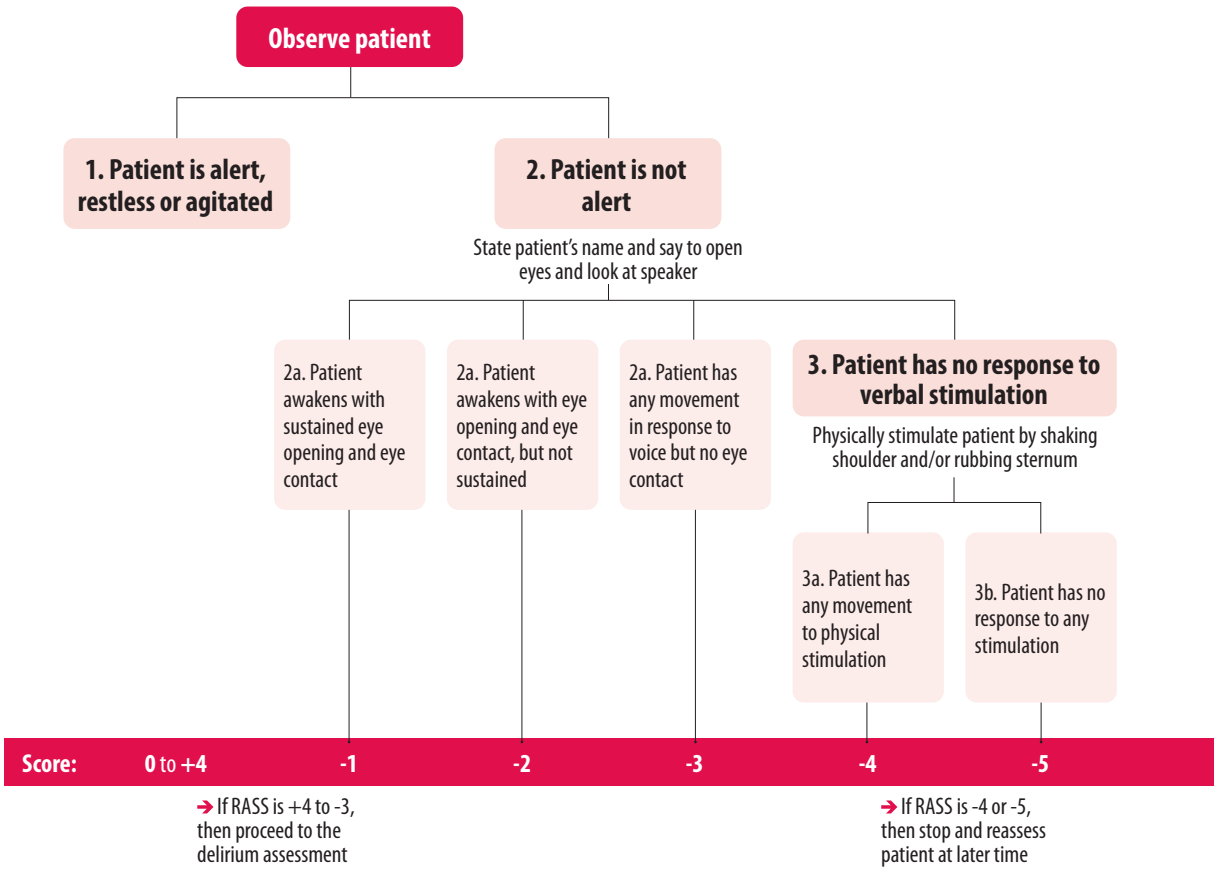
Assess agitation, anxiety and sedation levels on a regular basis using a standardized scale and set a daily sedation target based on clinical condition and management plans for the day. Consider the use of the Richmond Agitation-Sedation Scale (RASS). This has been validated in many clinical trials and can be easily taught to staff.

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (> 10 seconds)	Verbal stimulation
-2	Light sedation	Briefly awakens with eye contact to voice (< 10 seconds)	
-3	Moderate sedation	Movement or eye opening to voice (but no eye contact)	
-4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation	Physical stimulation
-5	Unarousable	No response to voice or physical stimulation	

Source: Adapted from Sessler et al (2002).

Algorithm for RASS assessment

In most patients, this assessment is very quick and takes only 30 seconds (only 10% take a few minutes).



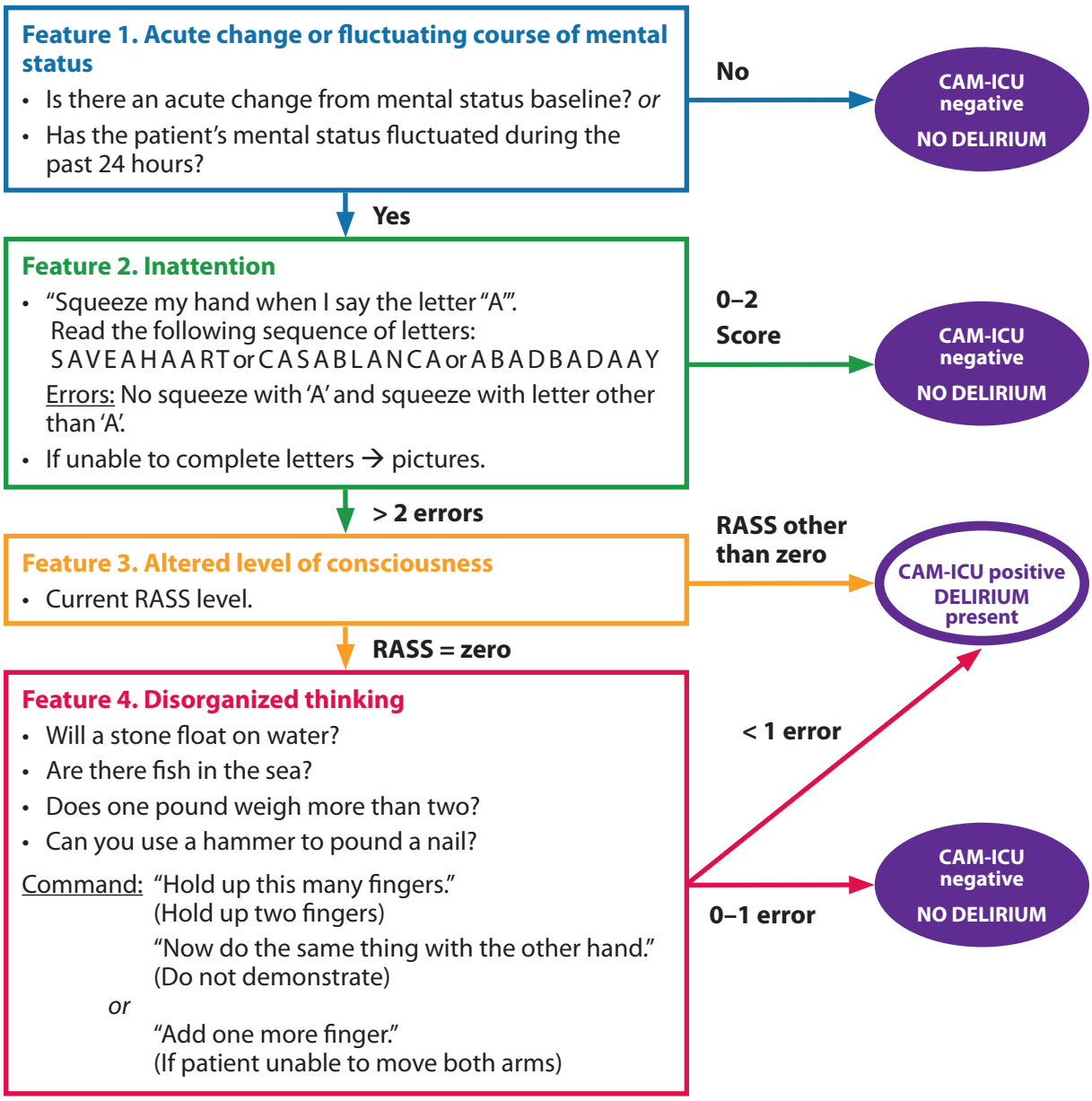
Source: Adapted from Sessler et al (2002).

10.5 Flowchart and worksheet for the Confusion Assessment Method of the ICU for adults (CAM-ICU)

Use the CAM-ICU flowsheets and worksheet (http://icudelirium.org/docs/CAM_ICU_training.pdf), reproduced below, to assess delirium in conjunction with the RASS scale. For additional training materials on how to do the CAM-ICU and train staff, visit https://www.icudelirium.org/medical-professionals/downloads/resources-by-category

CAM-ICU flowchart

The flowchart can be used as a pocket card or wall poster to easily reference the procedure to assess for the presence of delirium.



Source: Ely et al (2001).

CAM-ICU worksheet

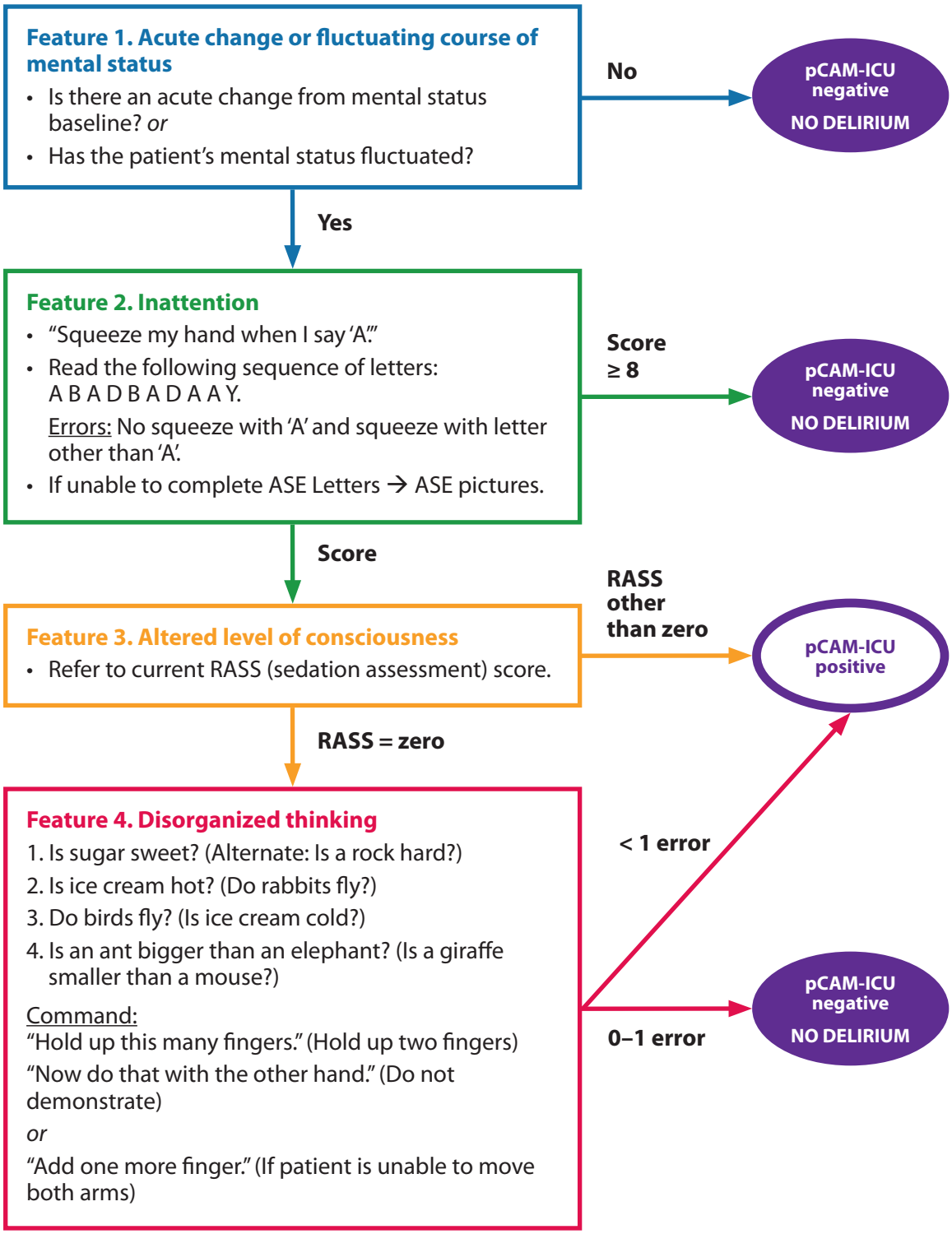
	Score	Check here if present
Feature 1: Acute onset or fluctuating course		
Is the patient different than his/her baseline mental status? *or* Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e. RASS/SAS, GCS or previous delirium assessment)?	Either question Yes →	☐
Feature 2: Inattention		
Letters attention test: Directions: Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A', indicate by squeezing my hand." Read the letters from the following list in a normal tone 3 seconds apart. S A V E A H A A R T *or* C A S A B L A N C A *or* A B A D B A D A A Y Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A". If unable to complete letters attention test → use pictures (see Tool 10.7)	Number of errors > 2 →	☐
Feature 3: Altered level of consciousness		
Present if actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	☐
Feature 4: Disorganized thinking		
Yes/No questions: Will a stone float on water? Are there fish in the sea? Does one pound weigh more than two? Can you use a hammer to pound a nail? **Errors are counted when the patient incorrectly answers a question.** Command: Say to the patient, "Hold up this many fingers." (Hold up two fingers in front of the patient) "Now do the same thing with the other hand." (Do not repeat the number of fingers) *Note:* If patient is unable to move both arms, for second part of command ask patient to "Add one more finger". **An error is counted if patient unable to complete entire command.**	Combined number of errors > 1 →	☐
Overall CAM-ICU **CAM-ICU positive =** **Feature 1** _____ + **Feature 2** _____ + *either* **Feature 3** _____ *or* **Feature 4** _____	Criteria met →	☐ CAM-ICU positive (DELIRIUM present)
	Criteria not met →	☐ CAM-ICU negative (NO DELIRIUM)

Source: Ely et al (2001).

10.6 Flowchart and worksheet for the Confusion Assessment Method of the ICU for children (pCAM-ICU)

This tool is adapted from Smith et al (2011) (see References and resources).

pCAM-ICU flowchart



pCAM-ICU worksheet

Feature 1: Acute change or fluctuating course of mental status		
A. Is there an acute change from mental status baseline? Yes or No B. Has my patient's mental status fluctuated during the past 24 hours? Yes or No Evidenced by fluctuation on a sedation scale (RASS), SAS, GCS or previous delirium assessment.	If either answer YES then circle ⊕ →	+ / –
Feature 2: Inattention → FEATURE POSITIVE if SCORE 0–7 on Vigilance "A" test *or* ASE picture test		
Vigilance "A" test: I want my patient to squeeze my hand when I say ONLY the letter "A". I will read the 10-letter sequence in the same order every day, with my normal voice, saying each letter once every second. Directions to patient: "Squeeze my hand when I say the letter 'A'. Let's practise, 'A'". To score: When I say the letter "A" and the patient does not squeeze my hand, I subtract 1 point. When I say the other letters and the patient squeezes my hand, I subtract 1 point. A___B___A___D___B___A___D___A___A___Y___	If the SCORE is 0–7 then circle ⊕ →	+ / –
or		
ASE picture test: I will show the patient **"5 memory pictures"**. I want the patient to remember the 5 **"memory pictures"** when shown a larger **"deck"** of 10 pictures. Directions to patient: "I am going to show you 5 pictures that I want you to remember". (Show 1 **picture** every **3 seconds** and state object's name.) Directions if patient can verbalize: "Say yes when you see **1 of those 5 pictures** again". (Show all pictures from **deck** and state object's name.) Directions to intubated patient: "Nod your head yes when you see **1 of those 5 pictures** again". To score: If the patient nods or says "yes" to ONLY the **5 memory pictures** they have completed the task successfully – SCORE 10/10. If patient does not nod or say "yes" to 1 of the 5 memory pictures, I will subtract 1 point. If the patient nods or says "yes" to the other pictures in the deck, I will subtract 1 point. Memory picture: _____ / 5 Deck pictures: _____ / 5	If the SCORE is 0–7 then circle ⊕ →	+ / –
Feature 3: Altered level of consciousness → FEATURE POSITIVE if the current RASS score is anything other than 0		
At the time of sedation assessment the RASS score was _____		+ / –

Feature 4: Disorganized thinking		
Directions if patient can verbalize: "I am going to ask you 4 questions, say 'yes' or 'no' to answer". Directions to intubated patient: "I am going to ask you 4 questions, nod your head yes or no to answer". **Set A:** 1. Is sugar sweet? 2. Is ice cream hot? 3. Do birds fly? 4. Is an ant bigger than an elephant? **Set B:** 1. Is a rock hard? 2. Do rabbits fly? 3. Is ice cream cold? 4. Is a giraffe smaller than a mouse? 5. Directions to patient: "Hold up this many fingers." (Examiner hold up two fingers for patient to see) Directions to patient: "Now do the same thing with the other hand." (Do not show fingers again to patient) Directions to patient if unable to move **both** arms: "Now, add one more finger." (Do not show fingers again to patient) To score: If the patient answers a question incorrectly, I will subtract 1 point. If the patient is not able to complete the command no. 5, I will subtract 1 point.	If the SCORE is 0–3 then circle ⊕ →	+ / –
Paediatric delirium = **Feature 1** _____ + **Feature 2** _____ + *either* **Feature 3** _____ *or* **Feature 4** _____		

10.7 Procedure for assessing attention: attention screening exam (ASE) for adults

This procedure is to be used to assess for feature 2 (**inattention** – a cardinal feature of delirium), when the patient is unable to complete the letters attention test (SAVEAHAART). This happens in only about 10% of patients.

Step 1

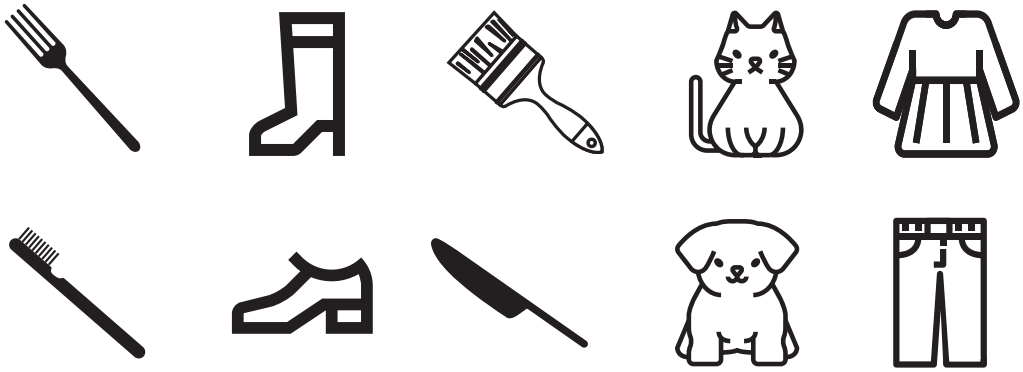
- Say to the patient: *"Mr or Mrs …, I am going to show you pictures of some common objects. Watch carefully and try to remember each picture because I will ask what pictures you have seen."*

- Present five pictures: naming them and showing them each for 3 seconds.

Step 2

- Say to the patient: *"Now I am going to show you some more pictures. Some of these you have already seen and some are new. Let me know whether or not you saw the picture before by nodding your head yes (demonstrate) or no (demonstrate)."*

- Present ten pictures (five new, five repeated): naming them and showing them each for 3 seconds.



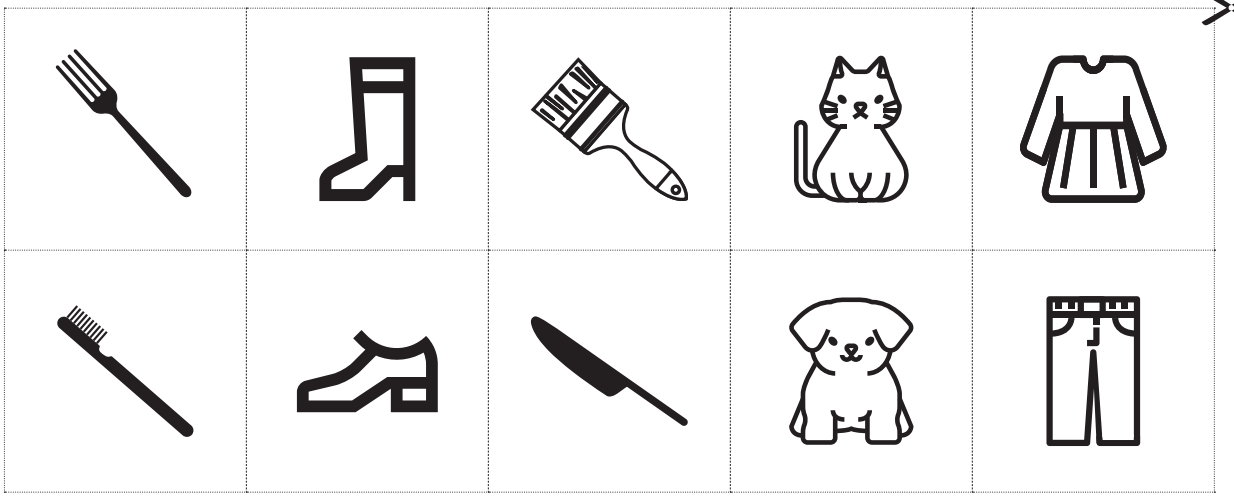
Scoring

This test is scored by the number of correct "yes" or "no" answers during Step 2 (out of a possible 10).

Important: Alternate daily between Forms A and B (see next tool) if repeat measures are taken. If a patient wears glasses make sure they have them on when attempting the ASE.

Source: Adapted from Ely and Vanderbilt University (2002).

Form A



Source: Adapted from Ely and Vanderbilt University (2002).

Form B

Source: Adapted from Ely and Vanderbilt University (2002).

10.8 Guide to commonly used sedatives in adults

There are many sedative medications available to treat agitation and anxiety. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. It is important to familiarize yourself with the basic pharmacokinetics and side-effects of any drug you use. The goal is to reach the sedation target with the lowest possible sedative medication to minimize toxicity. The doses provided below are intended to be used for patients who are intubated and receiving mechanical ventilation. Continuous infusions of benzodiazepines should be avoided when at all possible to reduce the risks of oversedation, prolonged days of IMV and delirium.

		Benzodiazepine[a]			
	Propofol	**Midazolam**	**Lorazepam**	**Diazepam**	**Dexmedetomidine[b]**
Onset	< 1 minute	1–5 minutes	5–20 minutes	2–5 minutes	1–3 minutes
Infusion	25–75 µg/kg/min	0.04–0.2 mg/kg/hr	0.01–0.1 mg/kg/hr (preferred vs midazolam)	Not used	0.2–1.5 µg/kg/hr
Time to arousal	10–15 minutes	1–2 hours	2–6 hours	2–4 hours	6–10 minutes
Risks	Respiratory depression Hypotension Idiosyncratic rhabdomyolysis and acidosis Raised triglycerides	Respiratory depression Hypotension Prolonged sedation with infusions due to active metabolite Reduce dose in renal and liver failure	Respiratory depression Hypotension Propylene glycol carrier may irritate veins and cause metabolic acidosis with prolonged administration	Respiratory depression Hypotension Oversedation with repeated boluses with accumulation of drug and active metabolite	Hypotension Bradycardia Atrial fibrillation More pronounced in elderly Safety data for up to 4 days of infusion Dose may need to be reduced in elderly depending on renal function

Notes:

[a] Reduce dose in the elderly;
[b] Less commonly available.

Note: Early in the course of severe ARDS, however, deep sedation targets may be needed to safely achieve LPV targets and reduce asynchrony. In cases when NMB are administered, remember to also give a continuous sedative for amnesia and analgesic for pain.

10.9 Guide to commonly used opioid analgesics in adults

There are several opioids available to treat pain. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. Familiarize yourself with the basic pharmacokinetics and side-effects of any drug you use. Be sure to set a therapeutic analgesia plan and communicate to all caregivers for a consistent approach.

These considerations are adapted from the *Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult* (Jacobi et al, 2002) (see References and resources).

The doses provided below are suggestions and will need adjustment based on the amount of pain and whether the patient is receiving mechanical ventilation.

	Morphine	Hydromorphone	Fentanyl
Intermittent dose IV	0.01–0.15 mg/kg every 1–2 hr	10–30 µg/kg every 1–2 hr	0.35–1.5 µg/kg every 0.5–1 hr
Infusion	0.07–0.5 mg/kg/hr	7–15 µg/kg/hr	0.7–10 µg/kg/hr
Half-life	3–7 hr	2–3 hr	1.5–6 hr
Equianalgesic IV dose[a]	10 mg	1.5 mg	200 µg
Situations where drug is preferred	Intermittent dosing	Intermittent dosing Haemodynamic instability Renal failure	Rapid onset in acutely distressed patients Haemodynamic instability Renal failure
Risks[b]	Histamine release causing hypotension Prolonged effect in renal failure due to metabolite		Rigidity with high doses Repeated dosing may cause accumulation and prolonged effects

Notes:

[a] These doses produce approximately the same analgesic effects;
[b] Side-effects common to all agents include respiratory depression, coma and delirium, hypotension (especially with morphine) and ileus.

Note: Meperidine and codeine may be available at many hospitals. However, meperidine has an active metabolite that causes neuroexcitation (apprehension, tremors, delirium and seizures) and may interact with antidepressants (contraindicated with monoamine oxidase inhibitors and best avoided with selective serotonin-reuptake inhibitors), so it is not recommended for repetitive use. Codeine lacks analgesic potency and is thus not useful for most patients.

10.10 Guide to using neuromuscular blockers in adults

In patients with moderate-severe ARDS (PaO_2/FiO_2 < 150), neuromuscular blockade by continuous infusion should not be routinely used.

A trial found that neuromuscular blockade improved survival in adult patients with severe ARDS without causing significant weakness (Papazian et al, 2010), but results of a recent larger trial found that use of neuromuscular blockade with high PEEP strategy was not associated with a survival benefit when compared with a light sedation strategy without neuromuscular blockade (NHLBI PCTN et al, 2019). Continuous neuromuscular blockade may still be considered in patients with ARDS, both adults and children, in certain situations: ventilator dyssnchrony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxaemia or hypercapnia.

	Pancuronium	Vecuronium	Cisatracurium
IV dose	Intermittent: 0.08–0.1 mg/kg Infusion: 0.2–0.6 µg/kg/min (usually 1–2.5 mg/hr)	Intermittent: 0.08–0.1 mg/kg Infusion: 0.2–0.8 µg/kg/min (usually 1–4 mg/hr)	Intermittent: 0.15–0.20 mg/kg Infusion: 3 mcg/kg/min for first 20 minutes then reduce to 1–2 mcg/kg/min (range: 0.5–10 mcg/kg/min)
Common points on dosing	Tailor intermittent dose to patient response. Titrate infusion dose clinically or to achieve one or two twitches with train of four stimulation on peripheral nerve stimulator, if available		
Onset	< 4 minutes	2–3 minutes	
Specific risks	Long duration of activity: ~90–160 minutes Accumulation in hepatic and renal dysfunction Dose-dependent increased HR and blood pressure (due to vagolytic and weak sympathomimetic effects)	Intermediate duration of activity: ~30–45 minutes Accumulation in hepatic and renal dysfunction	Duration of action: ~45–75 minutes Slight accumulation in hepatic and renal dysfunction
Common risks	Appropriate sedation and analgesia should be administered concurrently since these drugs have neither effect HR and blood pressure should be routinely monitored; increases may indicate inadequate sedation or analgesia ICU-acquired weakness if used for prolonged period		

10.11 Guide to commonly used antipsychotics (haloperidol) in adults

Antipsychotic agents can be used to control delirium. Haloperidol is a typical antipsychotic that has been available for many years. Atypical antipsychotics can also be used (e.g. quetiapine, olanzapine and risperidone). Dexmedetomidine is a newer agent that has both sedative and anti-delirium effects.

Haloperidol	
Loading dose	Begin with 2–5 mg IV Double dose every 15 minutes until desired effect is achieved **Do not** exceed total of 20 mg/day
Onset	10–20 minutes
Risks	Torsade de pointes arrhythmia, do not use if the QTc interval on ECG is prolonged to > 460 milliseconds Suspect neuroleptic malignant syndrome if patient develops hyperthermia, muscle rigidity and rhabdomyolysis

Dosing recommendations	
Quetiapine	Begin with 50 mg po twice daily Increase up to 200 mg po twice daily (halve dose in elderly)
Olanzipine	Begin with 5–10 mg IV/IM/po Repeat dose in 2 hours to maximum of 30 mg/day
Risperidone	Begin with 1–2 mg po daily Increase to maximum of 6 mg po daily

Side-effects of atypical antipsychotics are prolonged QTc interval and extrapyramidal effects (less common than with typical antipsychotic agents).

10.12 Guide to paediatric analgesics, sedatives and neuromuscular blockers

There are several agents available for analgesia, sedation and neuromuscular blockade. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. Familiarize yourself with the basic pharmacokinetics and side-effects of any drugs you use. The doses provided below are suggestions and will need titration in individual patients based on the amount of pain and whether the patient is receiving mechanical ventilation. Appropriate sedation and analgesia should be administered concurrently with neuromuscular blockade, which has no sedative or analgesic properties.

Propofol is contraindicated for sedation in children < 16 years old in the ICU because of the risk of propofol infusion syndrome (acidosis and rhabdomyolysis).

	Drug	Enteral dose	Bolus IV dose	IV infusion
Analgesia	Paracetamol	10–15 mg/kg po/pr 6 hrly	N/A	N/A
	Oxycodone	0.05–0.2 mg/kg/dose po 4–6 hrly	N/A	N/A
	Ibuprofen	5–10 mg/kg/dose po 6–8 hrly	N/A	N/A
	Morphine	0.2–0.4 mg/kg po 6 hrly	0.1–0.2 mg/kg	0–40 µg/kg/hr
	Fentanyl	N/A	1–2 µg/kg	0–8 µg/kg/hr
Sedation	Midazolam	N/A	0.1–0.2 mg/kg	0–4 µg/kg/min
	Diazepam		0.1–0.2 mg/kg	N/A
	Chloral hydrate	30–50 µg/kg pr 6 hrly	N/A	N/A
	Triciofos	30–50 µg/kg pr 6 hrly	N/A	N/A
	Allmemazine	1 mg/kg po 6 hrly	N/A	N/A
Neuromuscular blockade	Vecuronium	N/A	0.1 mg/kg as required	0–4 µg/kg/min